A Light for Science

ESRF news

Number 48 December 2008

Getting to the heart of health

From the ESRF to the pharmacy

Improved breast scans offer better diagnoses

The fight to arm our blood warriors

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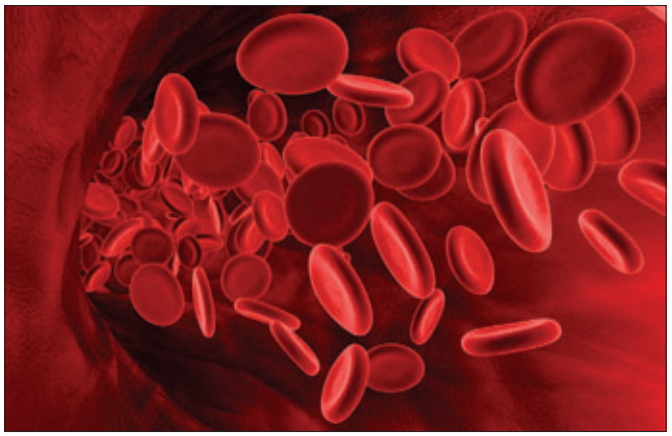
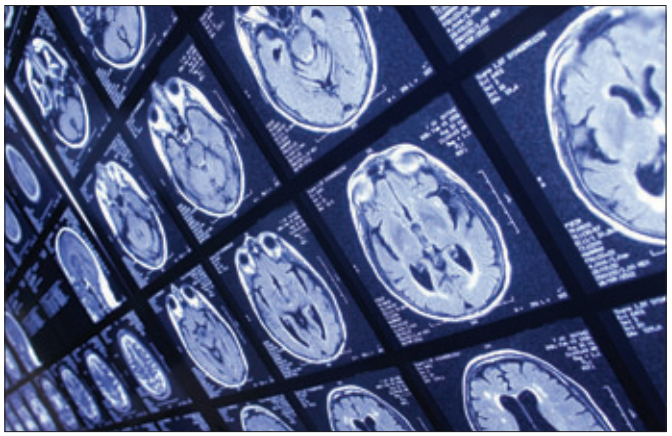
A light for science



The key to unlocking our immune system. p12



Developing new techniques to help treat brain tumours. p15

Bill Stirling has changed the face of the ESRF. p21

On the cover:
Synchrotron sources are helping to shed light on health research.

ESRFnews Number 48 December 2008

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ESRFnews

A new look for a new era

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Welcome to the first edition of the new-look ESRF science news magazine, *ESRFnews*. As the ESRF enters a new era with the realisation of our exciting Upgrade Programme, it is time to renew and restyle our old friend, the *ESRF Newsletter* – and with a new style and layout comes a new name. *ESRFnews* will inform the scientific community about the latest research being carried out at the ESRF. There are new sections – *In brief*, *Beauty of science* (featuring an especially striking image from research at the ESRF), *Careers* (focusing on jobs in SR as well as the movers and shakers of the synchrotron world) and finally *In the corridors* (presenting out-of-the-ordinary SR news). From this issue onwards, our news magazine will be published four times a year. I'd like to thank Montserrat Capellas and her colleagues at IOP Publishing for their imagination and for the energy that they have expended in the preparation of this redesigned magazine.

The ESRF's heroic phase of design and construction was followed by a second phase of operation and consolidation. Now we are waiting for the signal from Council to engage the first major expenditure of phase three of the ESRF's existence. After four years of preparation, four years of discussion and argument, the Upgrade Programme is about to start in earnest with major decisions on the future building programme. Under the guidance of the Science Advisory Committee, the floor plan for the extended Experimental Hall is taking shape, while a set of world-leading new beamlines is being defined. In parallel, a new project structure is being tested, while the Instrumentation Services and Development Division will be ready for implementation at the end of the year. I look forward to a positive formal decision on the Upgrade Programme by Council on 24 and 25 November. The VIP celebration of the ESRF's 20th anniversary will take place on 26 November and I am looking forward especially to that evening's party for all of the staff and their families.

I complete my period as director-general at the end of the year, so this is the last editorial I will write. I would like to thank everyone at the ESRF for their support over the last eight years and for their many contributions to the success of our organisation. This success is due, in my opinion, in large measure to the multinational nature of the ESRF. In saying goodbye I wish you all the best for a radiant and successful future – and, please, don't forget the European dream!

Bill Stirling, director-general

ESRF supports health research

Since the discovery of X-rays by Röntgen in 1895, they have been used to provide 2D images of the body that can be used in the diagnosis of diseases, while their damaging effects have been exploited in the radiotherapy treatment of cancerous tumours. Synchrotron radiation and the advanced instrumentation at the ESRF have given the medical application of X-rays a completely new dimension, as illustrated by recent results from the biomedical beamline. A new, efficient imaging method based on 3D computed tomography enables the earlier diagnosis of breast cancer, while the radiotherapy of previously untreatable brain tumours is moving towards clinical trials.

It is perhaps more difficult to envisage the impact on our health of the fully automated beamlines for macromolecular crystallography, which are optimised for the fast and accurate determination of protein structures. Human health depends on the function of the body: are all of the cellular processes operating normally and can its immune system defeat attacks by foreign organisms and molecules? These functions are intimately linked to the 3D structures of the molecules that play a key role in biological processes. An increased understanding of the function of the complex innate immune system and its activation by foreign organisms has recently been achieved by Piet Gros and colleagues from Utrecht University by the structure determination of proteins in the complement system. Many proteins bound in the cell membrane react to external stimuli, making them important for the functioning of the body. The G-protein coupled receptors are a particular class of membrane protein that is important in exhibiting a cellular response to external stimuli, and the results using X-ray microbeams obtained by Gebhard Schertler and his group from MRC Cambridge will contribute greatly to the development of future drugs. The successful use of structural knowledge to design a drug for the treatment of breast cancer was performed by Laurence Pearl and his team from the Institute of Cancer Research. The structure-based, drug-design method is used by numerous pharmaceutical companies in the development of new and more efficient drugs, which explains why the medical sector uses more than a quarter of the time at the macromolecular crystallography beamlines.

I hope that you enjoy reading in this first issue of *ESRFnews* about these examples of the multifaceted research at the ESRF, which is of great relevance and benefit to human health.

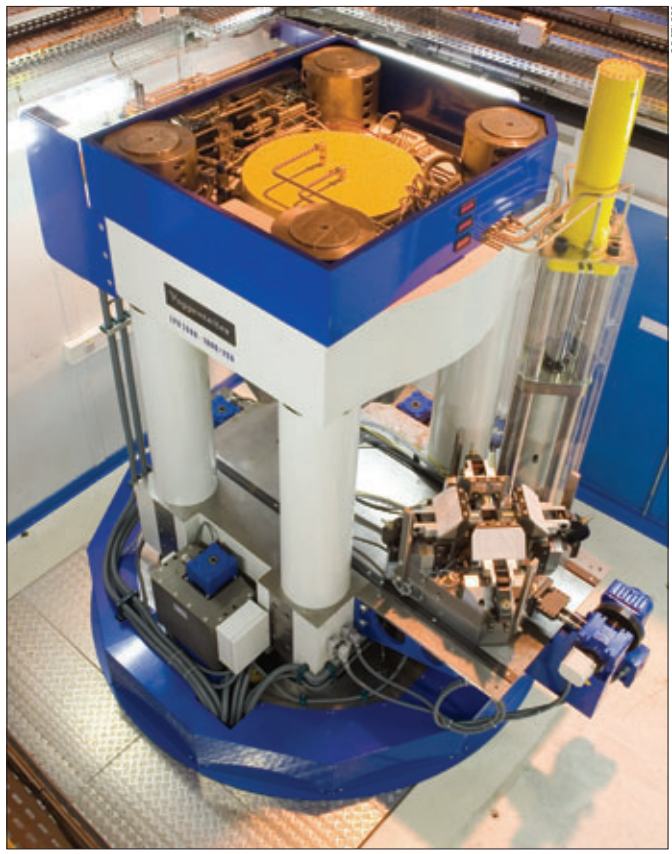
Sine Larsen, director of research

ESRF steadily increases the pressure

The levels of pressure are progressively going up at the ESRF as the new 40 tonne large-volume press is being installed on the ID06 beamline.

Built and installed by Max Voggenreiter GmbH in September, this device will offer higher pressures and larger sample volumes compared with existing large-volume devices. It will also extend the capabilities of the ESRF's current high-pressure programme.

The four-column press is capable of generating 2000 tonnes of force in the main ram. The anvil construction is a hybrid cubic/D-DIA with independent upper and lower anvils that can take cubes of up to 32 mm in a two-stage operation. It can also be run as a conventional D-DIA device for large-volume, high-pressure deformation studies. The sample can be placed on the rotation axis of the press through its two X-Y stages, while vertical adjustment is met through four independent spindles. All anvil gaps are modified for X-ray entry and exit, allowing conventional forward-scattering measurements and those where access to 90° or near-back scattering are required. Data collections can take place during rotation, making it possible to study highly oriented or textured samples, such as single crystals. The device will not be limited to diffraction measurements – in the medium term other imaging and spectroscopic techniques it will be possible. Other enhancements in the foreseeable future include the addition of ultrasonic capabilities.



CDETLEFS

The new large-volume press has now been installed at the ESRF.

Wilson Crichton, the scientist in charge, is confident about the machine's potential: "It has sufficient inherent qualities and flexibility to do the experiments that users want." The press is now in a period of calibration and commissioning, and it will gradually be opened up to the user community.

Future users are invited to contact Crichton (e-mail (crichton@esrf.eu) for any specific technical clarification or information regarding their experimental requirements.

Users' corner

Users' corner is a new section produced by the Users' Office. It features practical information for ESRF users. It will be a regular column in ESRFnews *and include news items aimed at those who are already regular visitors to the site, as well as for those who are considering applying for upcoming time at one of the beamlines.*

For your diary

- **The next Users' Meeting & Satellite Workshops** will take place on 2–5 February 2009. More information is available at www.esrf.eu/events/conferences/usersmeeting2009.

- **The next deadline for proposal submission is 1 March 2009**. For the 1 September 2008 deadline, 953 proposals for beamtime were received, representing a record number for the September rounds.

News from the beamlines

- **Scientists from ID28** have installed the second revolver-undulator segment on the beamline, resulting in a 30% flux increase at 18 keV.
- **Collaborating Research Group users of BM14** will have the opportunity to submit BAG-like proposals for 2009 to aid access to the beamline. Full information is available on the BM14 website at www.bm14.ac.uk. Proposals are still accepted at any time, on a soft deadline of six weeks before the start of each ESRF synchrotron run, the dates of which are posted on the CCP4 bulletin board.
- **New high-powered primary slits will be installed on ID14** in January 2009 to prepare for the installation of a new 11 mm U35 undulator (replacing the U42) during the March 2009 shutdown. This insertion device will allow the tunable beamline ID14-4 to operate independently of the fixed-energy stations on ID14.
- **ID32 has commissioned a new ultra-high vacuum system** with a unique hemispherical photoelectron analyser (PHOIBOS 225 from SPECS, Germany) for hard-X-ray photoelectron spectroscopy. This electron spectrometer features a low-noise, 2D delay-line detector and allows the analysis of electrons with kinetic energies up to 15 000 eV. In conjunction with the recently commissioned high-resolution post-monochromator, this new set-up allows electron spectroscopy measurements to be made with an energy resolution of 0.1 eV or better.
- **BM16 will upgrade the protein crystallography sample environment** with the installation of a complete beam conditioning unit from Huber and refurbishment of the first mirror bender capillaries.
- **ID03 has a new low-temperature set-up for the ultrahigh-vacuum diffractometer** that reaches temperatures as low as 25 K, with a maximum of about 1000 K. The only limitation of this set-up is that samples cannot be changed without breaking the vacuum. Regarding techniques, scientist can now carry out grazing incidence small-angle X-ray scattering and surface X-ray diffraction experiments simultaneously in both hutches, and they can correlate the surface-morphology changes with the surface structure. There is also a new flow reactor, which can be mounted in the vertical diffractometer.
- **A U22 insertion device has been installed on ID15** in addition to the existing asymmetric wiggler, giving a factor of 10 increase in flux at 70 keV.

ESRF reaches for growth in the east

The Czech Republic, Hungary and Slovakia have formed a consortium, CENTRALSYNC, to become an associate member of the ESRF. The group has a 1.05% financial share of the ESRF budget. The Czech Republic and Hungary have already been co-operating with the ESRF for several years, providing their scientists with access to the facilities. With the creation of CENTRALSYNC, these countries have gained the status of associate member of the ESRF and will participate in its governing bodies.

New beamline is ready for SAXS protein solutions

There has been a lot of activity on ID14-3 starting at the beginning of 2008 and lasting till the end of the summer. The beamline was converted from a protein-crystallography station into an experimental facility dedicated to small-angle X-ray scattering (SAXS) of solutions of biological macromolecules.

This new set-up is intended to complement the SAXS facilities already present at the ESRF, which are highly oversubscribed for experiments in biology, chemistry and materials sciences. With a rapidly growing interest in scattering protein solutions from the crystallography community, the limited time on the existing stations was set to become even more sought after. Establishing a bio-SAXS station at ID14-3 satisfies this demand.

An additional benefit of creating this new facility is close collaboration with the neutron scattering facility of the neighbouring Institute Laue Langevin. "We intend to allow users with a single proposal to have access to both facilities for appropriate experiments," explains Petra Pernot, who, together with Adam Round, EMBL scientist is in charge of ID14-3.

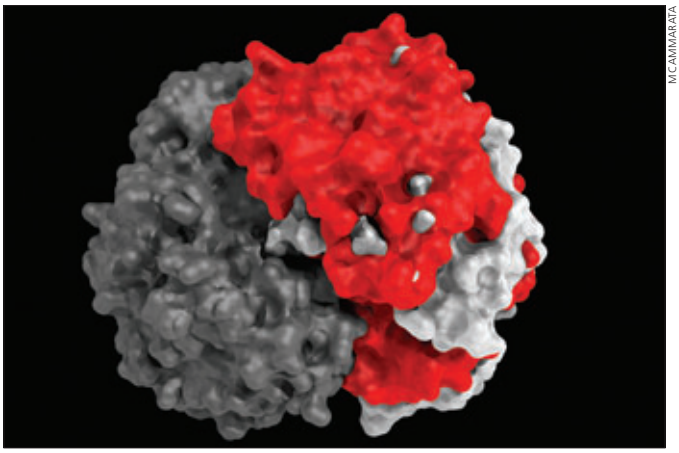
The conversion of ID14-3 was undertaken in stages starting in January and completing in August 2008. After a couple of months of commissioning, the first official users arrived in November.

Protein transition in action studied in natural habitat

Understanding how proteins behave is a tough nut for scientists to crack. Until today they have managed to observe proteins' actions on crystals of the proteins by using time-resolved protein crystallography or optical spectroscopy. These techniques work relatively well, but the crystals in the sample are arranged so close together that the protein cannot move freely when it changes – as it does in real-life conditions.

Scientists from the ESRF, Korea, Italy and the US have developed an approach to study protein function. The key to this method is that the proteins are in a solution that is similar to their natural environment. The challenge for the team was to measure small changes in a system without the ordered structure of a crystal.

Haemoglobin, which is responsible for the release of oxygen in the blood, was the first protein used to test the technique. Thanks to the high photon flux available at ID09B, the team determined the structural changes that occur, from the relaxed structure of the protein to the tensed structure. It used a laser pulse to excite the protein and followed its changes with nanosecond resolution. Surprisingly, the researchers realised that the transition between one state and another happens 10 times as fast – 2 ms – as had previously been proposed through optical-spectroscopy measurements.



M CAMMARATA

The structure before (red) and after (white) the transition. The part of the protein that doesn't move greatly during the transition is in grey.

Reference
Cammarata *et al.* 2008 *Nature Methods*. **5** 881–886.
doi:10.1038/nmeth.1255.

Experiments from the home

Participants at the IUCr meeting in Osaka followed a live experiment taking place in Grenoble at the ESRF.

Since 2007, macromolecular crystallography (MX) users have been able to control their experiments at the ESRF from anywhere in the world, thanks to the simple, robust and secure means of remote access implemented on all MX beamlines. While complete remote control is limited to daytime shifts, when ESRF staff are present to help if needed, a hybrid mode – where local contact for the experiment is shared between the ESRF and the User Group – is already popular with the MX user community.

Remote access assumes that users ship their samples to the ESRF while they stay at home. For this reason a tracking system for the dewars containing samples has been introduced.

By extending the existing IspyB database (the previous tracking system), a new tool has been developed in collaboration with the Scientific Management Information System (SMIS), MX group, Stores, Safety and the Users' Office. Using the new system, users now know where their samples are at any time on their journey from their home lab to the beamline, and back again. "This ensures the safe arrival of samples and is a great relief for the Users at the same time, particularly if they are sending special samples," explains Stéphanie Monaco of the MX group. Although the tracking system is currently undergoing trials on the MX beamlines, other beamlines will have access to this service once it is fully up and running.

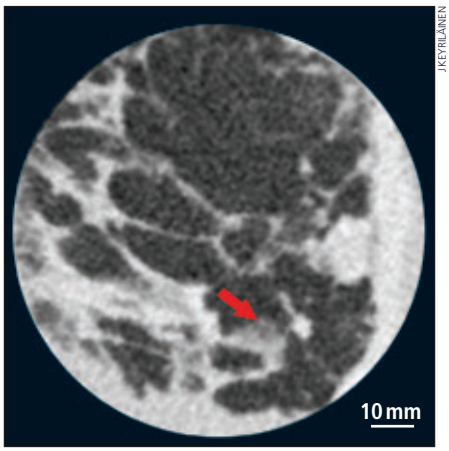
ESRF makes tweaks to the Upgrade brief

One aspect of the Upgrade Programme is the remodelling of the physical aspect of the Experimental Hall. In the spring, five teams of architects submitted proposals for how it might look like. In the summer, the evaluating team identified the best proposal but no clear winner was found. The boundary conditions for the Upgrade have evolved over the past few months, with several new technical requirements being added to the architectural specifications.

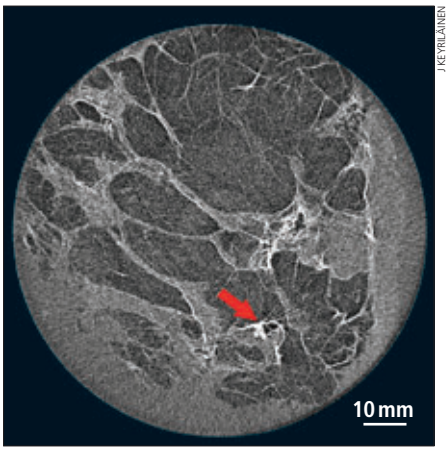
The major challenge of meeting the financial target of €41 million at 2009 prices while keeping very high technical and environmental standards remains. Therefore a request will be placed with the summer's winning architectural team to go back to the drawing board and address the issues added to the original outline of the Upgrade Programme brief.

Improved breast scans offer better diagnoses

Early detection of breast cancer is directly linked to successful treatment. A radical new screening method is improving the accuracy of scan results.



A conventional CT scan of a breast. The arrow shows the location of the tumour.



The new ABI technique shows tissue and tumour seven times clearer than CT scans.

Although X-ray mammography is currently the most widely used tool in diagnostic radiology, it fails to identify about 10–20% of palpable breast cancers. This is because some breasts are more dense than others, especially in young women. In such cases, glandular tissues can mask cancer lesions in mammograms.

Better results are obtained using X-ray computed tomography (CT). CT scans produce accurate 3D images of the entire breast, improving the detection of early diseases in dense tissue. The use of this technique in breast imaging, however, is limited by the radiation dose that can be delivered to a radiosensitive organ, such as the breast.

Now, a new CT technique has allowed scientists to overcome this problem. Teams from the Helsinki University Central Hospital, Turku University Central Hospital, Finland; the Radiation and Nuclear Safety Authority of Finland; the University Hospital of Grenoble, France; the European Molecular Biology Laboratory in Hamburg, Germany; and the Biomedical Experimental Station at the ESRF have managed to visualise breast cancer with an unprecedented contrast resolution and with clinically compatible doses.

The researchers, including physicists, surgeons, radiologists and pathologists, used the technique, called analyser-based X-ray imaging (ABI), on an *in vitro* specimen at the ESRF, using a radiation dose similar to that of a mammography examination. This corresponded to a quarter of that required for imaging the same sample with a conventional CT scanner, and the spatial resolution of the ABI images was seven times as good.

Researchers chose a particularly challenging specimen for the experiment: a breast invaded by a lobular carcinoma (a diffusely growing cancer), which is the second most common form of breast cancer and is notoriously difficult to scan clearly in clinical mammography. In this kind of sample, determining the extent of the cancer frequently fails in X-ray mammograms and ultrasonographs.

The results showed that high-spatial-resolution ABI-CT makes small, low-contrast anatomical details visible, which would otherwise only be seen by the microscopic study of an extracted sample of the breast tissue (histopathology).

"We can clearly distinguish more microcalcifications – small deposits of minerals that can indicate the presence of a cancer – than with radiography methods, and improve the definition of their shapes and margins," explains Jani Keyriläinen. "If we compare the images with X-ray mammograms and CT scans, we can confirm that this technique performs extremely well," he adds.

Despite only having studied *in vitro* samples, the team is optimistic that the method will be applied in future clinics. "The technique does not require sophisticated and expensive synchrotron radiation facilities," explains Alberto Bravin, the scientist in charge of the biomedical beamline at the ESRF. However, "it would not be viable to use X-ray tubes, as exposure times would be too long and this would be incompatible with clinical practice," concludes Bravin.

Scientists hope that the current worldwide development of compact, highly intense X-ray sources will enable the clinical use of this method. The biomedical beamline at the ESRF is directly involved in one of these projects, with the role of developing synchrotron techniques for clinical application on compact sources, such as the tabletop X-FEL machine of the Munich Advanced Centre for Photonics-MAP.

Once the method is confirmed and tabletop synchrotrons are on the market, the progression could be straightforward. "With these machines it would definitely be possible to apply this technique to clinical practice," explains Bravin, "and, in this way, contribute actively to a more efficient detection of breast cancer," he says.

MC

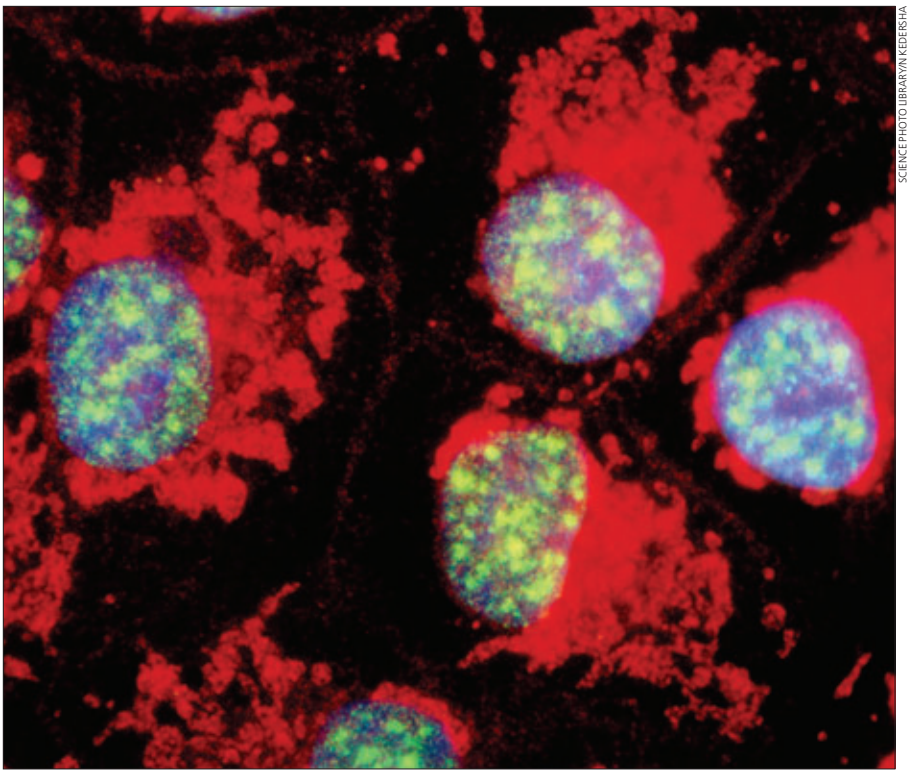
The pink ribbon is used as the international symbol of breast-cancer awareness.

Reference

J Keyriläinen *et al.* 2008 *Radiology* **249** 321–327.

Structural research reveals new ways to battle cancer

By investigating a protein molecule that can promote the growth of malignant cells, a British team has developed a drug that could help in the fight against some cancers.



SCIENCE PHOTO LIBRARY/KEDERSHA

Immunofluorescent-light micrograph of cultured drug-resistant human lung-cancer cells. The nucleus of each cell is an oval structure. DNA is stained blue and proteins associated with the nucleus are green. The cytoplasm around each nucleus is stained red owing to the presence of heat-shock proteins, where they indicate the presence of abnormal cancerous cell growth.

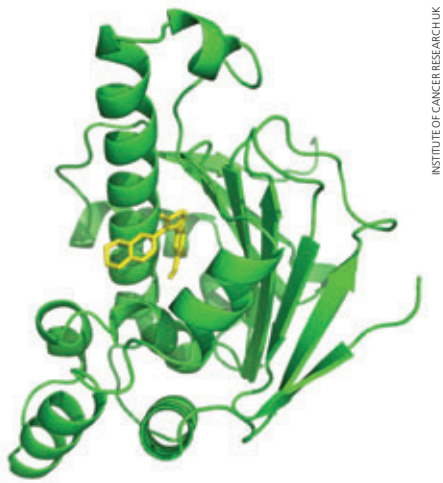
The body needs them to live, but at the same time they can contribute to making our health worse: heat-shock proteins (HSP) are molecules that protect other cellular proteins from breaking down in adverse environments, such as when the body is at a high temperature. These conditions increase production of HSP.

One particular HSP that has caught the interest of scientists around the world in recent years is the chaperone (a protein that assists in folding/unfolding other proteins) HSP90. As well as protecting cells when the body is under stress, HSP90 plays a role in the growth of tumour cells. In cancer, some of the body's key proteins become mutated, and HSP90 helps to protect them and keep them functioning.

The enzymatic function of HSP90 is powered by adenosine triphosphate (ATP). Researchers are trying to block it so as to inhibit the function of HSP90. A successful inhibitor would leave the cancer cells so debilitated that chemotherapy or radiotherapy could then control them. This would assist greatly in developing targeted treatments for a range of cancers, including prostate, breast, bowel, ovarian and kidney.

The section of structural biology at the Institute of Cancer Research in London, UK, has studied HSP90 extensively, and the ESRF played an important role in solving the structure of this molecule and its function. In 2006 the researchers solved the structure of the yeast HSP90 in complex with ATP and a co-chaperone molecule (a protein that assists a chaperone), thanks to data taken at the ESRF macromolecular crystallography beamlines. The crystals used to solve the structure were small and poorly diffracting, making the ESRF the best choice to collect the data. An understanding of the structure gave the team an insight into the behaviour of the chaperone and some initial ideas of how to control HSP90's progression through the chaperone cycle. The group found that the binding and turnover of ATP in HSP90 is crucial to this mechanism.

"We have come a long way," explains team head Laurence Pearl. After years of work the researchers have already proposed several inhibitors that have entered clinical trials. The first was the pyrazole compound CCT018159 – a small molecule that binds to HSP90. After solving the structure of the whole complex, the team realised that there were water-mediated hydrogen bonds holding the inhibitor in place. The scientists also established where additional atoms could be placed to increase the binding of the drug to the protein and improve the behaviour of the complex.



INSTITUTE OF CANCER RESEARCH UK

An illustration of an inhibitor (yellow) bound to the ATP site of an Hsp90 molecule.

The team decided to add an amide group to improve binding to the protein, which led to the creation of NVP-AUY922. This drug has so far proved successful in human breast-cancer models, potently inhibiting the proliferation of the cancer. It has been through several stages of clinical trials, with promising results. Further derivatives of this inhibitor could be on the market within the next 5–10 years.

MC

References

S A Eccles *et al.* 2008 *Cancer Res* **8** 2050–2060.
M M U Ali *et al.* 2006 *Nature* **440** 1013–1017.

From the ESRF to the pharmacy

Pharmaceutical companies are increasingly turning to synchrotron light in the development of drugs.

R DAVIES

The development of drugs is the ultimate aim of the pharmaceutical companies at the ESRF.

Next time you go to the chemist with a prescription, remember synchrotron light. Maybe the drug you will be buying has its origins in structural-biology experiments carried out at one of the world's light sources.

Pharmaceutical companies are regular industrial users at the ESRF, where they study complex molecules and their binding to ligands with potential inhibitor effects. This is one of the most important steps in the design of medicines. In the process of drug design, a target protein is crystallized and its atomic structure revealed using X-ray crystallography. The structure is then used as an aid in the design of potential drug molecules. The most promising ones are then tested both *in vitro* and *in vivo*, and after successful clinical trials they appear in pharmacies and clinics.

The proof of the pudding is in the eating: a new drug to combat type 2 diabetes might be on the market soon. This form of the condition results from the body's ineffective use of insulin. It often results from excess body weight and physical inactivity, and there are an increasing number of people affected by it.

Pharmaceutical company Sanofi-Aventis is carrying out clinical trials for a new medicine for type 2 diabetes, the development of which has involved X-ray crystallographic structure solution using data collected at the ESRF. Researchers crystallized the ligand-binding domain of the nuclear receptor protein PPAR delta with agonist molecules (molecules that increase the activity of the protein). Increased PPAR delta activity is considered to have a positive effect in the treatment of the condition. X-ray diffraction data collected at the ESRF allowed the researchers to understand the structural basis of interactions between PPAR delta and the agonist molecules, and they showed that the agonist-binding pocket of the protein is large and exhibits plasticity. This information provided the key for the team to develop novel agonists with improved properties.

"We have successfully used the ESRF for the last decade," explains Magali Mathieu, head of protein crystallization at Sanofi-Aventis' Vitry site. "It has happened in the past that the results from experiments at the ESRF have made us rethink the possible composition of a product," she adds.

Mathieu is a "veteran" user, having been coming to the facility for the last 10 years. Sanofi-Aventis was the first user of the MXpress service. Mathieu's team sends frozen samples to the synchrotron, and ESRF staff analyse them. "It has been a crucial development for us, especially in routine experiments. We all monitor progress from our end: chemists, technicians, biologists, drug designers...It is a bit like *Big Brother* – we can see how the experiment is going from our lab," she says. "We still come to Grenoble twice a year to carry out experiments and catch up with beamline and software developments, but MXpress is our preferred option in general," she adds.

Multidisciplinary research

Another big fan of MXpress is Michael Schäffer, CEO of Crelux, based in Germany. This is a service company for pharmaceutical and biotech companies that outsource their crystallographic activities. Despite being a newcomer to the ESRF – 2008 is the first year that Crelux has used the facility – Schäffer claims that results are already extremely positive. "We are even considering a visit to the ESRF so that we can collect our own data and solve many structures in one go," he says.

Mathieu and Schäffer agree that a big part of the success of MxPress is the team involved at the ESRF: Elspeth Gordon and Stéphanie Monaco. "You need to trust the scientists who are collecting the data, otherwise it does not work," explains Mathieu.

The use of synchrotron light by drug companies is well established, and they represent about 25% of user activity at the ESRF's macromolecular crystallography beamlines. Mathieu explains that the capabilities of the beamlines have improved a lot: "In the past we would have considered a crystal of 100 μm just big enough; today the definition of 'big enough' is 30 μm."

Denis Zeyer, CEO of French biotech company Alix, a contract research organisation that provides services in fragment- and structure-based drug discovery, sees the future of synchrotrons as bright: "Synchrotron sources can't be detached from structural biology. At the ESRF we can test 100 samples per shift, which is huge compared with what we can do with classical sources. The idea in the Purple Book of having a dedicated beamline to test crystals and another for data collection is excellent."

Schäffer demonstrates the health of synchrotron sources with his own example: "Our company was created three years ago and we are now self-sustaining. There is an increasing trend from pharmaceutical companies to outsource because they are cutting down their discovery departments. There is also a rise in the demand for structure solution, and synchrotron sources play a significant role in that."

In terms of scientific discoveries, Mathieu, Schäffer and Zeyer agree on the next big challenge for structural biology: the routine determination of the structures of membrane proteins will be the key to discovering many new medicines. Membrane protein structure solution is a field currently dominated by academic groups, but pharmaceutical companies hope to jump on the bandwagon once recent technological advances can be implemented. Schäffer thinks that this will happen soon: "It's a matter of effort to solve this kind of structure, and in only 10 years we may be solving them systematically; I believe it will not take a long time."

MC

The fight to arm o

Researchers from Utrecht University, the Netherlands, work on unlocking the mysteries of the C3 protein, which is key both to understanding and to helping our immune system.

The body becomes a battlefield when viruses and bacteria attack, but, thanks to its various defence mechanisms, it wins the battle most of the time. The immune system includes not only antibodies but also a system of "innate immunity" that pre-dates the evolution of antibodies and is at least 700 million years old.

The immune system in blood is activated by the so-called complement system, which consists of more than 20 large proteins that normally circulate in an inactive form. The most central of these are equipped with a highly reactive molecular "warhead". When stimulated, these proteins trigger a chain of reactions to fight against pathogens.

One of these proteins, C3, is currently the object of study by scientists around the world. Understanding its particular structure is of utmost importance to research, not just for a knowledge of how it works but because of the danger that it represents in cases where it malfunctions. For example, if C3 fails to function correctly it can turn against the host tissues and lead to kidney disorders or macular degeneration (loss of central vision in the eye, potentially resulting in total blindness).

Researcher Piet Gros and his team from the University of Utrecht, the Netherlands, have studied C3 for five years. They are regular users of the macromolecular crystallography beamlines at the ESRF and their research there has appeared in high-profile journals, including *Nature* and *Science*.

Little was known about C3 until 10 years ago. Today, the structure of its inactive state is no longer a secret, nor is the structure of some of the proteins that it produces when it attacks bacteria or viruses. When Gros' team published the structure of C3 in 2005, the editor of *Nature* asserted that "it may be the largest protein structure [the longest chain and the most domains] so far determined".

Getting ready for the battle

The so-called "warhead" is the key part in C3 and is therefore of particular interest. When activated, it binds to chemical acceptor groups on many pathogens and marks them out for destruction by immune cells. There are three ways to activate C3: an antibody recognises the pathogen and guides C3 to its target; C3 reacts to the actions of lectin (a protein that binds to the sugars found in pathogens); or it is activated spontaneously.

Specifically, what happens in the activation process is the cleavage of C3. Gros and colleagues studied the protein and its warhead inside the thioester domain (TED), which is tucked into the body of the protein. When the protein is activated, it separates into two fragments: C3a and C3b. Research at the ESRF allows scientists to observe how the TED becomes exposed and shifts 8.5 nm at the same time. This separation of the TED facilitates its binding to a target-pathogen surface – which is when C3a and C3b carry out their respective functions.

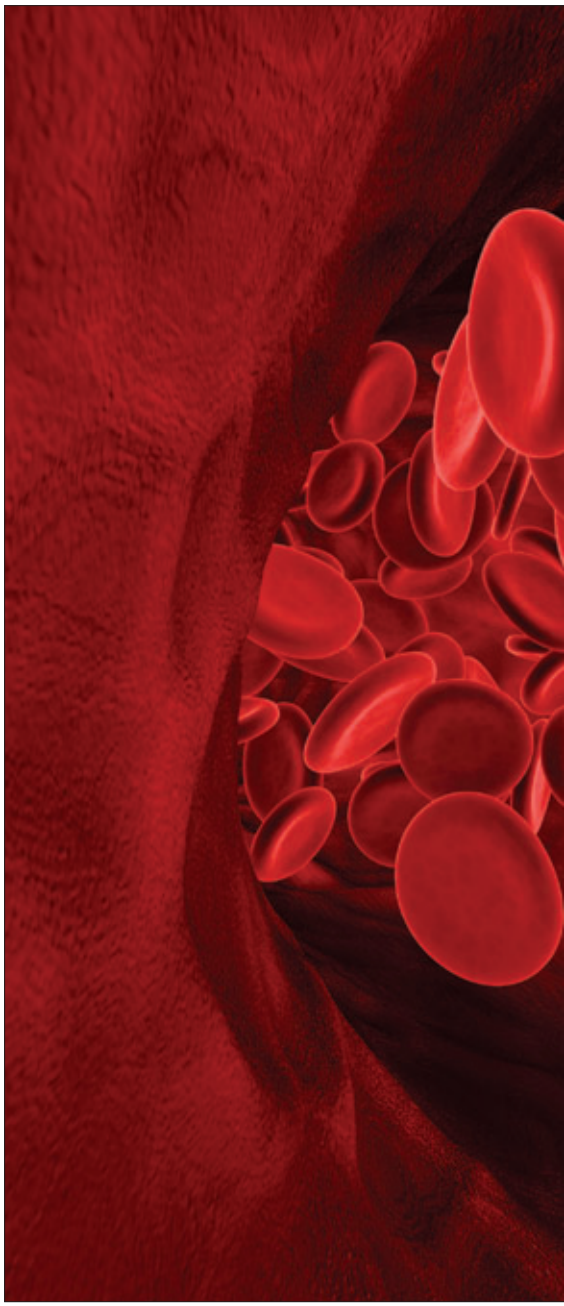
Inflammation effect

When the body is attacked by a virus or bacterium the injured area may become inflamed. This is caused by the action of C3a, which activates mast cells. The chemicals cause blood vessels in the area around the infection to dilate and become more permeable, so that it is easier for all of the components that fight disease to get to the site of infection. C3a also activates white cells when it binds to cell receptors. In contrast, C3b binds to sugars on the pathogen surface. It subsequently starts a series of reactions and cleavages that result in the formation of "attack" complexes. This fragment also triggers the recognition by immune cells of the virus or bacterium, which destroy the micro-organism.

C3b was the particular focus of a study by Gros' team and other teams that was featured in *Nature* in November 2006. In his article Gros explains that the C3 molecule undergoes huge structural changes at the same time as C3b is created. These changes activate the warhead to bind to pathogens. This is a critical step in the defence against the pathogen because, once C3b is bound to the pathogen surface, it also binds to a series of other proteins that then proceed to target immune responses to the pathogen. If C3b does not bind to the pathogens, then the blood can become infected with bacteria (bacteraemia), and this may result in blood poisoning.

The terminal pathway of the complement system consists of proteins that protect blood against bacteria. When this pathway is deficient, bacterial infections – such as meningitis – can easily take hold in humans.

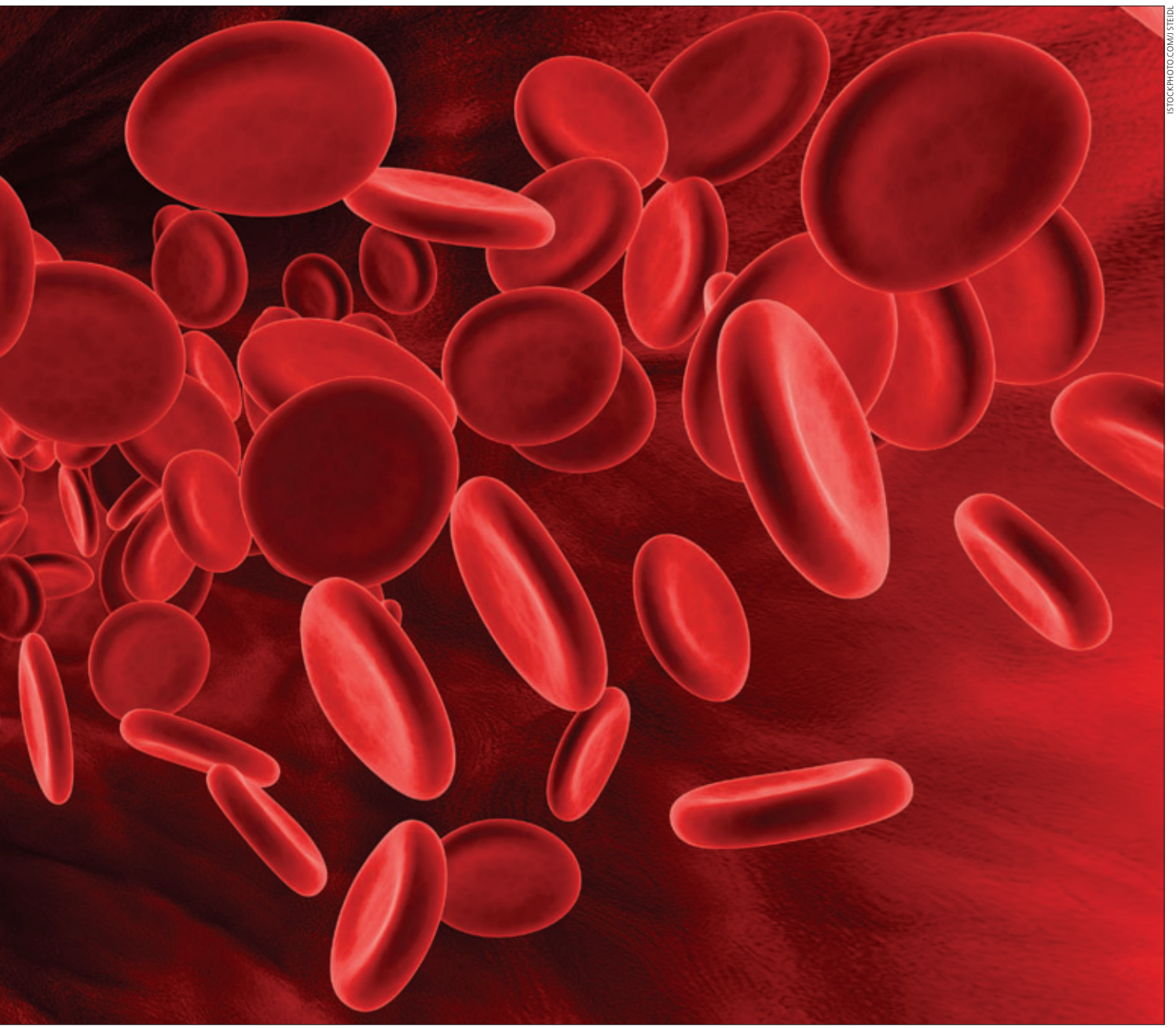
In the terminal pathway there are membrane attack complex/perforin (MACPF)



The C3 protein is responsible for marking out invading path

C3 is currently the object of study by scientists around the world

ur blood warriors



ISTOCKPHOTO.COM/JSTEIDL

nogens for destruction by immune cells. An internal "warhead" is activated, fragmented and unleashed through the bloodstream to fight infection.

domain pathways. These disrupt the membranes of any invading micro-organisms or infected host cells. The scientists from Utrecht solved the structure of one of these domains, namely C8, and realised that it is almost identical to pore-forming, cholesterol-dependent cytolysins (proteins that are toxic to certain cells) from Gram-positive bacteria. The way in which cytolysins produce pores is understood, so scientists concluded that C8 and the other MACPF proteins may use a similar mechanism to disrupt cell membranes.

Despite its successful extensive investigations, Piet Gros' team continues to work on the complement system. "There is still a lot to do. Our next challenge is the protein complexes that are formed. They will teach us how the molecules become activated in this process," he explains. "These insights should tell us how our body controls this immune response, and how it manages to attack only the infectious microbes and not our own cells," he concludes.

MC

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Unlocking GPCRs is key to drug design

G protein-coupled receptors play an important role in the body and are pivotal targets in drug development. A UK team from Cambridge has figured out these structures with the help of the ESRF.

The postman knocks on the door and gives the man a letter. The man goes to his wife and they open the envelope together. They discover a card from their friends, congratulating them on their wedding anniversary. The couple pick up the phone and call their friends, thanking them for the card.

This is analogous to something that happens in cells. First, an activator (the postman) outside the cell binds to the receptor molecule, called G protein-coupled receptor (GPCR; the man), which is located at the surface of the cell (the house). These transmembrane proteins are bound to a G protein (the wife) and set off a series of events (calling their friends) inside the cell.

The role of GPCRs in humans is of great importance to the functioning of the body. Since these molecules can interact with the environment both inside and outside the cell, they receive chemical signals and activate certain cellular reactions in response. They are vital to functions such as heartbeat, digestion and neural activity. Their actions allow humans to process light and smells; and to regulate behaviour, mood and immune response. Much drug development today is focused on locating chemicals that affect the ability of ligands (agonists or antagonists) to bind to their GPCRs, thereby either inhibiting or accelerating specific cellular process.

A team at the Medical Research Council (MRC) in the UK has worked out three challenging structures of GPCRs in the last year alone.

"We have been studying the structure of GPCRs for more than 10 years. Our recent results have provided us with some spectacular insights into the function of GPCRs at the cell surface," explains Gebhard Schertler, group leader at the Laboratory of Molecular Biology at Cambridge.

ISTOCKPHOTO.COM/I KARJALAINEN

Scientists hope to find the key to the helices of the stress hormone receptor.

GPCRs tend to be difficult to crystallise because of their instability. Despite there being hundreds of different GPCRs in the body, the structure of only one of them (rhodopsin) had been solved prior to last year. Rhodopsin is a protein that enables vision in low light conditions and is the most stable of the GPCRs. The team has determined several structures of this visual pigment using electron-crystallography and X-ray microcrystallography.

New strategies

The team works on other GPCR proteins using the most advanced microprotein crystallography available at the ESRF. It devised a new strategy to stabilise the receptors, as well as solving the structure of recombinant rhodopsin and the stress hormone receptors beta 1 and beta 2 adrenergic receptor. These two receptors help regulate to heart rate, blood pressure and lung constriction, making them important drug targets. Last year the scientists, together with a team from Stanford University, determined the structure of the human beta 2 adrenergic receptor. To crystallise the molecule they used an antagonist (beta blocker), which keeps the receptor stable and inactive.

They then studied the samples on the microfocus beamlines ID13 and ID23-2.

"In collaboration with Manfred Burghammer and David Flot, we adapted the existing microfocus beamlines at ESRF to produce the smallest and most intense beams available in the world for protein crystallography. This allowed us to work with extremely thin and weakly diffracting crystals, which are typical of GPCRs. By solving their structures we were able to see a beta blocker bound to the binding pocket of the stress receptors for the first time," explains Schertler.

Independently, the Cambridge researchers developed a stabilisation strategy for the beta 1 adrenergic receptor that will allow them to solve the structures of other GPCRs.

Comparison of the two beta-receptor structures shows that the two proteins are surrounded by near identical ligand-binding pockets. Furthermore, the structure of 67% of the transmembrane region of these receptors is similar. However, the team identified two amino acid residues close to the ligand-binding site that are different, which may explain ligand selectivity. These findings are vital to the future of rational drug design.

The structure of the beta 1 adenergic receptor shows a well defined helix that is not found in the structures of rhodopsin or the beta 2 receptor protein. This helix may be essential for receptor activation, as well as cell signalling. These structures have helped to reveal ligand binding in greater detail and they are important in understanding the mechanism of receptor activation.

However, this is just the start of fully understanding GPCR signalling. "We now know the structures of three out of more than 800 GPCRs. There is still a lot to be done. Our next challenge is to determine the structure of an activated receptor in complex with the G protein to find out how the signal is handed on to the cell. Our knowledge of these receptor structures, coupled with state-of-the-art technology, is letting us make significant steps towards a better way of tackling GPCR-related illnesses," says Schertler.

MC

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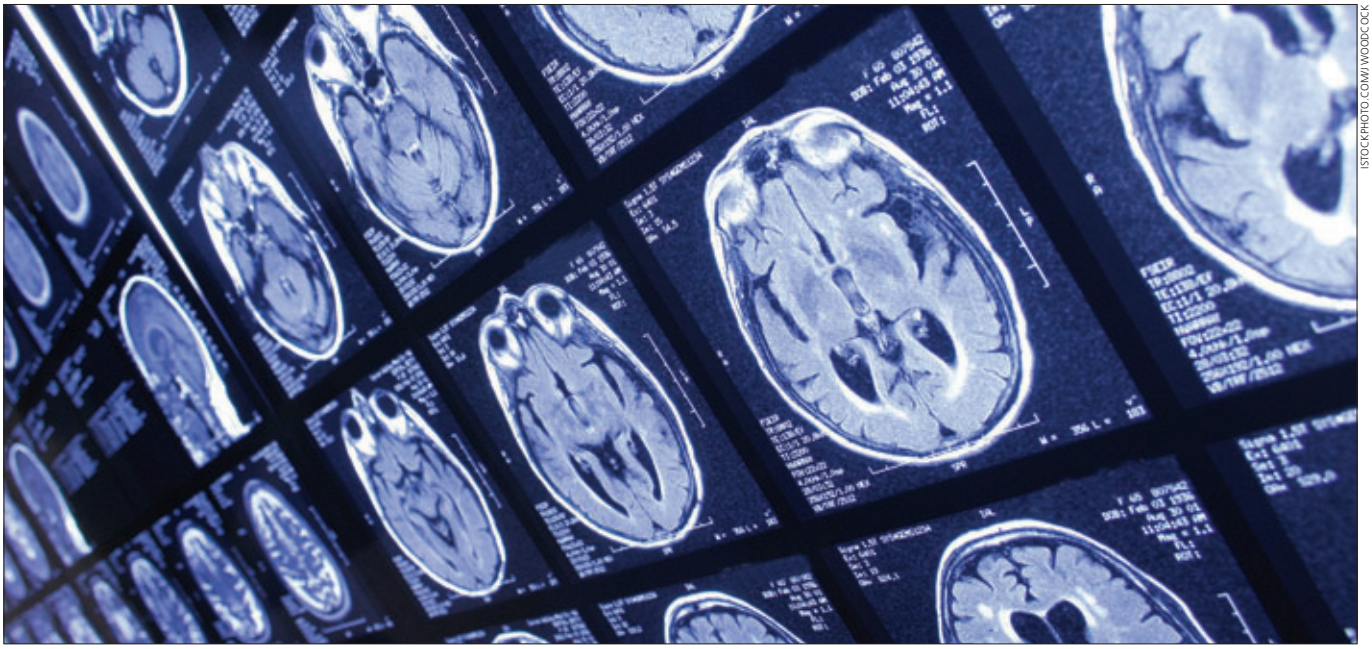

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The state-of-the-art medical beamline at the ESRF is currently being used to develop two techniques that may help in the treatment of certain types of brain tumour. Researchers hope that the expected results from advances in SSRT and MRT could soon lead to human clinical trials.

Newly renovated beamline has tumour patients in mind

Positive preclinical results from the treatment of brain tumours in recent years have been the motivation for major infrastructural changes on the medical beamline at the ESRF.

From late 2009 the new-look experimental station will allow scientists and doctors to perform clinical trials on patients with certain types of brain tumour.

The medical beamline is a melting pot of backgrounds, with physicists, biologists, medics, engineers and technicians. It represents a true convergence of scientific ideas, which have pushed medical research at the ESRF one step closer to human application. There are two techniques being developed by these teams: stereotactic synchrotron radiation therapy (SSRT); and microbeam radiation therapy (MRT).

The success of SSRT is thanks to a collaboration between the University Hospital of Grenoble (CHU), the Université J Fourier, Grenoble, the INSERM U836 Equipe 6 and the ESRF. In 2004 the teams came across some astonishing results when treating rats suffering from glioma – a brain tumour that affects 5–10 adults out of every 100 000 and has a median survival of less than a year.

The scientists treated the rodents with cis-platinum and monochromatic synchrotron X-rays. By "marrying" chemotherapy with radiotherapy, they increased the lifespan in treated rats six-fold compared with those that received no treatment. Back then, Dr François Estève from the CHU was convinced that it was worth moving forward to treat humans: "Taking into account the impossibility today of healing this brain tumour in humans, it is a must to try this method."

Four years and several scientific publications later, the beamline is ready to welcome patients next year. One of the main changes involves the adaptation of the set-up that was previously used in coronary angiography, so that it can be used for the radiotherapy treatments. For the SSRT technique the team has added a series of masks, next to the treatment chair, that will define the size of the beam depending on the tumour dimensions and several additional safety features. The content and objectives of the different phases of clinical trials are defined and regulated by international protocols.

"These are early days. However, we are advancing slowly but surely."

The first phase aims to show that this technique does not produce any secondary effects. Patients with brain metastases from lung tumours will take part. Only when the first phase has been completed and reviewed will phase two start. Scientists and doctors will select a specific group of the population and try to improve the lifespan of those affected, primarily, by brain tumours.

This technique may one day be used in hospitals. "These are early days. However, we are advancing slowly but surely. If we succeed, this will be a great advancement for medicine," explains Alberto Bravin, the scientist in charge of the medical beamline.

There is another reason for hopes of success in the treatment of gliomas. In addition to SSRT, the ESRF teams are using the promising MRT, a technique developed in the late 1990s by a Swiss team in collaboration with the ESRF. Following the encouraging results from preclinical trials on different brain-tumour models, the ESRF has supported a large refurbishment of the MRT station to prepare for possible human clinical trials.

MC

Earth's interior contains unusual electron structure

High-pressure, high-temperature experiments at the ESRF on the Earth's most abundant mineral reveal stable partial spin-pairing of ferrous iron.

The Earth's interior is mostly inaccessible, so scientists primarily use indirect methods to construct models of it. These include comparing geophysical data (e.g. from earthquakes) with measurements taken in the laboratory. Models such as these tell us not only how properties such as temperature and chemistry change with depth but also how the movement of material inside the Earth affects surface processes, such as plate tectonics and the chemistry of the atmosphere.

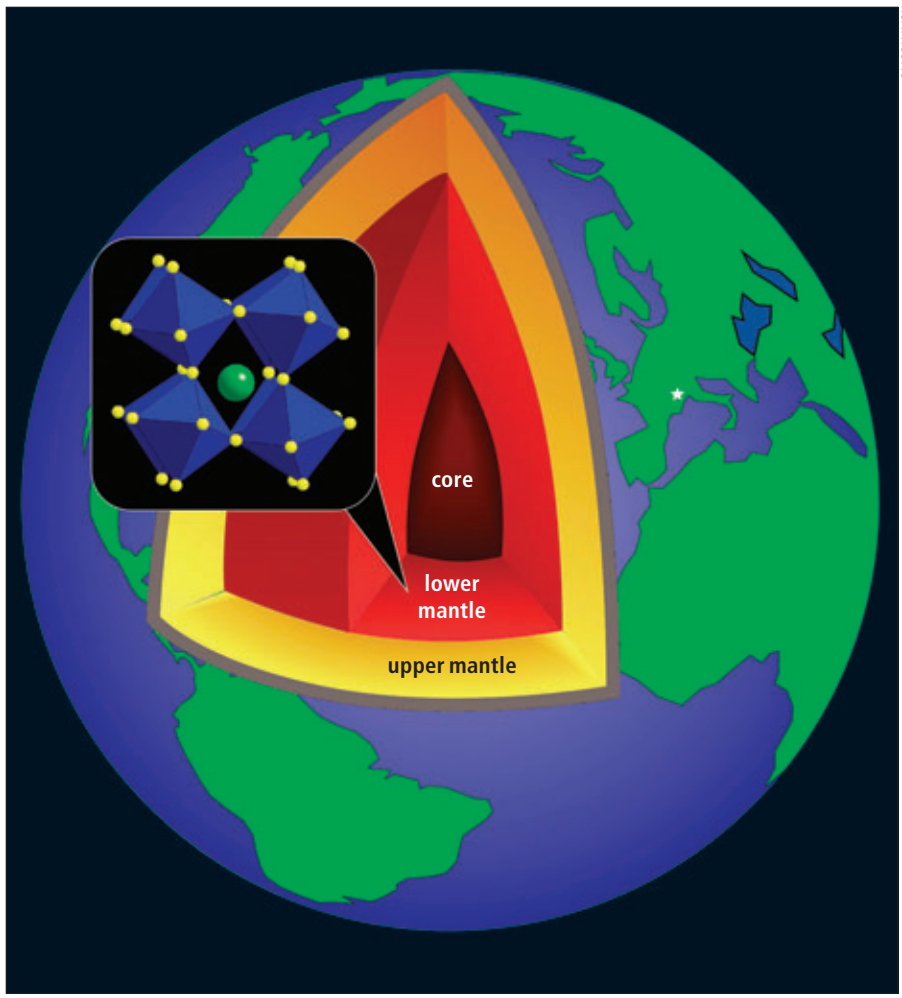
Many laboratory studies have focused on the Earth's most abundant mineral: a magnesium- and iron-containing silicate with a perovskite structure (lower-mantle perovskite). Not all of the studies have included iron, because experiments without the metal are generally easier to perform. However, iron is a transition element that can change its electronic structure and, consequently, the way that the Earth's interior behaves. Spin-state transitions, for example, are changes in the pairing of electrons in the atomic orbitals. These have been studied since 2004 for lower-mantle perovskite, but each study has reached a different conclusion, so spin state of iron in lower-mantle perovskite remains a puzzle.

Now, researchers from the University of Bayreuth, Germany, and the ESRF have clear evidence of a spin transition in lower-mantle perovskite. With the combined advantage of the four-bunch timing mode at the ESRF and the small, intense beam at beamline ID18, they collected high-quality nuclear resonance data on lower-mantle perovskite at a pressure of up to 110 GPa and 1000 K using a diamond anvil cell fitted with a miniature heater. The team carried out Mössbauer spectroscopic studies of the same sample at the University of Bayreuth, as well as X-ray studies on beamline ID27 and at the Advanced Photon Source. It found that iron in lower-mantle perovskite is stable in a partial electron-paired configuration (intermediate spin state) throughout most of the lower mantle.

The stability of the intermediate spin state is completely unexpected and may be related to the unusual environment of the iron atom in lower-mantle perovskite. Computer simulations have so far failed to reproduce the stability of intermediate-spin iron using conventional approaches, suggesting that more-complex calculations are needed to recreate what nature has already produced.

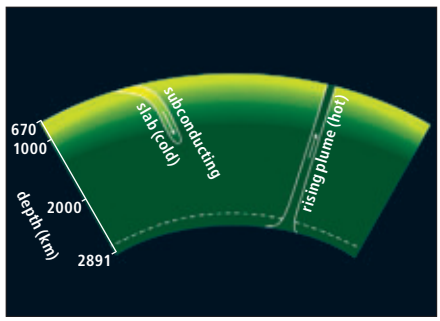
These new findings suggest that some of the assumptions on which Earth models are based will have to change. By how much will be decided by the results of some upcoming high-pressure experiments.

C McCammon, I Kantor, O Narygina, J Rouquette, U Ponkratz, I Sergueev, M Mezouar, V Prakapenka and L Dubrovinsky



C MCCAMMON

Inside the Earth's structure the lower mantle consists mostly of lower-mantle perovskite (inset). In the crystal structure the iron atoms (green) are in a distorted atomic environment.



C MCCAMMON

A cross-section of the lower mantle shows how high-spin iron (minimum electron pairing; yellow) transforms rapidly to intermediate-spin iron (partial electron pairing; dark green). Changes in temperature at the top of the lower mantle associated with the movement of material change the relative proportion of the two spin states.

Reference

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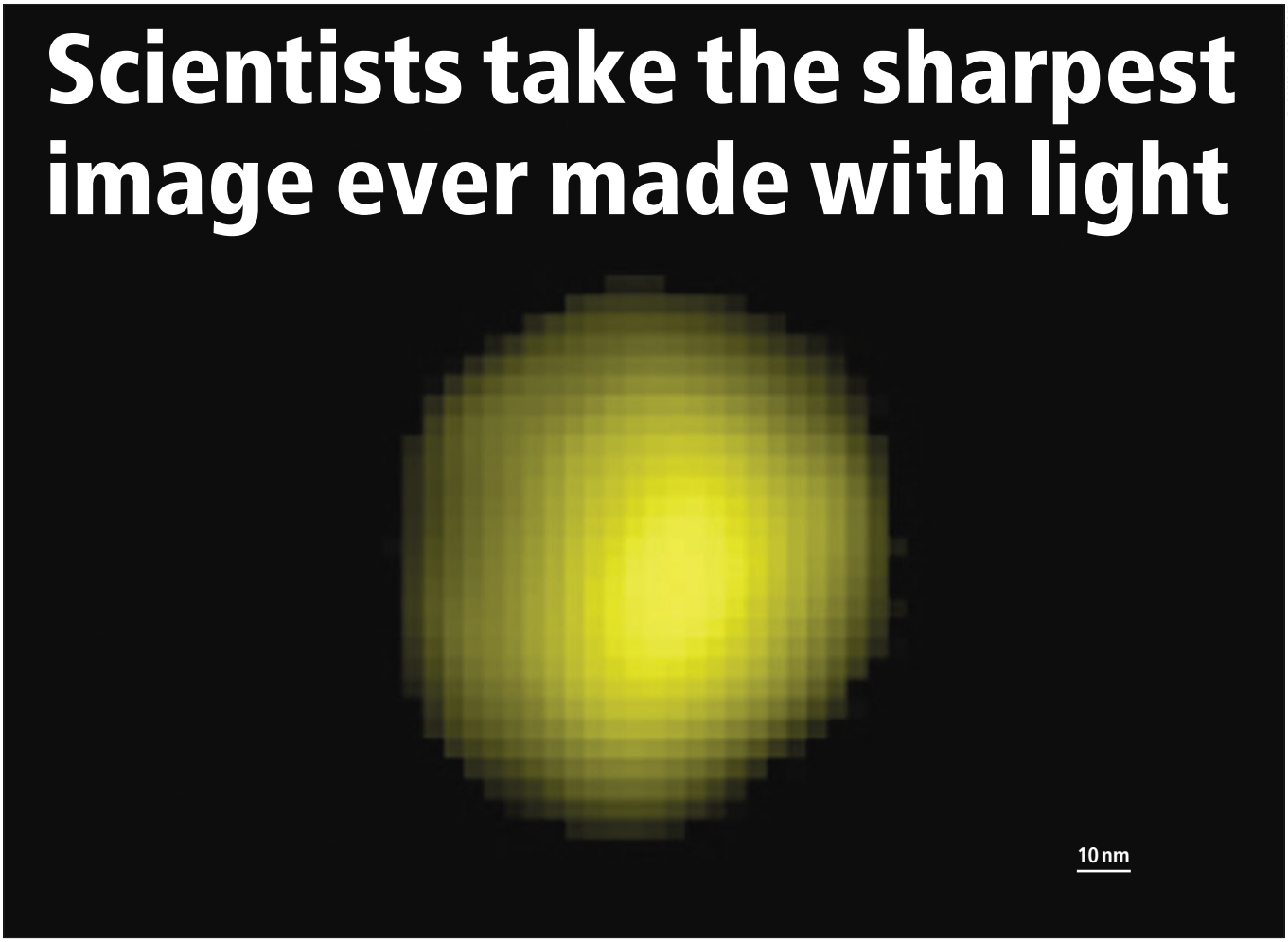
Scientists take the sharpest image ever made with light



TU DRESDEN / C SCHROER

This image of a gold nanoparticle was reconstructed using data from its diffraction pattern. The brightness indicates the thickness of the gold. The diameter of an average human hair measures some 300 times that of a nanoparticle.

Diffraction-imaging techniques offer several advantages over other microscopy-imaging methods. The main benefit is that they can be used in almost any environment.

The image above may not appear out of the ordinary. However, if you note the scale bar, the object suddenly takes on a new dimension. This image represents the first time that something has been "photographed" at such a high resolution using X-ray light.

Researchers from the Technische Universität Dresden, Germany, and the ESRF staff on ID13 reconstructed a 100 nm gold particle fixed onto a substrate with an astounding 5 nm resolution. Unlike other techniques, X-ray imaging works in real-life environments, such as chemical processing.

The key to the success of this research is coherent X-ray diffraction imaging. The team made a big step forward in pushing the resolution from some tens of nanometres to just 5 nm, which is 100 times as sharp as anything achievable using a good-quality optical microscope.

This breakthrough was possible because scientists improved both the quality and the intensity of the coherent X-ray beam by narrowing the focus of an incoming 15.25 keV beam to a diameter of 100 nm, while at the same time maintaining a pencil-like shape. The beam illuminated a single nanoparticle for 10 minutes, after which a detailed diffraction pattern made it possible to render an image of the particle.

Coherent X-ray diffraction is not the only technique that can achieve nanometre resolution. Transmission-electron microscopy, for example, yields the highest resolutions but requires thin samples to be put into a vacuum. The benefit of X-ray techniques is that they can be used in almost any environment, such as chemical reactors and high magnetic fields. They are also suited to the study of how a sample changes according to its environment.

The technique is non-destructive and can assess the shape, size, strain and composition of individual nanostructures such as quantum dots in semiconductors and nanoparticles in catalytic converters.

Coherent diffraction imaging will play a major role in the future of the ESRF. The Purple Book – the document outlining the ESRF's Upgrade Programme 2008–2017 – highlights the method as a toolset for extensive development. The team now plans to push the resolution farther towards the nanometre limit and apply its record-breaking technique to answer some real-world scientific questions.

CH

"Coherent diffraction imaging will play a major role in the future."

Reference

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Many paths lead to health research

Three scientists talk about their career paths and how they found their way to positions at the ESRF.

Less than a year ago, Yolanda Prezado was working as a medical physicist at the Hospital of Navarra in Spain. Her work consisted of calculating the dosage of treatment for cancer patients, or treatment planning, as well as experimental dosimetry and quality assurance of the equipment used for cancer therapy. She was in charge of determining how much radiation they should receive.

"This job was very focused on the patients. It was very practical," explains Prezado. "I missed research a lot, so when I discovered the advert for a scientist at the ESRF medical beamline on the website of the Spanish association of medical physicists, I went for it." She already had experience of particle accelerators from the days of doing her PhD in physics, a big part of which was carried out at CERN. What attracted her to the job at the ESRF was the project to develop new radiotherapy techniques. Today she works on the clinical trials of radiotherapy techniques on that beamline.

Matthew Bowler has a very different background. He arrived at the ESRF last year after being hired as the beamline scientist for ID14-2. He knows the MX beamlines well from being a user there since 2001. Bowler studied biochemistry at the University of Exeter, UK, followed by an MSc at Oxford University and then a PhD in structural biology at the Medical Research Council/Cambridge University.

"During my MSc I started coming to the ESRF as a user and I realised that what I liked was the process of data collection, the methodology and the instrumentation," he explains. This is why he applied for the job at the ESRF. "My main interest is to make the beamline as easy to use as possible and to develop the instrumentation," he says. In fact, the beamline should go through an upgrade in the next few years, and this is where Bowler hopes to continue its development.

C.ARGOUD

Ganesh Natrajan combines his working knowledge of biology and physics, and describes himself as a jack of all trades.

Another member of the macromolecular crystallography team, Ganesh Natrajan, arrived at the ESRF for quite different reasons. "The scientific project of my postdoctoral position was very attractive and I couldn't let it go," he says. Natrajan currently studies *Helicobacter pylori* in the Macromolecular Crystallography Group. His start in science was, however, far removed from biology. "I did my degree in physics, but I changed in my PhD, which I did in structural biology in the Netherlands Cancer Institute," he explains. There he learned from all the biologists working alongside him in the lab, which helped him to overcome the fact that he hadn't studied biology. Today he gladly describes himself as "a jack of all trades and master of none". "It is interesting to be versatile; I know a bit about many subjects," he states.

These seemingly "unusual" and varied backgrounds have had a positive effect in each of these scientists' positions. Natrajan's physics has definitely proved useful in his current role: "There are things like thermodynamics, and other biophysical aspects of structural biology, where a knowledge of physics can be quite handy." Prezado, too, feels that her background helps her do her job better: "In the hospital I acquired a knowledge of treatment-planning systems and the dosimetry needed to treat patients at the ESRF in future."

MC

Movers and shakers

ESRF director-general
Francesco Sette

Francesco Sette will become director-general at the ESRF in 2009. He will succeed Bill Stirling, whose eight-year term of office finishes at the end of 2008.

Since 2001 Sette has been a director of research at the ESRF, playing a pivotal role in maintaining the facility among the world's leading synchrotron radiation sources, as well as enlarging its user base, which today comprises more than 4000 scientists.

C.ARGOUD

An Italian born in 1957, Sette holds a PhD in physics from the University of Rome. A pioneer in research with synchrotron radiation, he spent eight years at the AT&T Bell Laboratories in Murray Hill, US, and has received prestigious awards for his work. Some 20 years ago, he co-invented the world's first high-energy resolution, high-intensity soft-X-ray source, which quickly found its way into many synchrotron light facilities around the world. Later, as group leader at the ESRF, he developed a new generation of inelastic X-ray scattering beamlines that made it possible to study the atomic motions and electronic properties of condensed matter at an unprecedented energy resolution.

Sette is also a member of the advisory committees of major light sources at DESY in Hamburg, Germany, and LCLS at Stanford, US.

Director of administration
Angelika E Roehr

Angelika E Roehr is director of administration at the ESRF after her predecessor, Helmut Krech, finished his term last October after six years in the position.

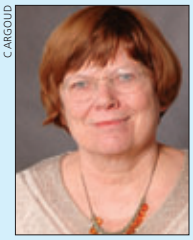
C.ARGOUD

Roehr was born in Germany. She got an MBA at the University of Munich and gained professional experience at Deutsche Bank, including two years as an analyst at the New York branch. She also worked in the finance department of the Max-Planck Society, where she was responsible, in particular, for the national and international subsidiaries, industrial co-operation, tax matters and central accounting.

Roehr's position prior to coming to the ESRF was as the administrative director of the Municipal Museums of Vienna, Austria.

President of the International Union of Crystallography
Sine Larsen

One of the directors of research at the ESRF, Sine Larsen has recently been appointed president of the International Union of Crystallography. This is a three-year position that has rarely been occupied by a woman. The last was Nobel laureate Dorothy Hodgkin, 36 years ago in Japan. The challenges she has set for her presidency involve the development of solid crystallographic communities in the world, especially those under-represented in the union today. Larsen also wants to encourage the crystallography communities to build strong relationships with each other.



C.ARGOUD

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Applicants should submit a curriculum vitae and a research plan and arrange three letters of recommendation to be sent separately by the referees to

Dr. D. J. Huang, Head of the Scientific Research Division
National Synchrotron Radiation Research Center
101 Hsin-Ann Road, Hsinchu Science Park
Hsinchu 30076, TAIWAN
E-mail:science@nsrrc.org.tw

The deadline for applications is January 1, 2009, but submissions received after this date will be considered if the positions are not yet filled.

The ESRF offers exciting opportunities to work in an international atmosphere in the French Alps. The facility opens about 75 posts for researchers and engineers every year, from PhD students to positions for senior scientists and group leaders. In the next six months the following posts are likely to be opened:

Macromolecular Crystallography Group:
Two scientists and up to three postdoctoral researchers

Materials Science Group:
Two postdoctoral researchers (ID11/ID31)

Soft Condensed Matter Group:
Three postdoctoral researchers (ID02, ID10A and ID13)

X-Ray Absorption and Magnetic Scattering Group:
One scientist and three postdoctoral researchers (ID20, ID24/BM29)

X-Ray Imaging Group:
One post-doctoral researcher (ID21/ID22)

The ESRF also regularly offers PhD programmes. For details about any of these posts please visit the ESRF jobs pages at www.esrf.eu/Jobs regularly or subscribe to mailings for new job advertisements at **www.synchrotronjobs.com**.

ESRF

Bill Stirling: a man with a vision

Malcolm Cooper presents a personal portrait of the departing director-general of the ESRF.

Bill Stirling completes his period as director-general of the ESRF at the end of 2008, a role he stepped into in 2001. The facility now looks and feels very different from how it did back then, which, of course, it would. The current positive feeling at the establishment owes much to the changes that he has worked with great care and indefatigability to make a reality.

Stirling, known to many simply as Bill, had what he regards as the finest European education possible: a Scottish high school in Dunfermline; and a Scottish university in Edinburgh, where he gained a first-class Honours degree. It was with his PhD that he commenced a career in neutron scattering by studying that archetypal material strontium titanate. He followed this with postdoctoral positions in Edinburgh and Jülich, leading to a long period at Institut Laue Langevin and culminating in his position as a staff scientist. In fact, Bill and his wife Jenny have spent more of their married life in Grenoble than anywhere else.

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Bill Stirling (middle) has undoubtedly made the ESRF known around the world. He is pictured here playing host to the European commissioner for science and research, Janez Potocnik (left), during a visit to the ESRF in 2007. Richard Wagner (right) is director of the neighbouring Institut Laue Langevin.

A bright vision

In 1987 Brian Fender, the vice-chancellor of Keele University (who just happened to be a former director of ILL) tempted Bill to move to England. He must have been persuasive because Keele is in the English Midlands, not the Scottish Lowlands. There he became acquainted with the pleasures and pains of the Daresbury Synchrotron Radiation Source (SRS), where he performed magnetic diffraction studies. He also learned about university management, becoming first head of school then dean of the board of natural sciences at Keele. In 1995 he moved to Liverpool University (marginally closer to Scotland), to head up the Department of Physics, before his 2001 move to become director-general of the ESRF: a return to his "home", Grenoble.

Bill has done seminal work, not only on lanthanide and actinide magnetism but also

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on the condensate fraction in liquid helium. His career achievements have been most notably recognised in the UK by the award of the Institute of Physics Glazebrook medal and prize this year.

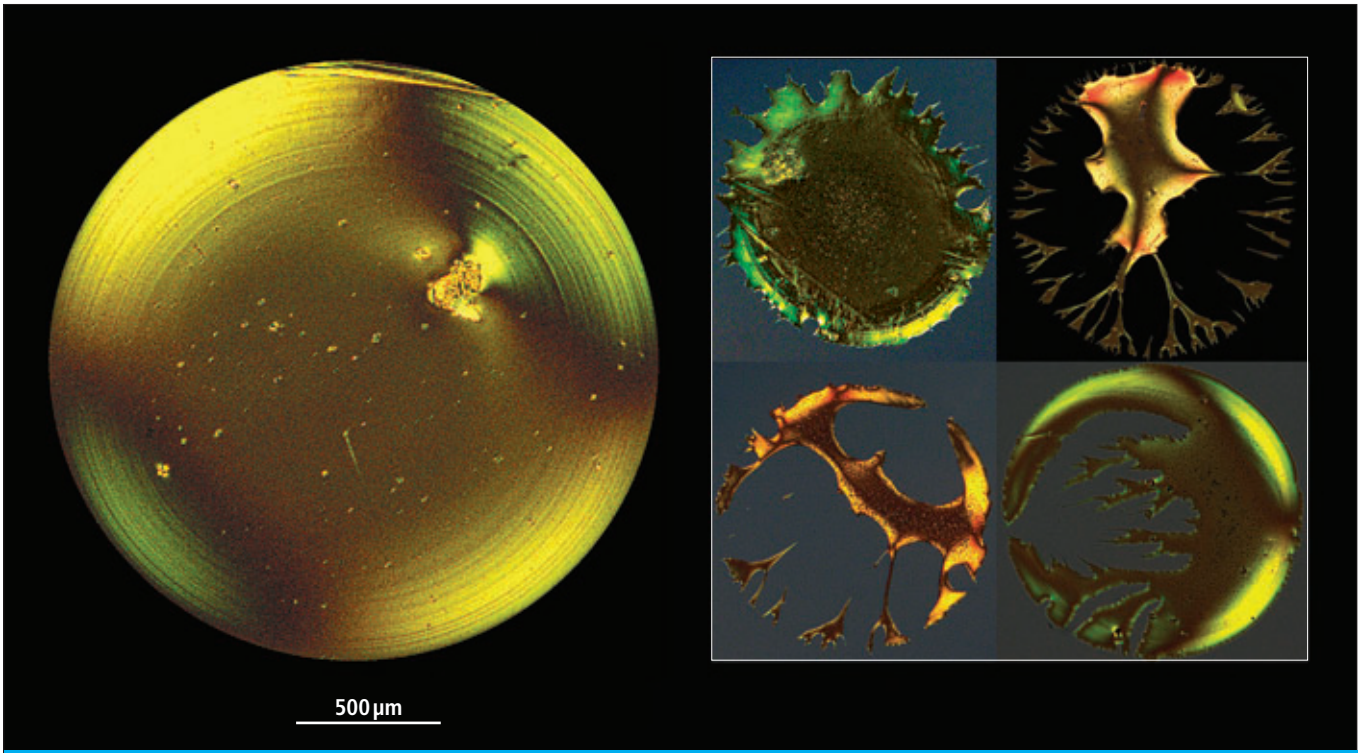
Serendipity has played its part, as far as the ESRF is concerned. In 1991, at the annual UK SRS Users' Meeting, over a glass of lukewarm white wine, he and I hatched a plot to build a materials diffraction UK Collaborative Research Group beamline at the ESRF. The rest is history: XMaS came to the ESRF, Bill became a European synchrotron scientist and frequent face around the facility, and the ESRF noticed.

"Vision" is an easily overused word, but Bill has always seen the big strategic picture while at the same time paying attention to the details and, most important, the people involved. He never forgets that organisations are composed of individuals, and that helping them to achieve their own goals is the only way to promote the success of the whole venture.

The ESRF Council chose wisely in appointing Bill director-general. The changes that he introduced, culminating with the ESRF Upgrade Programme, will ensure that the facility remains a premier synchrotron laboratory for the foreseeable future. The next generation of ESRF staff, as well as the current one, will continue to owe him a debt of gratitude.

Malcolm Cooper

S RATHGEBER



Millimetre-sized droplets of conjugated polymers on glass substrates deposited from solution.
These pictures were taken using a microscope in transmission geometry with crossed polarisers. Silke Rathgeber from the Max-Planck-Institute for Polymer Research studies the correlation between optical and structural properties of conjugated polymers in droplets because of its relevance to the technologies applied in inkjet printing. The fingered pattern seen in the four samples on the right originates from an instability occurring during the retraction of the evaporating droplet. This unwanted effect is nevertheless beautiful.

In the corridors

A journey through the digestive system of a mite

Imagine travelling through the body of a mite, starting from the mouth and exiting from the anus. Scientists from the ESRF and the University of Tübingen, Germany, have done just that, making it possible to "travel" inside the digestive system of an oribatid mite. This organism is difficult to study because of its tiny size, which is less than 1 mm. The researchers used the technique of tomography at beamline ID19 to gain an insight into the internal structure of these animals without destroying them. They have published the results (main author Michael Heethoff) in the *new Journal of Visualized Experiments* and posted a video of their work online.

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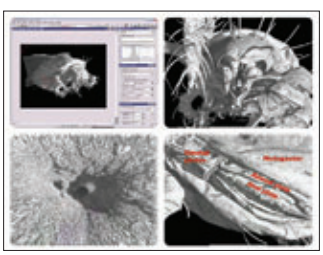

This video takes you along the full path of a mite's breakfast.

Take a ride while waiting for scans

Working late hours is routine for many users conducting experiments at the ESRF. Waiting for a scan in the middle of the night can be tedious, especially a long one, and there is a risk of falling asleep at the computer. However, as a simple search for "ESRF" on *YouTube* shows, users have found a novel remedy for sleepiness and boredom: to cycle around the ring and film it.

On a more serious note, the ESRF now has its own video channel on *YouTube*, featuring many interesting clips about the facility.

● **www.youtube.com/user/LightforScience.**

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