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Number 52 December 2009

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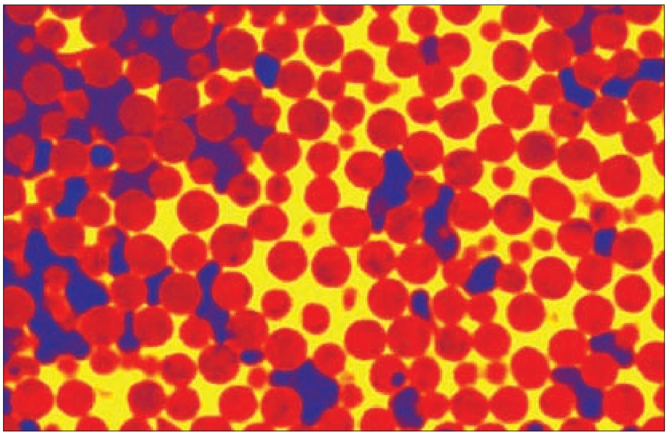

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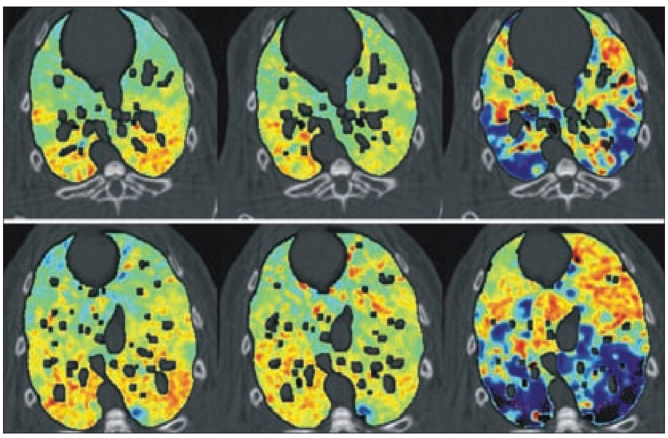

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On the cover: Many time-resolved experiments take place at the ESRF. The sand clock symbolises the idea of time.

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ESRFnews is produced for the ESRF by
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Dirac House
Temple Back
Bristol BS1 6BE, UK
Tel +44 (0)117 929 7481
www.iop.org

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ISSN 1011-9310

Experiments that improve with time

The performance of synchrotron radiation sources has been continuously rising for decades, enabling us to carry out new experiments that we could not even dream of only a few years earlier. Many experimental techniques employing synchrotron radiation such as diffraction, spectroscopy, imaging and tomography, had originally been developed as static applications. With the rapidly improving performance of the experimental stations they have all been extended into the time domain.

Time-resolved experiments are being performed at many beamlines at the ESRF, most notably at ID09TR, ID10A/C and ID24. Many other beamlines including ID02, ID06, ID11, ID15, ID18, and ID19, to name just a few, perform time-resolved experiments bridging many orders of magnitude in time from the picosecond regime (60 ps at ID09TR) to many hours. You will find, in this issue of *ESRFnews*, recent examples of time-resolved experiments performed at different ESRF beamlines in the fields of materials science (pp9, 10 and 12–13), biology (p10) and physics (p11).

Synchrotron radiation studies in the time domain has developed into a rapidly expanding field being pushed around the globe in many institutions. They are identified as one of the five key areas defining the core of the ESRF Upgrade Programme. Owing to their high average brilliance and the flexible time-structure of the source, synchrotron radiation facilities will continue to play an important role in time-resolved studies of materials. And beyond that, new horizons are opening up with the advent of free electron lasers for the soft and hard X-ray regime, which will push the limits in time resolution into the femtosecond regime.

"Time-resolved experiments are being performed at many beamlines at the ESRF"

The 2009 Nobel Prize for Chemistry recognises investigations that have led to the deciphering of one of life's core processes, i.e. how the DNA code is turned into life via ribosome translation and subsequent production of proteins. Besides controlling the chemistry in all living organisms, ribosomes provide major targets for new antibiotics. The Nobel prize has been awarded for studies of the structure and function of the ribosome to three scientists: Venkatraman Ramakrishnan, Thomas A Steitz and Ada E Yonath, who succeeded in establishing its three-dimensional structures at the atomic level and demonstrated how it functions. All three have used synchrotron X-ray crystallography to locate the hundreds of thousands of atoms that make up the ribosome. They have produced not only a static picture of the ribosome but also caught it in the act in many different stages while it performs its function.

Two of the three laureates, Ada Yonath and Venkatraman Ramakrsishnan, performed their experiments at the ESRF, among other synchrotrons. At the ESRF they made use of the unique facilities provided by the seven structural biology beamlines dedicated to macromolecular crystallography. The extreme complexity of the ribosome samples required data collection from thousands of protein crystals. It is those challenging projects that have inspired the scientists of the Structural Biology group at the ESRF to push for unique facilities and develop automation and strategies for sample evaluation. This approach will be taken to the next step and is at the heart of one of the major upgrade projects of the ESRF referred to as MASSIF: the massively automated sample selection integrated facility. The fantastic impact that the work of the Nobel laureates has accomplished by deciphering the three-dimensional structure of the ribosome is also a recognition of a facility proud to have served and contributed to a most ambitious scientific endeavour.

Serge Perez and Harald Reichert, directors of research

Macromolecular crystallography unveils protein linked to the evolution of sperm

Sperm are the only cells in our bodies that swim and speed is crucial in their objective of fertility. These cells have developed the means to be exceptionally streamlined and an international team of researchers has used the ESRF structural biology beamlines to find out how. The presence of the Bromodomain testis-specific protein (Brdt) in developing sperm directs tight repackaging of sperm DNA.

Because it is such a long and unwieldy molecule, our DNA is packaged for convenience into a complex structure called chromatin: long DNA strands are wound around proteins called histones. In sperm, however, this package has become even more compact, reducing the size of the sperm head and making it more hydrodynamic.

The nature of chromatin – how open or compact it is – is intricately regulated. Histones are marked with different chemical tags, often several per histone, that act as a code to direct changes in chromatin structure. Different proteins bind to the tags, the combination of which deciphers the code. Until now, scientists thought that these proteins bind using one or more modular "domains", with each domain docking to just one tag. However, this new study reports the discovery of an extra level of sophistication. The researchers studied histone-binding of Brdt, finding that it binds most strongly to a histone with two tags of a particular kind (in this case, acetyl groups) and, contrary to expectations, uses just one protein domain to do so.

The key experiments took place on ID23-1 and ID23-2. "We could only obtain a few small crystals of Brdt bound to a doubly tagged ligand," explains Carlo Petosa, researcher at the Institut de Biologie Structurale in Grenoble and member of the team. "What's more, the crystals initially appeared to be unusable because they were highly disordered internally. However, exposing the edges of a crystal to a grazing beam of X-rays revealed that the thinnest tips gave a well-ordered diffraction pattern. Using the microfocused beam at ID23-2, we could collect enough data from a single crystal to solve the structure."

The researchers believe that their work will shed light on potential problems in sperm development and are now looking at the role that this protein plays in human male infertility.

ISTOCKPHOTO.COM

Sperm (the only cell in our body that swims) racing to get to the egg.

Reference

J Morinière *et al.* 2009 *Nature* **461** 664–668.

Users' corner

Following the 1 September deadline, 985 proposals for ESRF beamtime allocation were received. The next deadline for submission of standard proposals will be on 1 March 2010. The next deadline for submission of long-term proposals is 15 January 2010.

The plenary session of the 20th ESRF Users' Meeting will take place on 10–11 February 2010. Two workshops and a school will be associated with the Users' Meeting:
- "Science with X-ray nano-beams" workshop;
- "Science at high pressure" workshop;
- "Getting the most from the MX beamlines" Macromolecular Crystallography School.

The plenary session of the Users' Meeting has been extended to one and a half days in order to include a wider range of scientific talks as well as a discussion session. During this session, feedback from the different parallel sessions can be exchanged and questions can be addressed to the ESRF management.

More information about the Users' Meeting can be found at www.esrf.eu/events/conferences/usersmeeting2010/users-meeting-2010-associated-workshops.

News from the beamlines

- **Shutdown of ID24 and BM29:** one of the first upgrade projects concerns the renewal of the XAS beamlines ID24 and BM29. Scheduled interventions on both beamlines will become effective during or after the next scheduling period (2010/II from March to July 2010). The current planning includes:
  - the shutdown of BM29 on 26 May 2010 for relocation to BM23. The current plan is to reopen the beamline at the beginning of 2011.
  - the shutdown of ID24 on 28 July 2010 for reconstruction on the same port. The renewed ID24 will comprise two stations, which will be commissioned in 2011. Current planning is to reopen the first branch of the renewed beamline in the second half of 2011.
- **At ID01 the *in situ* AFM and the nanodiffraction set-up were combined** allowing *in situ* coherent diffraction imaging while deforming a nano-object by the AFM-tip. The sample positioning stage was equipped with an additional piezo rotation stage to facilitate the sample alignment, in particular, for in-plane stress and strain studies of individual nanostructures. Moreover, the AFM tuning fork was mounted on a second positioning tower equipped with three piezo translation stages for x, y and z movement. All piezo stages of both the sample and the tuning fork positioning tower are now controllable by SPEC. Thus, the above-mentioned improvements facilitate the alignment of the sample and the AFM-tip with respect to the X-ray beam. It enables the accurate positioning of a pre-chosen nanostructure in the focal beam spot that can currently be as small as 300 nm.
- **A new wavelength-dispersive spectrometer is now available for the users at ID21 beamline**. The newly developed instrument can be operated for X-rays between 1.2 and 7.2 keV. Energy resolution, in the range of 10–30 eV, provides new possibilities for X-ray micro-fluorescence analysis at ID21 beamline.
- **The wiki site presenting best practices** to perform *in situ* measurement of electrical polarisation on multiferroics, announced in "Users' Corner" in the September issue of *ESRFnews*, has been moved to http://interactive.npl.co.uk/multiferroics/index.php/Main_Page.

ESRF gets good marks from study

The American Physical Society has recently completed the study "Access to Major International X-ray and Neutron Scattering Facilities", which explores how scientists' access to light and neutron sources has been evolving not only in the US but also internationally. The final report has been posted on the APS website at www.aps.org/programs/international/resources/facilities.cfm. It positions the ESRF as the leader in synchrotron facilities for the next decade.

For the study, 32 facilities and user groups across the globe completed a questionnaire on access issues and policies. The authors based their report on these data and on discussions that they had with individuals in the US and abroad. In their findings, they put many aspects of interest to light source users in Europe into a global perspective. These include different ways to access beamtime, notably the relation between Collaborating Research Groups and facility beamlines, the role of the facilities' scientists, support given to users technically and for travel and logistics, and effective availability of a facility for a user.

Ruprecht Haensel (1935–2009)

It is with great sadness that we have to report that Ruprecht Haensel passed away on 19 October after a long illness.

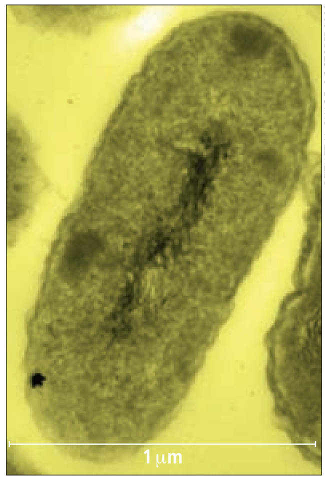
In 1986 he became the first director general at the ESRF where he stayed until the machine was running and the first beamlines were taking shape, in 1992. Haensel was the first synchrotron radiation user at DESY in Hamburg. In 1974 he became professor of physics at Kiel University, where he later became dean, and he stayed there until he retired in 2000. During this time he moved to Grenoble and became director of the Institut Laue Langevin (1985–1986).

Bacterium helps to form gold

Australian scientists have found that the bacterium *Cupriavidus metallidurans* catalyses the biomineralisation of gold by transforming toxic gold compounds to their metallic form using active cellular mechanism.

Researchers reported the presence of bacteria on gold surfaces but have never clearly elucidated their role. Now, an international team of scientists has found that there may be a biological reason for the presence of these bacteria on gold grain surfaces. "A number of years ago we discovered that the metal-resistant bacterium *C. metallidurans* occurred on gold grains from two sites in Australia. The sites are 3500 km apart, in southern New South Wales and northern Queensland, so when we found the same organism on grains from both sites we thought that we were onto something. It made us wonder why these organisms live in this particular environment. The results of this study point to their involvement in the active detoxification of gold complexes leading to formation of gold biominerals", explains Frank Reith, leader of the research and working at the University of Adelaide (Australia).

The experiments showed that *C. metallidurans* rapidly accumulates toxic gold complexes from a solution prepared in the lab. This process promotes gold toxicity, which pushes the bacterium to induce oxidative stress and metal resistance clusters as well as an as yet uncharacterised gold-specific gene cluster in order to defend its cellular integrity. This leads to active biochemically mediated reduction of gold complexes to nano-particulate, metallic gold, which may contribute to the growth of gold nuggets.



REITH ET AL, PNAS 5–9 OCTOBER 2009

A TEM image of a *C. metallidurans* ultrathin section containing a gold nanoparticle (in the middle).

For this study scientists combined synchrotron techniques at the ESRF and the Advanced Photon Source (APS), and molecular microbial techniques to understand the biomineralisation in bacteria. It is the first time that these techniques have been used in the same study, so Reith brought together a multinational team of experts in both areas for the success of the experiment.

The team was made up of scientists from the University of Adelaide, the Commonwealth Scientific and Research Organization, the University of California (US), the University of Western Ontario and the University of Saskatchewan (both Canada), Martin-Luther-Universität (Germany), University of Nebraska-Lincoln (US), SCK.CEN (Belgium), the APS (US) and the ESRF (France).

This is the first direct evidence that bacteria are actively involved in the cycling of rare and precious metals, such as gold. These results open the door to the production of biosensors: "The discovery of a gold-specific operon means that we can now start to develop gold-specific biosensors, which will help mineral explorers to find new gold deposits. To achieve this we need to further characterise the gold-specific operon on a genomic as well as proteomic level. If funding for this research is granted I believe that we can produce a functioning biosensor within 3–5 years," concludes Reith.

Reference

F Reith *et al*. 2009 *PNAS*. **doi:10.1073/pnas.0904583106.**

ESRF and SOLEIL host SRI in 2012

The two lightsources based in France, the ESRF in Grenoble and SOLEIL in Paris, will welcome the next Synchrotron Radiation and Instrumentation (SRI) meeting in 2012. The decision was announced at this year's SRI conference, which took place in Melbourne (Australia) in October.

The international committee of directors of synchrotron sources worldwide voted for the ESRF and SOLEIL because of the excellence of the scientific programme presented, the scholarships and tutorials offered to young scientists and the push for more involvement of industry and other lightsources in the event.

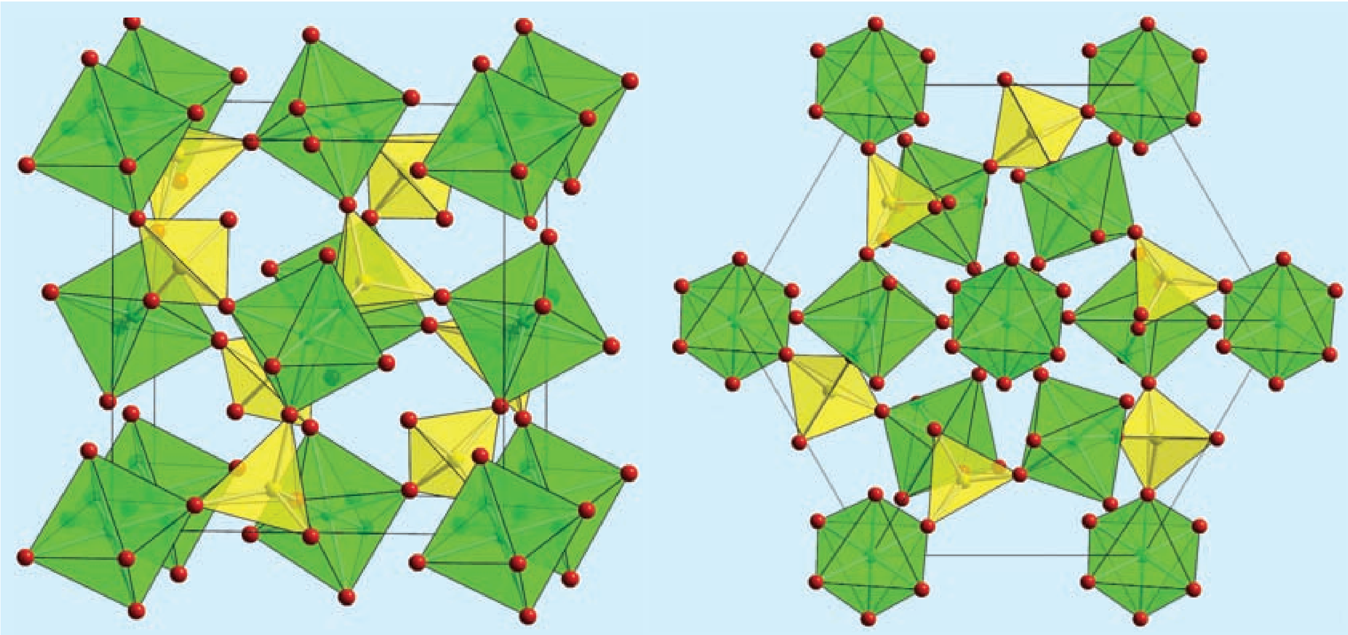
As it's a joint collaboration, the meeting will take place in Lyon, a thriving French city in the heart of Europe, one hour away from Grenoble and two hours from Paris by high-speed train.

UMR-CNRS MAP-ENSAL

View of the Lyon Convention Centre (right), the venue for SRI 2012.

Other European sources are welcome to participate at this event and some have already signed up for satellite workshops.

As well as the ESRF, the Spanish synchrotron ALBA (currently under construction) also placed a bid to hold the event. Despite not winning, the synchrotron, based in Barcelona, and due to be up and running from next year, will host a satellite workshop before or after the main conference.



Two views of $ZrMo_2O_8$ from different angles. Right: viewed from the three fold axis. ZrO_6 octahedra is shown in green, MoO_4 tetrahedra in yellow.

Scientists follow the synthesis of an NTE material as it happens

A team of European scientists and the ESRF has, for the first time, enabled the rapid synthesis of a negative thermal expansion material that was thought to be metastable, from its component oxides.

A vast majority of materials expand on heating, which can have adverse consequences on their applications. Negative thermal expansion (NTE) materials, on the other hand, contract on heating. These materials are of great interest to industry, because they can potentially counteract the expansion of another material upon heating.

For instance, glass–ceramic stoves used in many households can resist dramatic changes of temperature without cracking. The reason for this resistance is the crystalline component of thermal glass–ceramics, which has a negative coefficient of thermal expansion and contrasts with the positive coefficient of the glass. This is one example of a common use of NTE materials, but there are many others, such as dental composite fillings or substrates for high-precision optical applications.

Most NTE materials expand anisotropically, (differently in all dimensions). However, for materials with a cubic crystal structure the symmetry forces them to contract equally in all dimensions – isotropic contraction. This helps to minimise problems such as micro-cracking during repeated thermal cycling.

The most famous cubic NTE material is zirconium tungstate (ZrW_2O_8), which contracts over a temperature range of 0.3–1050 K. However, at about 450 K, it suffers a transition from an ordered structure to a disordered one, and above 0.2 GPa of pressure it becomes significantly denser and loses NTE properties. These transitions could limit the industrial uses for this material.

Researchers from Durham University (UK), the University of Kiel (Germany) and the ESRF have now found a rapid synthesis of an alternative to this well studied material.

Cubic $ZrMo_2O_8$ had been thought to be metastable at all temperatures and, unlike cubic ZrW_2O_8, it had not been possible to synthesise it directly from the constituent oxides – until now.

The researchers noticed in their lab that they might be able to form the supposedly metastable cubic phase by firing the constituent oxides at high temperatures (~1450 K) for a few seconds followed by rapid quenching. The team used the ID11 beamline to carry out *in situ* experiments to monitor the evolution of the metal oxides as they reacted at high temperatures, using the technique of powder diffraction. They benefited from the high flux and high-energy X-rays of the beamline, and the FRELON camera provided them with a unique real-time insight into the synthesis of the new material. This camera was particularly important due to the extremely short timescales over which the different phases appeared.

The reaction took place extremely quickly at elevated temperatures with $ZrMo_2O_8$ formation occurring within seconds at ~1360–1400 K. Reaction occurs via the melting of MoO_3, the formation of trigonal $ZrMo_2O_8$ and then the formation of cubic $ZrMo_2O_8$. The reaction is complete within a few seconds and the material can be quenched from the reaction conditions, where it appears to be thermodynamically stable, to room temperature.

Because the researchers discovered that this NTE material can be synthesised in this way, it means that lengthy precursor routes requiring careful thermal transformations may no longer be necessary.

John Evans, leader of the team, from Durham University, comments that "the use of extremely rapid quantitative powder diffraction at the ESRF was crucial to unravelling this chemistry and similar techniques could provide significant insight in other areas of materials synthesis".

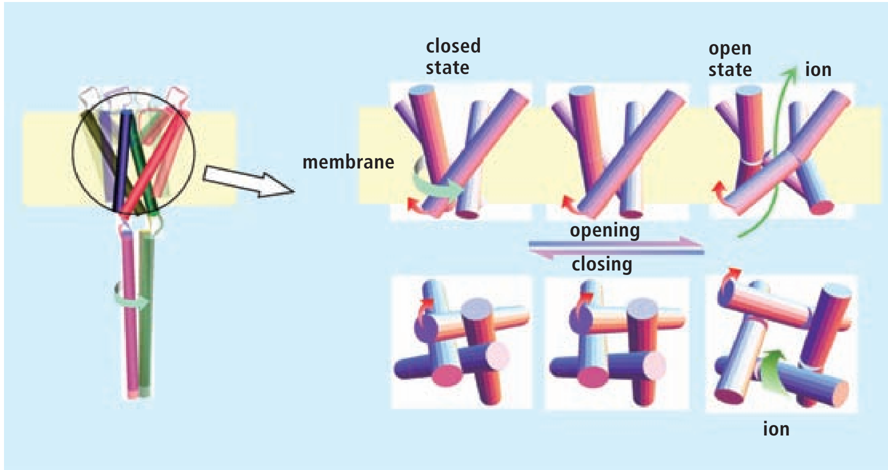
M Capellas

Reference

J E Readman *et al.* 2009 *J. Am. Chem. Soc.* **doi:10.1021/ja907648z**.

Excitement, changes, new sample: this is pump probe

In recent years, pump and probe experiments in synchrotron sources have allowed scientists to trespass boundaries that seemed unattainable a decade ago.



JOURNAL OF THE JAPANESE SOCIETY FOR SYNCHROTRON RADIATION RESEARCH

Helical architecture of the full-length KcsA channel and functional domains (left). Schematic representation of the twisting motion of the KcsA channel upon gating (right).

In some materials, ultrashort laser pulses can change the materials physical properties, turning them from magnetic to non-magnetic, or from isolating to conductor. These materials with photoactive multifunctional molecules could have applications in optical devices, including ultrafast data-storage technology. However, the mechanisms of how the flashed materials actually change at the atomic level are still not well understood.

Scientists from the University of Rennes, Tokyo Institute of Technology and the ESRF have made a step forward in understanding these materials by observing how the magnetic and optical states in molecular crystals can be controlled by light.

The reaction, which switched the material from a low-spin to a high-spin state, took place in a Fe(III) spin-crossover solid with a switching time of about 1 ps. The researchers followed the structural response by combining ultrafast optical measurements and X-ray diffraction on ID9B. They found that the sample, excited by the light, triggers a reorganisation of its structure.

The results showed that the photo switching of the sample happened in less than 1 ps, and it was followed on the nanosecond timescale by a volume expansion and on the microsecond scale by thermal switching. These results shed new light on the complex switching pathway from molecular to the macroscopic length and timescales, explains the team in a recent paper (Lorenc *et al.* 2009).

Technologically, this experiment proved how a new material can be designed with highly specific properties. In the spin-crossover system mentioned above, the high-spin state is trapped by a structural reorganisation in the bulk material. "The pump-probe instrument on ID9B is very versatile as it can probe materials properties from the atomic to the macroscopic level. The novelty is the high time resolution, from sub-nanoseconds to seconds, which adds a new and fourth dimension to material's science," explains Michael Wulff, the scientist in charge of ID9B.

The next big thing: ion channels

Even more challenging experiments will take place on the beamline soon. "Filming how ions move in and out of living cells is a new and very important development that is a spin-off of nanotechnology," says Wulff. This research refers to time-resolved studies on molecular signalling and recognition. The task of translating environmental changes into signalling pathways in our bodies belongs to ion channels in the membrane of the cell, which switch ion permeation pathways on and off (gating).

Scientists from the University of Fukui in Japan, led by Shigetoshi Oiki, are trying to monitor the activity of ion channels as they are gated chemically or electronically. For this, they will use the very intense white beam on ID9B to map out how the channel opens and closes. By attaching gold nano-particles to the channels, the movements of single channels can be measured thanks to the super intense white beam. The diffraction spots are traced in real-time with 5000 frames per second. Occasionally a white spot moves across the screen of the detector, like a falling star in the sky: it comes from a single molecular event.

This project is the follow-up of initial studies on the pH-dependent gating of KcsA channels. At neutral pH, the KcsA channel fluctuated slightly in its structure. At acidic pH, the channel exhibited twisting conformational changes. Clockwise and counter-clockwise twistings continued at the steady state, reflecting random opening and closing events (Shimizu *et al.* 2008).

The goal of the new research is to build the energy landscape for the gating conformational changes of channel proteins. Reaction processes driven by laser-activation of caged chemicals will be traced by using two dynamic diffraction methods. Recordings with high spatial and temporal resolution, and taking ensemble average of these traces will eventually enable mapping the energy landscape whether it has a smooth surface or a ragged one. This has never been attained experimentally, not only for the channel proteins but also for any other proteins.

First tests at the ESRF have shown the team that the combination of its image intensifier and its high-speed camera allows the scientists to trace the diffraction spots at 5000 frames per second, more than 100 times faster than they could previously do. This improvement was enabled through manipulating the shape and bandwidth of "white" X-rays on the beamline ID9B. The background noise was dramatically attenuated. Also, the broad spectrum of white X-rays enabled tracing of the wide range of channel motions.

The aim of the scientists is to have a better understanding of the mechanisms of ion channels and ultimately to be able to improve drugs. Currently, drugs are designed using the crystal structure of proteins. With better knowledge of the dynamics of these proteins, drug manufacturers will be able to develop new medicines keeping the proteins in their normal environment.

M Capellas

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M Lorenc *et al.* 2009 *Phys. Rev. Lett.* **103** 028301.

H Shimizu *et al.* 2008 *Cell* **132** 67–78.

Reaching high magnetic fields with time-resolved experiments

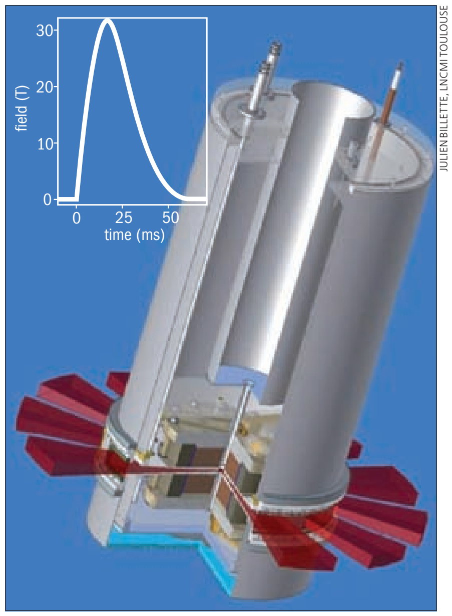
Magnetic fields affect the structural and magnetic state of matter. The use of pulsed magnets and time-resolved acquisition techniques allows scientists to combine high magnetic fields and synchrotron radiation. X-ray diffraction and spectroscopy offer new insights to the underlying physics that cannot be gained with more traditional methods.

Magnetic fields, similarly to temperature and pressure, allow tuning matter through various structural and magnetic phases with novel and exotic properties. All electrons carry a spin, therefore, in principle, all kinds of matter are potentially influenced by magnetic fields – although in many cases the interactions are weak and the critical fields are very large.

Systems studied under high magnetic fields today include the normal state of superconductors at low temperature, the spin structures of frustrated magnets or the interaction between magnetic and structural degrees of freedom. Often, scientists require very high magnetic fields to reach these phases – fields larger than what can be generated by the best available superconducting magnets. Consequently, these systems are usually studied in dedicated high magnetic field laboratories operating high-field resistive magnets. The choice of measurement techniques that these laboratories can offer is, however, limited. X-ray and neutron spectroscopy and diffraction techniques, in particular, are not available in any high-field laboratory. Therefore, the possibility to build such a facility on the ESRF and ILL site is currently under consideration. The major challenge is supplying the high currents required to generate the field and to cool the dissipated power of the order of tens of megawatts.

In the meantime, pulsed magnets are an economical and flexible intermediate step. Here the current is only supplied for a fraction of a second and the dissipated power can be cooled away between the pulses. Due to the short pulse duration, all pulsed field experiments require time-resolved acquisition techniques on the scale of 10 μs to 10 ms. Scientists at the ESRF have applied X-ray powder diffraction, X-ray magnetic circular dichroism and nuclear forward scattering in fields up to 30 T. Similar efforts are underway at Spring-8 in Japan and at the Advanced Photon Source in the US.

The first experiments at the ESRF in this domain started at BM26, which teamed up with the Laboratoire National des Champs Magnetiques Intenses in Toulouse (France) to perform the first X-ray powder diffraction experiments in pulsed magnetic fields. In their pioneering experiments the collaboration succeeded in the first direct observation of the magnetic field effect on the Jahn-Teller distortion in $TbVO_4$ (C Detlefs *et al.* 2008).



A split coil featuring panoramic access for diffraction experiments (red fans) is to be installed at ID06. Overlay: field pulse. Very high fields are reached for short times.

> **"Today, time-resolved diffraction and spectroscopy are key to accessing very high magnetic fields at synchrotron light sources"**

In parallel, ID24 has been working with the Sample Environment Support Group to develop X-ray Magnetic Circular Dichrosim (XMCD) using miniature coils. Ordered double perovskites have recently found renewed interest in view of applications for magnetoelectronic devices. In part, their desirable properties were found to be linked to a magnetostructural transition between phases that are characterised by different spin-orbit coupling. In their work on Ca_2FeReO_6 scientists from ID24 made use of the orbital sensitivity of XMCD to map for the first time the relative abundance of the two phases as a function of both temperature and field (M Sikora *et al.* 2009).

Scientists at ID18 have taken the challenge of pulsed field experiments one step further by performing the intrinsically time-resolved, photon-counting technique of nuclear forward scattering in time-varying fields. In order to extract the time-delayed signature of transitions in iron nuclei after excitation with short pulses of synchrotron light, the data was explored on two very different scales: the nanosecond scale of the nuclear decay, and the millisecond scale of magnetic field pulse. Using the iron nuclei as a probe, they were able to study the spin structures of the various field-induced phases of the frustrated triangular lattice antiferromagnet $CuFeO_2$.

The pulsed field activities evolve continuously. Researchers at ID06 have constructed a dedicated station for experiments in fields up to 30 T and at low temperatures down to 1.5 K around a unique split coil with panoramic access developed in the Laboratoire National des Champs Magnetiques Intenses. This station will be available to perform single crystal diffraction and magnetic scattering experiments in the near future.

The day that a high-field facility providing continuous field on site is a reality, pulsed fields will once more allow to push the limits further – to even higher fields.

C Strohm and C Detlefs

References

C Detlefs *et al.* 2008 *Phys. Rev. Lett.* **100**, 056405.

M Sikora *et al.* 2009 *Phys. Rev. B* **79**, 220402.

Scientists picture sli

Using time-resolved X-ray tomography, scientists want to investigate granular systems and flow in porous media, whether it is in oil extraction or in solidification of alloys.

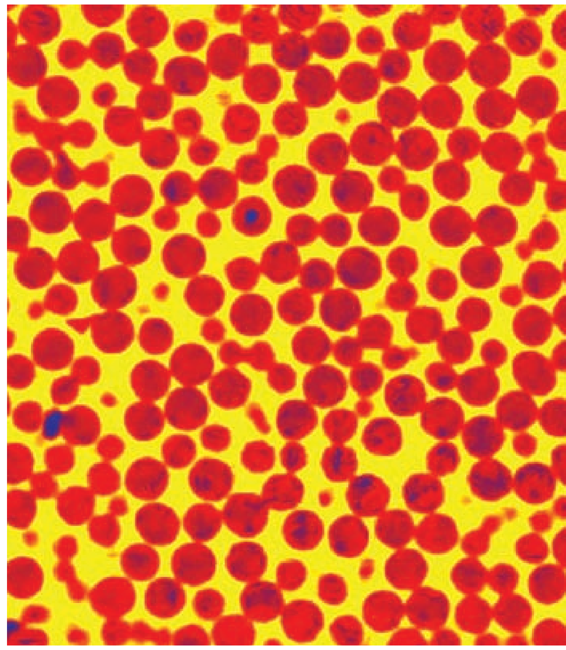


Fig. 1: these images were taken at an overall imaging time of 2
taken 600 s after injecting water. Right: taken 900 s after inje

In a petrol-dependent society such as ours, it is striking to discover that typically only 40% of the stored oil underground is actually being extracted. In order to remove oil, industries pump water into the oil wells and push the petrol laterally to the extraction area, but only a fraction of the oil makes it to the end. This situation could possibly be avoided with a better understanding of the behaviour of liquids in porous media.

With the aim of tackling this problem, an international team of scientists from the Saarland University (Germany), the Max Planck Institute for Dynamics and Self-Organization (Germany) and the University of Santa Barbara (US) has started a long-term collaboration with the ESRF. The researchers will try to overcome the challenges inherent to the experiments that try to reproduce the process of liquid flow in a porous medium. Until now, dynamic experiments on the multiphase flow could only be done for 2D model systems allowing for the required lateral and temporal resolution. However, there are no *in situ* results on 3D systems, with, for instance, columns of glass beads that copy realistic conditions.

The scientists are trying to reproduce the oil-extraction process in a set-up on the high-energy beamline ID15A. In the first tests they have managed to resolve the global shape of a driven liquid front in granular sphere packs with good lateral and time resolution. They clearly observed the formation of liquid pockets (of oil surrounded by water or the other way round) behind the liquid front. This means that some of the oil stays trapped. Another finding was that an area that might be filled with liquid will not necessarily stay filled as the liquid front propagates. This explains why oil mining is still not producing as much petrol as it could.

"The preliminary tests have been very successful and we are now ready to carry out experiments at the same typical speed as the oil-extracting process," explains Ralf Seemann, from Saarland University. "We hope to find rules to explain the behaviour of these liquids," he adds.

The team is familiar with this kind of study. Last year, its research on complex fluid structures of moist granules (in this case water and sand) on ID15, allowed them to demonstrate that grain roughness is not an important parameter in forming a bond. They first measured the distribution of liquid inside a pile of glass beads and also analysed wet sand (which behaved qualitatively identical). As liquid was added to the mixture they discovered that simple liquid bridges formed between the particles. These merged into polyhedral structures, such as trimers, tetrahedra and pentamers. Surprisingly, the mechanical stiffness, or bond, of the wet sand remained more or less constant with moisture levels ranging from less than 1% to more than 50% of the available pore space, although the internal fluid structure changed enormously. However, beyond a certain point, the sand became saturated with liquid and the granules lost their "stickiness".

Deformation of alloys in a semi-solid state

A different type of study, also involving grains, liquids and time-resolved X-ray tomography, is the research that is being carried out on the solidification of alloys. Luc Salvo and Michel Suéry, from the SIMAP Laboratory (Université de Grenoble, France), focus their research on aluminium alloys and have used ID15 and ID19 to study the mechanisms of solidification of these materials in 3D. The challenge is to understand the hot-tearing phenomenon (crack formation during solidification) in aluminium–copper alloys. This research has a great industrial impact. They have worked with a team from INSA Lyon on a specific tensile device that can be mounted on the tomograph in order to perform tensile testing during solidification. This requires extremely fast acquisition and very good temperature control.

The scientists can perform tensile experiments while the material is held at a constant temperature in the semi-solid state (above the eutectic temperature of 548 °C). The aluminium–copper alloy used is a cylinder of 2 mm in diameter and 8 mm in length, the extremities of which are inserted into alumina tubes and fixed with ceramic glue. To localise the deformation of the specimen in a region of interest where X-ray images are recorded, the cross-section of the specimen was locally reduced to about 1.5 mm in diameter. The specimen was heated by the induction coil and the temperature was controlled and monitored by using a thermocouple of 0.5 mm in diameter inserted in the tube and in close contact with the specimen. It was heated at 0.5 °C/s until 555 °C was reached (i.e. above the eutectic temperature), and then held isothermally for 3 min at this temperature to reach thermal homogenisation. The tensile test was then performed at a displacement speed of 0.1 μm/s. During the test the tensile rig and the specimen were allowed to rotate over 180° in 16 s while the heating coil itself was fixed. During this rotation, 400 transmission images of the useful zone of the specimen were recorded.

The results showed that the deformation of the material is very heterogeneous: the liquid that is present in the material accumulates in the region where strains are highest (figure 2). Pores appear rapidly and the variation of the pore volume fraction is not smooth, but exhibits few abrupt variations (figure 3). These variations can be correlated with the sudden appearance of "new" pores (coloured in red) with a significant volume. More precisely, because these pores are interconnected, the crack linking all of them propagates in a jolty, rather than a smooth motion.

"It was a big challenge to carry out this experiment since it is technically very complicated. The next challenge is to increase spatial resolution and to perform tensile experiments during solidification to be closer to hot tearing conditions," explains Salvo.

Pushing boundaries

"We have greatly improved the time resolution throughout these last years," explains Marco Di Michiel, who has been in charge of the fast tomography project at ID15. Indeed, the first time-resolved tomography sample took one hour to be characterised, so

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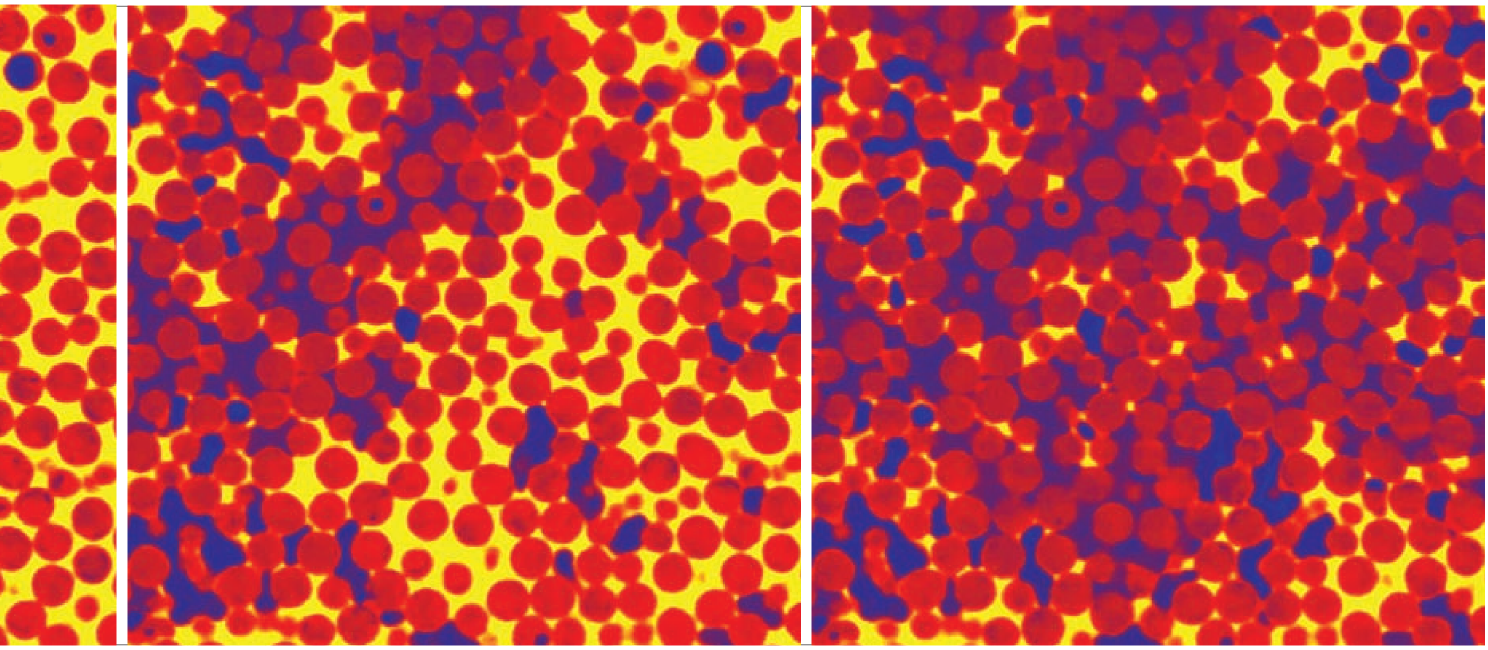
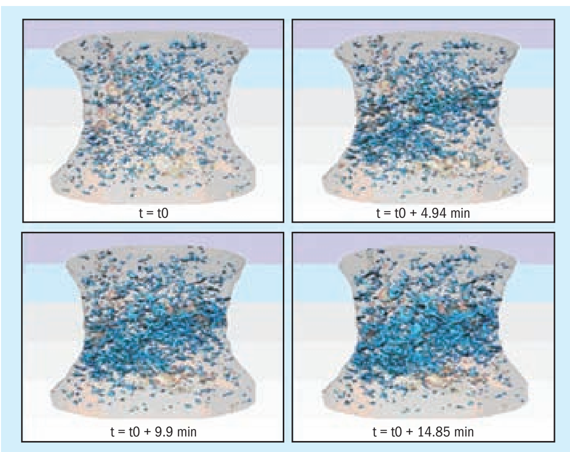


2 s per image and show 2D slices through a 3D image. Left: taken 200 s after injecting water into the oil-filled matrix (glass spheres, 355–425 μm diameter). Middle: cting the water. The colours represent glass beads (red), oil (yellow) and water that is pushed in, having different salt concentrations (different shades of blues).



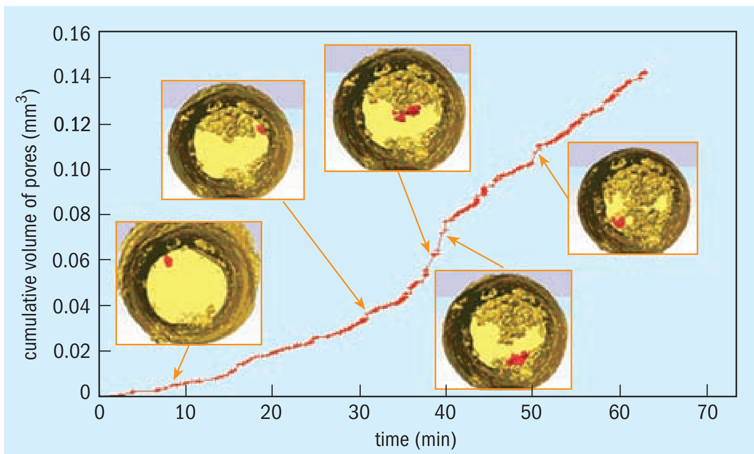


Fig. 2 (left): sequence of 3D images of the notched zone of the specimen after various times of deformation. It shows the variation of the liquid volume fraction in this zone (blue regions). Fig. 3 (right): variation with deformation time of the cumulative volume of pores in the notched zone of the specimen. It shows additional images of the pores at various times, seen from the top, with the new pore (shown in red) that is forming.

it was difficult to copy industrial processes. Scientists would merely measure the starting and final stages of the process, so "it was somehow very limited", adds Di Michiel. Things have now changed and a scan can take less than 1 s. During December a new low-noise high-speed CMOS camera will be installed at ID15. It will be possible to perform a tomographic scan in approximately 100 ms.

When asked about their decision to use the ID15A beamline at the ESRF over other synchrotron sources, Seeman reflected for a while and simply said: "speed and high energy." On the other hand, Salvo mentions that ID19 is more suitable for studies on aluminium alloys, but in the framework of a long-term project with the ESRF dedicated to *in situ* ultrafast X-ray microtomography experiments during high-temperature mechanical testing and thermal treatment of materials, some partners need high-energy beamlines such as ID15.

All in all, the ESRF offers different options for time-resolved X-ray tomography studies, each involving different kinds of samples. "It is important to highlight that without the work of the ESRF scientists and technicians, we would not be able to do these experiments today. Thanks to the long-term project we aim to push the present limitations in terms of acquisition time and spatial resolution and making all these *in situ* devices (furnaces, tensile machine etc) work on both ID15 and ID19 beamlines," concludes Salvo.

M Capellas

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Optimising the beams for time-resolved experiments

Time-resolved experiments on the beamlines require specific time-structure of the electron beam along the ring circumference. The accelerator and source division has worked throughout the years and is still working to develop a number of different filling patterns optimised to the various needs of the broad scientific community.

For the benefit of the "time-structure" user community, the ESRF has the ability to deliver a beam with a filling pattern that could vary from one week to another, and that follows a schedule that is established six months in advance. The versatility of the injector complex allows all types of filling patterns in the storage ring, from one bunch of electrons to a uniform filling of 992 bunches, with the possibility to fill any one of the 992 bunches with a specific number of electrons.

Since the start of the ESRF, filling patterns have evolved mainly following the specific requirements of the nuclear resonance scattering users, who need a pure pulsed beam at a high repetition rate and the Laue experiments on proteins, which isolate short intense X-ray pulses using a chopper. In addition to these two communities, a few other ESRF beamlines also take advantage of the time-structure filling patterns.

In the early days of the ESRF it was possible to deliver intensities of up to 20 mA in single bunch, the current is now limited to 10 mA in operation. This is due to the large number of low aperture chambers installed in the insertion device straight sections, which has increased the coupling impedance of the vacuum chamber of the storage ring. The heat load capacity of the front-end absorbers and dipole crotch absorbers set the beam current limit to 300 mA in multibunch filling mode where the current per bunch is a few tenths of a milliamp. But as the current per bunch is increased, some power is deposited locally in the vacuum chambers and in particular in the so-called RF fingers, which shield the dilatation bellows from the strong electromagnetic radiation produced by the electron beam. High voltages can develop across such fingers, followed by discharge and high local power density deposition. Therefore, this may result in the damage of the RF fingers. To avoid such damages, in 16 bunch mode, the total current is limited to 100 mA (6.25 mA per bunch).

The rms bunch length is 20 ps at low current per bunch and reaches 60 ps at 10 mA per bunch due to the interaction with the impedance of the surrounding vacuum chamber. Regarding short X-ray pulses, storage rings cannot compete with single-pass free electron lasers. Nevertheless, the high reproducibility, stability and reliability of the storage ring still makes it attractive for a number of experiments.

In addition to the specific needs of the time-structure user groups, the basic requirement of a brilliant and stable beam is a critical issue for many experiments. The stability of the beamline optics during an experiment is largely determined by the beam current decay over time. The decay rate depends greatly on the current per bunch through a process of collision of electrons inside a bunch (the Touschek effect). Consequently, the beam lifetime, which is close to 60 h with a uniform fill, is reduced to 6 h when the current per bunch reaches 10 mA. In few bunch modes with high current per bunch, the vertical emittance is voluntarily increased from 20 pm-rad up to 60 pm-rad in order to decrease the electron density in a bunch and increase the lifetime. It is worth noting that, with a proper calibration of beam position monitors, positional stability does not now depend on the filling pattern.

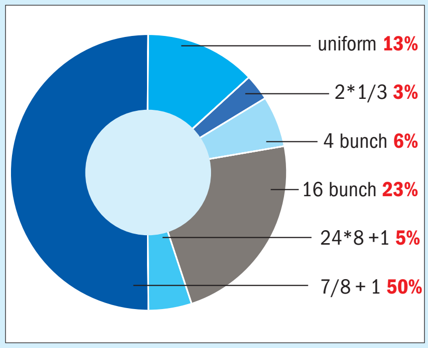
Since 2003, the implementation of refills with front ends open has greatly improved the thermal stability of the beamline optics. Thanks to the long lifetime in multibunch modes, only two short refills are performed every day. Between each refill the beam is delivered fully stable with a continuous and smooth current decay of 15% for 12 h. In contrast, the 16 bunch and 4 bunch filling modes result in a larger current variation that makes topping-up (or more frequent injection) quite attractive in time-structure modes. The high contrast ratio (better than 10^{-9}), which is needed between the filled and unfilled bunches, is obtained after a cleaning process is performed in the storage ring after each refill. This results in a temporary blow-up of the vertical beam size for a few seconds following every injection. A R&D programme is underway to reduce this perturbation and allow a more frequent injection into the ring.

J-L Revol and L Hardy

The filling patterns

The filling patterns effectively delivered to the beamline result from a fine compromise between user requirements and the tuning capabilities of the accelerator. Six filling patterns are routinely offered to the user community:

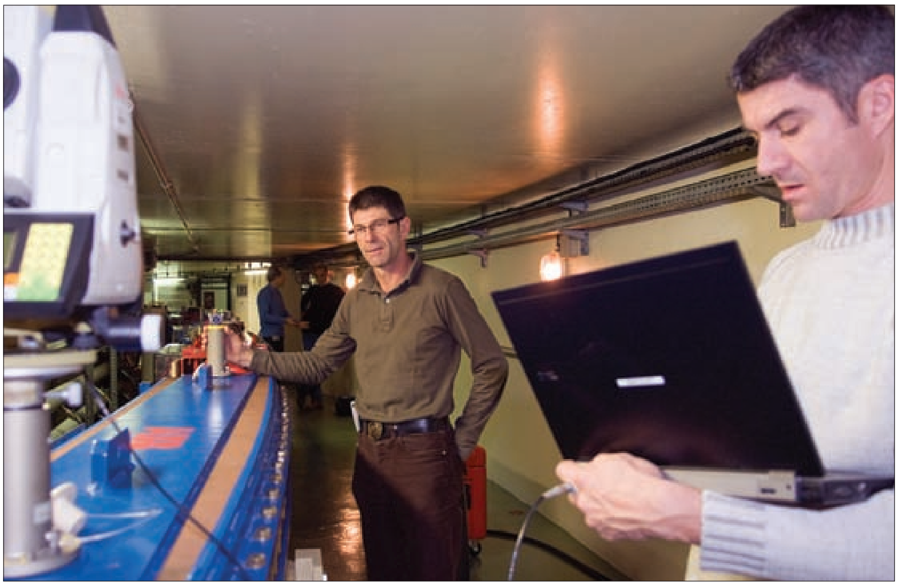
- **Uniform filling**
  200 mA, lifetime 60 h, 2 refills per day.
- **2*1/3 filling**
  200 mA, lifetime 55 h, 2 refills per day.
- **7/8+1 bunch**
  200 mA, lifetime 65 h, 2 refills per day. The simultaneous demand for time-structure studies, high intensity and long lifetime is served by a filling pattern composed of a uniform filling of 7/8 of the circumference leaving an empty gap of 1/8 in the middle of which a single bunch of 2 mA is placed. This mode, which is now the standard multibunch mode, was introduced in 2007.
- **24*8+1 bunch**
  200 mA, lifetime 30 h, 2 refills per day. This filling pattern is composed of a train of 24 groups of eight consecutive bunches with 1 mA per bunch and a single bunch of 4 mA in the gap.
- **16 equidistant bunches**
  90 mA, lifetime 12 h, 4 refills per day.
- **4 equidistant bunches**
  40 mA, lifetime 6 h, 6 refills per day.



Distribution of the various filling patterns in-time during 2009. The 7/8+1 filling mode combining high current per bunch and single bunch using in-time structured experiments is the one most in demand.

Measuring it right: the important role of calibration at the ESRF

The ALignment and GEodesy (ALGE) laboratory at the ESRF is in the process of receiving an official accreditation for the calibration of several angle-measuring instruments.



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Left: the calibration is a direct comparison between the interferometer and the instrument that is being calibrated. Christophe Lefevre (right) and Daniel Schirr-Bonnans (left), technicians in the Alignment and Geodesy group, carry out alignment measurements in the booster of the ESRF. Right: the ESRF calibration bench is 50 m long. A laser interferometer is on a concrete pillar at one end while the instrument station is on a concrete pillar at the other end. The interferometer prism and measuring reflector are on the motorised carriage that is moved along the bench.

The ESRF will obtain an official accreditation for the calibration of angle-measuring instruments, in particular high-precision robotic stations and laser trackers. This adds to the existing accreditation for the calibration of distance-measuring instruments, a service used by the ESRF and several external companies to maintain instrumentation in optimal operational condition.

In Malaysia, mapping the country is not a trivial task. The authorities impose strict rules on the Department of Survey and Mapping (JUPEM), the agency responsible for it. To get the measurements right, JUPEM needs to take its surveying instruments to a calibration laboratory to ensure traceability of its distance measurements to the definition of the metre. The lab at the ESRF, among the most accurate ones in the world, is its destination.

The ESRF calibration bench assesses the precision of measuring instruments used by governmental agencies (in the case of Malaysia) as well as industries, such as Electricité de France (EDF) or the transport company in Paris, RATP, for its topographic calculations. These companies are obliged to follow strict rules of calibration. However, this is not compulsory in many other companies around the world. Therefore it is possible that some topographic measurements are inaccurate. David Martin, head of the ALignment and GEodesy (ALGE) group at the ESRF, in charge of the calibration lab, explains that: “trying to standardise the measuring system worldwide is complicated, especially when authorities in many countries do not force companies to keep their measuring systems well calibrated.”

Since 2001, the French national accreditation body (COFRAC–COmité FRançais pour l’ACcréditation) has accredited the bench for the calibration of electronic distance-measuring instruments. Currently, calibrations can be made between 1.9 and 50 m, with an enlarged uncertainty of 0.15 mm, and from 1.9 to 113 m, with an enlarged uncertainty of 0.18 mm.

The ALGE group has studied 55 instruments and has found that about 2% of operationally employed field instruments sent to the ESRF exhibited suspicious behaviour or didn’t work correctly and consequently gave false measurements of up to several millimetres. At least, though, if you travel to Malaysia you can be sure that the maps are right.

The ALGE group’s main mission is, however, the installation, control and periodic realignment of the ESRF accelerators and experiments. Due to the conscientious work of the ALGE group it is very rare that the team finds badly aligned material in-house. “The ESRF tends to move downwards more than sideways,” explains David Martin. “This is mainly due to the geological situation of the valley and the two rivers adjacent to the ESRF.” Does the ESRF move a lot? “Not in real terms,” explains Martin. Accumulated vertical motion over the life of the ESRF has been less than 10 mm. Generally, movements are less than ±0.3 mm per year. However, with alignment tolerances in the order of microns, these movements can have significant effects on machine and beamline alignment. The quality of the calibration lab has also attracted other synchrotron sources, such as Diamond (UK) or Soleil (France), to use the services of the ALGE group for the calibration of their instruments.

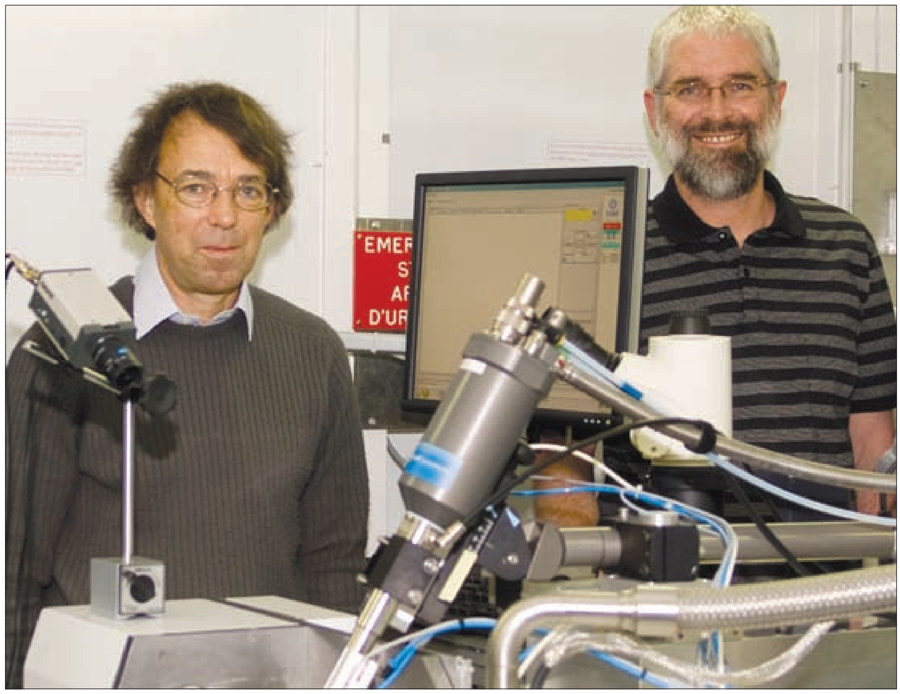
The next step is to get customers for its Horizontal Circle Comparator machine to calibrate angles. JUPEM has already expressed strong interest in this service. “Calibration of angles is particularly important in the alignment of the ESRF storage ring,” explains Martin. The storage ring is a long, narrow machine, like most accelerators, and the direction that is most sensitive to alignment errors is also the most sensitive to horizontal angle errors. This is also true for the alignment of the ESRF beamlines, particularly the new long Upgrade beamlines.

In the long-term, the goal is to improve overall alignment at the ESRF.

M Capellas

Answers to swine flu uncertainty

A year ago, not many people had heard of swine flu. Now it has entered our lives and it doesn't look like it will disappear any time soon. Rob Ruigrok, deputy director of the Unit of Virus Host Cell Interactions (UVHCI) in Grenoble, has been studying the flu virus and uses the ESRF on a regular basis. He gives some insight into this new phenomenon.



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Rob Ruigrok (right) has been studying the flu virus on ESRF beamlines such as ID23 (pictured) together with Stephen Cusack (left), director of the EMBL Grenoble outstation.

Where does swine flu come from?
All flu viruses have the same basic make-up. It is a virus originating from ducks. Ducks are infected in their intestines from drinking the water where they defecate, but they are not ill. Duck viruses can then infect chickens and pigs, where the virus can mutate and subsequently infect humans. Pigs can be ill from flu and chickens die (avian flu).

Sometimes pigs can be infected by human viruses and duck viruses at the same time. If this happens it is possible that new viruses emerge in which the bird and human virus chromosomes have been mixed up. In the case of swine flu, this is what has happened. We are now facing a human virus adapted to human cells, but with the outside aspect of a bird virus, so everyone can get it.

What is the difference from seasonal flu?
There is a general immunity in the population, called "herd immunity", against seasonal flu. This type of illness is triggered by three different viruses: influenza A virus H1N1 (existing since 1918), H3N2 (since 1968) and influenza B virus. One in every 1000 infected people die of influenza and that is still a lot. The type of virus you get is random: last winter the epidemic in Europe was mainly from the H3N2 virus and in the US it was H1N1. This new strain of H1N1 virus will infect many people because there is no general immunity.

Some differences with seasonal flu include the fact that the new one affects young people, while seasonal flu affects old people. The seasonal one affects the upper respiratory tracts, while swine flu also affects the lungs in ferrets, macaques and mice, and if it exhibits the same way in humans there may be more cases of pneumonia in healthy people, who could die as a consequence.

The number of infected people is growing relatively slowly. When is swine flu going to attack the population more virulently?
Flu is easily transmitted when environmental conditions are very dry. You get the ideal environment in winter, when it is freezing outside and houses are heated. My prediction is that once it starts freezing, flu will take off. We are just waiting and seeing what happens. So far, most of the people that have bad colds and that are tested in France are negative for this flu. However, with the extensive surveillance we have also noticed that there is seasonal flu in summer and nobody expected that. This opens up a whole new world of epidemiology that no-one knew about.

Did you see it coming?
We were expecting a pandemic sooner or later. Pandemics happen in cycles. For example, in the 20th century there were four pandemics: in 1918, 1957, 1968 and 1977. The first one of the last century was the well known Spanish flu. Apart from the very deadly human pandemic, humans also infected pigs and a new lineage of pig viruses was started. This virus remained very close to the original 1918 virus and later mixed up with chromosomes of other pig and bird viruses. This mixed-up pig virus mutated and could infect humans. Because the antigens of this H1N1 pig virus are still close to those of the human H1N1 virus circulating in 1920, people born before 1920 might still have antibodies against the H1N1 swine flu.

"If the vaccine works well and enough people get vaccinated then we won't get a pandemic"

Do we know what is going to happen?
If the vaccine works well and enough people get vaccinated then we won't get a pandemic because we'll create herd immunity. It is important to vaccinate people. If enough people get the jab, we may get a similar epidemic to that caused by seasonal flu, nothing more.

Does avian flu have anything to do with it?
Absolutely nothing, but it is still there and it is still killing people, mainly children. It could mutate anytime and become a nasty virus. No-one talks about it, but it exists as much as it existed two years ago.

Do you think that the media exaggerates?
No. All of the pandemic plans that were developed for avian flu are now being used. I really think that the campaign about washing hands or carrying a mask works and this will fall out once people are vaccinated. Before school classes started, the media were talking about it more than now. Estimates are that 350 000 people get infected every week in France. This is well below the level of an epidemic, but the figures are there.

How long could a pandemic be?
Nobody knows how long it will be.

In what way do you study flu?
We study the polymerase of influenza – the enzyme that produces new viral RNA in influenza. This polymerase is almost the same for all of the influenza A viruses. We can easily make avian versions, human versions, etc. The active sites are all the same, only the outside appearance can change. The polymerase has three subunits and we know almost the entire structure of the first subunit and about half the structure of the second one. We are trying to know more about the complete polymerase. We also want to study the polymerase as a whole with all of the subunits, which is very complicated. We have worked on it for many years, but it is difficult to make them in large quantities and it is not stable when you make them outside the human body and try to crystallize them.


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Wearing a mask can reduce the spread of flu.

How important is polymerase?
It is already very relevant today because it is a good target for new anti-influenza drugs. In 2008 Stephen Cusack, my colleague and director of the EMBL Grenoble outstation, published the structure of a part of the polymerase and he is now working with an Austrian company to try to find polymerase inhibitors that will stop virus replication.

How good is Tamiflu?
Tamiflu works nicely – also in seasonal flu – so far. It is possible, however, that the virus will mutate the active site targeted by Tamiflu and then the medicine won't work. The solution is to treat with three or four drugs at the same time, which attack three different sites. This is the way it is done with HIV patients and it works. This makes the chance of the virus mutating all of the targeted active sites at the same time very low. We can be sure that H1N1 will mutate so that Tamiflu won't work.

How can the ESRF contribute in the search for new drugs?
Crystallizing the proteins is, in theory, the most difficult part. There is so much development at the ESRF that it has all become so easy. The biology was easier than the crystallography in the past, but now the crystallography is easier. This doesn't mean it is not difficult though.

The UVHCI is located in the same building as the Partnership for Structural Biology (formed by the ESRF, ILL, EMBL and IBS) and this has been an amazing change in the way that we do science because we have so many different platforms. Crystallographers are now using Nuclear Magnetic Resonance, which would have been unheard of a few years ago. Personally, I am excited about the new developments in small scattering using X-rays and neutrons. We all want to do science and that is why the partnership works. It is really amazing that every partner invests for the benefit of the others.

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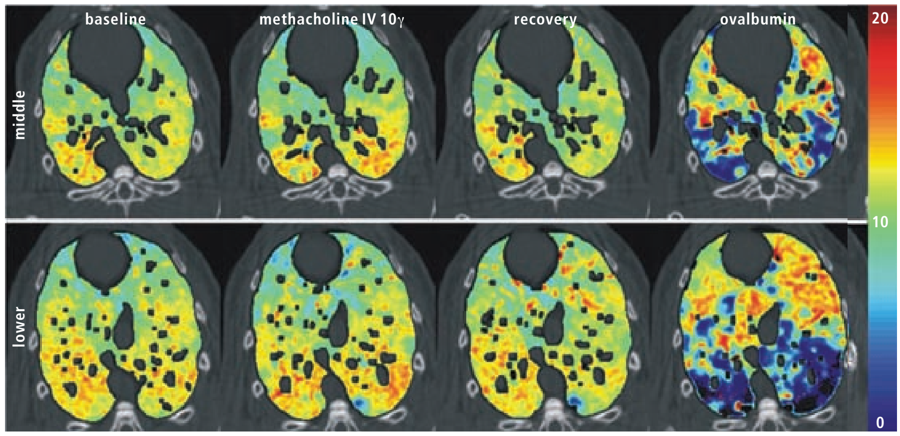
Physicians picture ventilation pattern in a model of asthma

An international team uses technology developed at the ESRF to improve its knowledge of asthma.



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Images of specific ventilation in one representative sensitised rabbit in normal conditions, during methacholine (Mch) infusion, upon recovery and after ovalbumin provocation. The colour scale goes from red (high regional ventilation) to black (no regional ventilation).

Asthma, a widespread disease in the western world, is characterised by a reversible airway narrowing that causes wheezing and breathlessness. An international team of physicians and researchers has recently used synchrotron radiation to image how this narrowing alters the pattern of ventilation inside of the lung, and what the mechanisms of these alterations could be. Better understanding of these mechanisms could improve the knowledge of how inhaled medications in asthma should be administered.

Recent imaging studies have shown that in asthma patients, the ventilation of alveoli in the lung periphery becomes very uneven. The exact mechanisms behind this heterogeneity are still not well understood, despite the importance of this phenomenon in the treatment of asthmatic individuals, where inhaled aerosols are commonly prescribed.

Most of the knowledge on lung function in asthma comes from measuring the flow of air and changes in lung volume at the mouth. Traditional measurements give little insight into what happens deep in the lung. A diagnostic feature of allergic asthma is the exaggerated reaction not only to inhaled allergens, but also to various non-specific stimuli. Physicians use the response to methacholine, a pharmacological agent that triggers constriction of the airways, to determine whether patients present the airway hyperresponsiveness that characterises asthma.

A multinational team of researchers from the University Hospital/University of Picardie, Amiens (France), the University Hospital/Department of Physics, University of Helsinki (Finland), the Geneva Children's Hospital (Switzerland), the University of Szeged (Hungary) and the ESRF used synchrotron imaging on the biomedical beamline ID17 to track regional ventilation in the lungs. For this study, the Computed Tomography dual energy subtraction technique was used.This technique, developed at the ESRF fully benefits from the characteristics of synchrotron radiation, namely high flux and monochromaticity .

The scientists imaged both lung structure and regional ventilation, with a spatial resolution sufficient to study small animals. Their aim was to determine whether the mechanism through which the airways are stimulated plays a role in the pattern of ventilation in the lung periphery. They were able to compare the ventilation pattern in the lung and the airway responses to an allergic reaction with the one produced by methacholine. To do this, they combined synchrotron imaging with a technique that measures the mechanical properties of the lung, called Low-Frequency Forced Oscillations (LFOT), which was developed by scientists in Hungary.

The researchers found that in rabbits sensitised to ovalbumin (a protein contained in egg white and used here to create an allergic reaction) the exposure to the protein caused both the constriction of large bronchi and severe patchiness in the ventilation of the lung periphery. Exposure to methacholine, however, produced a radically different pattern. It showed a prominent constriction in large airways and little, if any, heterogeneity in the peripheral lung ventilation. Surprisingly, this reaction took place despite similar changes in the overall resistance of the airways to the flow of air in both experiments.

Another unexpected finding of the study was that when the methacholine was inhaled (instead of being injected intravenously) it also caused the appearance of large patchy areas with poor ventilation. These results suggest that the route of the airway stimulation of methacholine may also play a role in the appearance of peripheral patchiness, possibly due to the uneven deposition of the inhaled aerosol particles.

"Next step is to see how aerosols reach the lungs"

The team compared the imaging results with the oscillatory lung mechanics parameters, which allow separate estimations of the mechanical properties of the airways and lung tissue. For the first time they were able to demonstrate very good correlations between the two techniques, confirming the mathematical model predictions provided by the LFOT method for many years.

The next step for the researchers is to find out how aerosol medication reaches the lung periphery during asthma attacks. In most of the cases these medicines dilate the bronchi by either acting directly on the airway smooth muscle, or by reducing inflammation and mucus secretion within the airway. Sam Bayat, physician at the Amiens University Hospital and co-author of the report, is convinced that a better knowledge would help to make more effective drugs. "In some studies, a large percentage of asthma patients haven't got good control of the disease. Perhaps if the medications could reach the peripheral lung more efficiently, patients could get better control," he says.

The ultimate goal of the researchers is to combine the quantification of the ventilation and the blood flow in the lung using synchrotron imaging. This will allow physicians to get the full picture of what goes on and where in an experimental asthma episode.

M Capellas

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ESRF users awarded 2009 Nobel prize

Ada Yonath (Weizmann Institute) and Venkatraman Ramakrishnan (MRC Laboratory of Molecular Biology) are two of the recipients of this years' Nobel Prize in Chemistry. In separate interviews they discuss how their work at the ESRF has contributed to their award.

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Ada Yonath, Weizmann Institute, Israel.

What does it mean to you to be awarded this prize?
It meant recognition of the scientific community. In the 1980s it was widely assumed that ribosome structure may never be determined, because it was clear that alongside the improvement of the ribosome crystals, ribosome crystallography required the development of innovative methodologies that didn't exist at the time. Therefore, this prize means a lot after many years of scepticism.

How has your work at the ESRF contributed to this prize?
My work at the ESRF provided many of the structures that led to the understanding of the ribosome function.

How long have you been using the ESRF for?
From the start of its existence.

How has the facility changed over the years?
It has developed tremendously. I am sincerely thankful to the ESRF because I was accepted even though it was quite clear that the experiment would not work at the beginning but I was allowed to try it again and again, and they improved the beamlines according to our needs constantly.

What do you think of the ESRF Upgrade Programme, especially in the field of structural biology?
It should be extremely useful.

How far are we from the development of antibiotics acting on the ribosome?
It is difficult to predict this, but synchrotrons sources have enabled the determination of the structures of complexes of ribosomes with antibiotics targeting it. This revealed the principles allowing for their clinical use, as well as the resistance mechanisms and it showed the bases for discriminating pathogens from hosts, hence providing valuable structural information for antibiotic improvement.

What is the next big scientific challenge in your field? How can the ESRF contribute to it?
It is certain that the ESRF will contribute significantly to all areas of structural biology, including the medicinal aspects.

What does it mean to you to be awarded this prize?
Above all it is recognition of the field of ribosomes and for the contributions of our lab towards the problems in this field. I am truly grateful for the recognition, considering that the ribosome is a field to which many groups have made important contributions.

How has your work at the ESRF contributed to this prize?
The work at the ESRF was crucial in several ways. We used the ESRF extensively to screen crystals, but also to collect the data on the first six antibiotic structures to be published, which also gave us our insight into decoding. The first of these papers was published back to back with the 30S structure in *Nature* in 2000, and the structure itself included data from the ESRF.

How long have you been using the ESRF for?
I've been using it since 1999 when I moved to England from the US.

How has the facility changed over the years?
To be honest, in 1999 when we began, it was not clear whether it would give us the type of data that we needed to solve the high-resolution structure. However, luckily for us, at about that time, a lot improved to the point where it gave us excellent data. Further improvements (more beamlines besides 14-4 for high intensity), more automation, better visualisation and use of more sophisticated goniostats such as the mini-kappa, have all been welcome advances. Especially important in recent years has been the ESRF's automatic crystal-changing robot. You cannot imagine how much easier this has made our lives, but it wouldn't be as useful without the other advances in visualisation, alignment and automation.

What do you think of the ESRF Upgrade Programme, especially in the field of structural biology?
This is excellent news. I think that increased automation and more reliable crystal handling are always good. In addition, the new generation of detectors based on the direct readout of pixels is going to improve the point–spread function, dynamic range, data-collection speed and signal to noise even further, making possible ever more difficult problems.

MRC

Venkatraman Ramakrishnan, MRC Laboratory of Molecular Biology, UK.

How far are we from the development of antibiotics acting on the ribosome?
I think that we may be reasonably close. The company Rib-X founded by Tom Steitz in New Haven, US, has used the structures to make several compounds that are in clinical trials, so I am hoping that it is only a matter of time before some useful drugs reach the market.

What is the next big scientific challenge in your field? How can the ESRF contribute to it?
Like many others in the field, I would like to work on trapping the ribosome in defined functional states to help unravel the mechanism of translation. This is quite tricky and some states, because of their intrinsic instability, may prove very difficult. We would also like to make progress towards the structures of ribosomes from other kingdoms, for example eukaryotes or mitochondria. They should be important for both biological reasons as well as for potential medical uses.

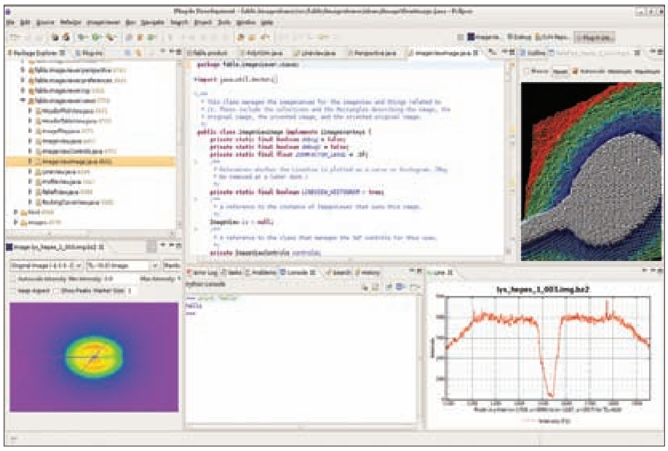
Making science software at the ESRF

ESRF software groups merge to maximise resources and to keep on top of developments.

Software is present in every aspect of the functioning of a synchrotron: whether it is in the accelerator, on the beamlines or back in the users' lab when the scientists analyse the results.

Six months ago, the three existing software groups merged into one, with the aim of "maximising resources and to be more effective at providing solutions", explains Andy Gotz, leader of the new software group. There are still three subgroups: the accelerator control group, the beamline control group and the data analysis group.

One of the main aims of the new group for the upgrade programme is to provide users with online data analysis while they are carrying out their experiment. This can help them to assess whether the experiment is working out as they had expected or not, and whether they need to make changes in its parameters. To date, there is no general solution for online data analysis that could be used in different beamlines and this is one of the challenges that the group faces. Another challenge is how to modernise the beamline control programme called SPEC. Today the group is evaluating different solutions and doing an added-value analysis.



A GOTZ

A programmer's workbench preparing a workflow for data analysis.

Another goal for the team is to keep improving the protocols and solutions that they have developed over the years. The work of the software group has already created standard solutions that are now used in different synchrotron sources. For instance, Soleil, Alba, Elettra, Max Lab and Petra III are all employing the control system toolkit and protocol called TANGO, which allows programmes running on different computers to interconnect with each other. TANGO has been around for 10 years, but ESRF developers continue to improve it with new emerging technology. The fact that it is constantly updated is the key to its success and the reason for its implementation in other sources. Both the accelerator and the beamline teams use it.

The profile of the 42 staff of the software group is very varied. "A lot of them are self-taught programmers and they don't have a computing science degree," explains Gotz. But this is not a problem because there is a constant need to learn new programming languages and techniques. Engineers, scientists and technicians all work together in a group where experience and abilities often count for more than academic curriculum does.

The work of the software group is a hidden, but a necessary element in running a scientific institution such as the ESRF. Gotz points out that, despite the fact that software development is present in many research labs, industry is pushing technology more than the labs: "Since the 1980s, research centres like CERN and the ESRF have been following the advances and standards that industry has created, whereas it used to be the other way round. This is the reason why it is important to have a solid team to keep up with new developments."

M Capellas

Movers and shakers

New Council vice-chair
Jean Moulin

Jean Moulin, general adviser of the Belgian Federal Science Policy Office, has been the new vice-chair of the ESRF Council since May. He replaces Helmut Dosch and has been in the Council since November 2002.

New Science Advisory Committee vice-chair
Keijo Hämäläinen

Keijo Hämäläinen, the chair of the Laboratory of Electronic Structures and Microtomography at the University of Helsinki (Finland), is the new vice-chair of the Science Advisory Committee (SAC) of the ESRF. Hämäläinen, a regular user of the ESRF, has been in the SAC since 2006 and was previously chairman of the Users' Organisation.

Nobel prize laureates
Venkatraman Ramakrishnan and Ada Yonath

Ada Yonath, from the Weizmann Institute (Israel), and Venkatraman Ramakrishnan, of the MRC Laboratory of Molecular Biology in Cambridge (UK), both ESRF long-term users, have been awarded the Nobel Prize in Chemistry 2009. The award was given for the study of the structure and function of the ribosome, the protein factory in the cell. They share the prize with Thomas Steitz, from Yale University (US).

Ramakrishnan and Yonath have been regular users of synchrotron sources around the world for many years, as well as the structural biology beamlines at the ESRF since the early days of the facility. Yonath is also a member of its Science Advisory Committee.

The seven structural biology beamlines at the ESRF have evolved over the years and turned into automated machines, partially thanks to feedback from Yonath and Ramakrishnan and their groups. "Their research helped to push the automation and sample evaluation methodology at the ESRF," says Sean Mc Sweeney, head of the Structural Biology group at the ESRF. "The challenge of the project that they had was so huge that it kept us thinking of new developments in order to make it fruitful," he adds. Today, the teams of both winners visit the ESRF once a month on average and they analyse around 500 samples every time.

For an interview with the laureates, see p19.

New permanent scientists

Two scientists, Mark Newton, who works on ID24, and Gema Martínez-Criado, scientist in charge of ID22, have been appointed as permanent ESRF staff. The decision was taken by the Science Advisory Committee (SAC) in May.

The SAC also decided to change Manfred Burghammer's position from beamline operation manager of ID13 to scientist in charge, also on a permanent basis.

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MAX-lab is a national facility operated jointly by the Swedish Research Council, and Lund University. We are the only laboratory of its kind in Sweden, but it belongs to a family of a dozen synchrotron radiation sources located world wide. The laboratory is a highly international forum. Nearly half of the scientists working at the laboratory are from foreign countries. The common language at the laboratory is English. The construction of the new MAX IV project will begin in 2010.

Synchrotron Radiation Based Science 2 Year Master Programme at MAX-lab

MAX-lab offers the unique opportunity to study science at a Swedish synchrotron radiation facility in a cross-disciplinary and highly international setting. Student participation in discussions is actively encouraged and an atmosphere of informality enables easy contact with leading experts. A study program is developed for each student with the guidance of the program directors. General introductory courses such as introduction to Synchrotron Radiation Science, introduction to Accelerators and Free Electron Lasers (FEL) form the base for more advanced and specialized study in areas such as Spectroscopy, Accelerators and FEL and X-ray Based Basic Research.

Study is tailored to both the scientific interest of the student and future plans in the industrial or academic arenas. Since the students studies are at the same site as the laboratory a unique combination of theoretical studies and practical work and demonstrations will be on hand.

The presence of a large number of research groups at MAX-lab facilitates the choice of suitable thesis project. Students will find teams working in a very wide range of subjects from medicine and biology to industrial applied research.

The application process will begin in December 2009, details about which can be found on the following pages:

http://www.lu.se/lund-university/master-programmes

http://www.maxlab.lu.se/maxlab/education/master/index.html

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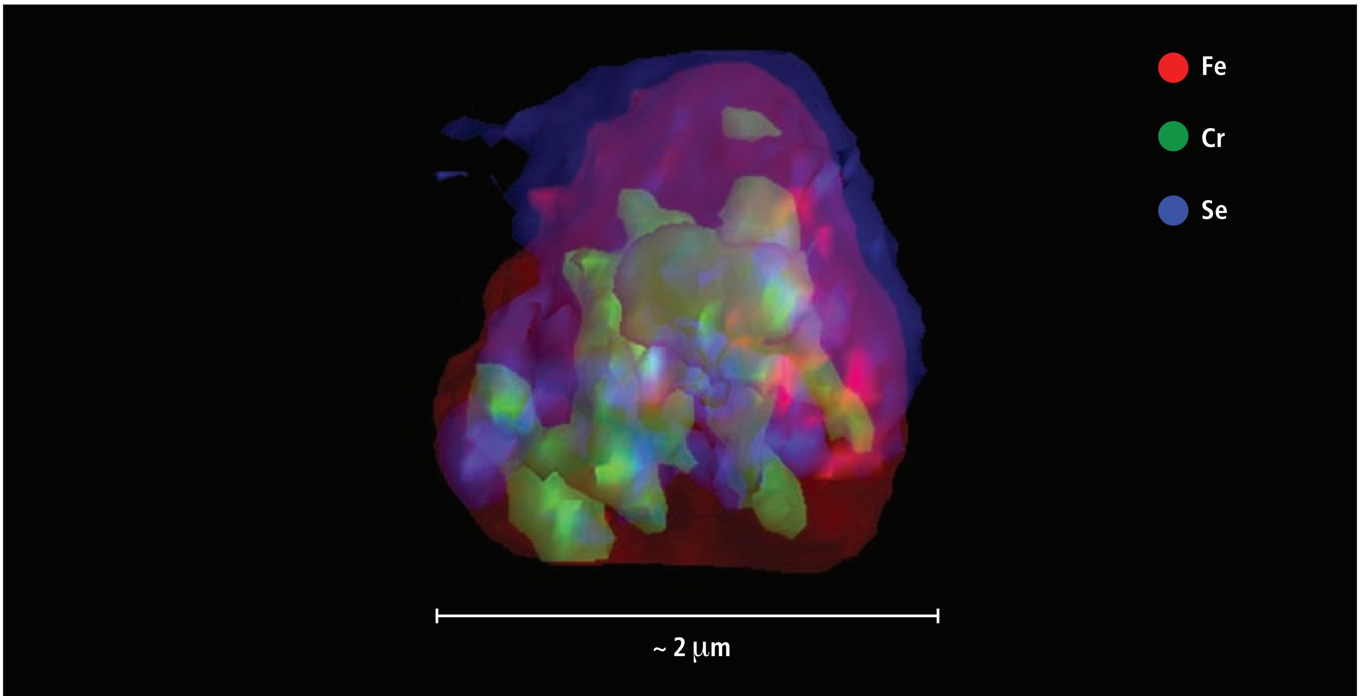


The picture shows a reconstructed comet coma particle returned by the NASA Stardust mission, with colours showing the distribution of different minor and trace elements (red: iron; green: chromium; blue: selenium). These results came out from an X-ray fluorescence tomography experiment on ID13, the microfocus beamline. This image was published in G Silversmit *et al.* 2009 "X-ray Fluorescence Nanotomography on Cometary Matter from Comet 81P/Wild2 Returned by Stardust" *Analytical Chemistry* **81** 6107–6112.

In the corridors

Small science on big machines

Scientific activity is not, per se, linked to politics. However, the latter has had an influence in the creation of several lightsources. Olof Hallonsten, from Lund University (Sweden), dedicated his thesis to this matter. The work, entitled "Small science on big machines: politics and practices of synchrotron radiation laboratories", is a study of the institutionalisation of synchrotron radiation – its scientific and technological, but also political and sociological, development.

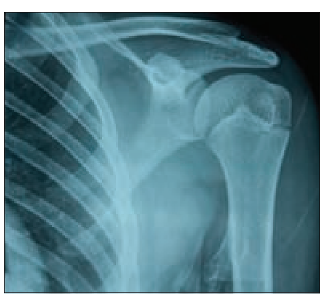
Three case studies, chosen to complement each other, highlight different aspects of this process. The Stanford Synchrotron Radiation Lightsource in Menlo Park, California, was a pioneering laboratory in the early days of synchrotron radiation. MAX-lab in Lund originated as a small-scale university project and expanded gradually to become a national and international user facility. The ESRF is portrayed as a multinational collaborative European project and one of the world's largest synchrotron radiation laboratories.

The analysis is organised around three themes: the changing dynamics of science, changes in science policy, and the identification of scientific entrepreneurs – actors with particularly strong roles in the institutionalisation of the facilities.

Reference

http://lup.lub.lu.se/luur/download?func=downloadFile&recordOId=1419054&fileOId=1419183.

X-rays voted top scientific invention



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X-rays named as best invention.

On the occasion of its centenary, the Science Museum in London (UK) asked its visitors what had made the biggest impact on the past, present and future. Out of nearly 50 000 votes, one in five people named the X-ray machine as the best invention. Ten of the most significant objects in science, engineering, technology and medicine were nominated for the vote and the outcome is:

- 1st – X-ray machines
- 2nd – Penicillin
- 3rd – DNA double helix
- 4th – Apollo 10 capsule
- 5th – V2 rocket engine
- 6th – Stephenson's rocket
- 7th – Pilot ACE computer
- 8th – Steam engine
- 9th – Model T Ford
- 10th – Electric telegraph

Reference

www.sciencemuseum.org.uk/Centenary/Home/Icons/XRay_machine.aspx.

NASA detects iron on Mercury

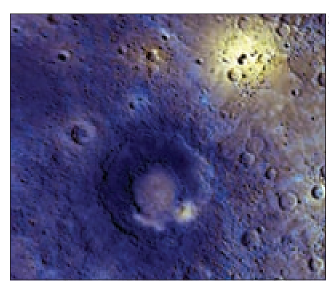
NASA Messenger spacecraft's third and final flyby of Mercury has given scientists, for the first time, an almost complete view of the planet's surface and provided them with new scientific findings about this relatively unknown world. Many new features were revealed including new information on the abundances of iron and titanium in Mercury's surface materials.

Earlier Earth and spacecraft-based observations showed that Mercury's surface has a very low concentration of iron in silicate minerals, a result that led to the view that the planet's crust is generally low in iron.

The spacecraft also spotted a region with a bright area surrounding an irregular depression, suspected to be volcanic in origin.

Reference

http://science.nasa.gov/headlines/y2009/03nov_hiddenterritory.htm.



NASA

NASA discovered that Mercury appears to have volcanic areas.

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724	± 1.125 / ± 5	EP1C4/ EPIC20	Single Ended Differential	100	40	14	0.5/4	✓ 8 ch	✓ 4 ch	✓ 4 ch	Coming Soon
720	± 1	EP1C4	Single Ended Differential	250	125	12	1.25/10	✓ 8 ch	✓ 4 ch	✓ 4 ch	Coming Soon
721	± 0.5	EP1C4	Single Ended Differential	500	250	8	2	✓ 8 ch	-	-	-
731	± 0.5	EP1C4	Single Ended Differential	500-1000	250/500	8	2-4	✓ 8-4 ch	-	-	Coming Soon
740	± 1 / ± 5	EP3C16	Single Ended	65	30	12	0.19/1.5	✓ 64 ch	✓ 32 ch	✓ 32 ch	-
751	± 0.5	EP3C16	Single Ended Differential	1000-2000	500	10	1.8-3.6	✓ 8-4 ch	✓ 4-2 ch	✓ 4-2 ch	-
742(1)	± 0.5	EP3C16	Single Ended	5000	Tbd	12	0.128	✓ 32+2 ch	✓ 16+1 ch	✓ 16+1 ch	-

(*) AMC: ADC & Memory controller FPGA. ALTERA models available: EP1C4: Cyclone (4.000 LEs), 1C20: Cyclone (20.000 LEs), EP3C16: Cyclone III (16.000 LEs).
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