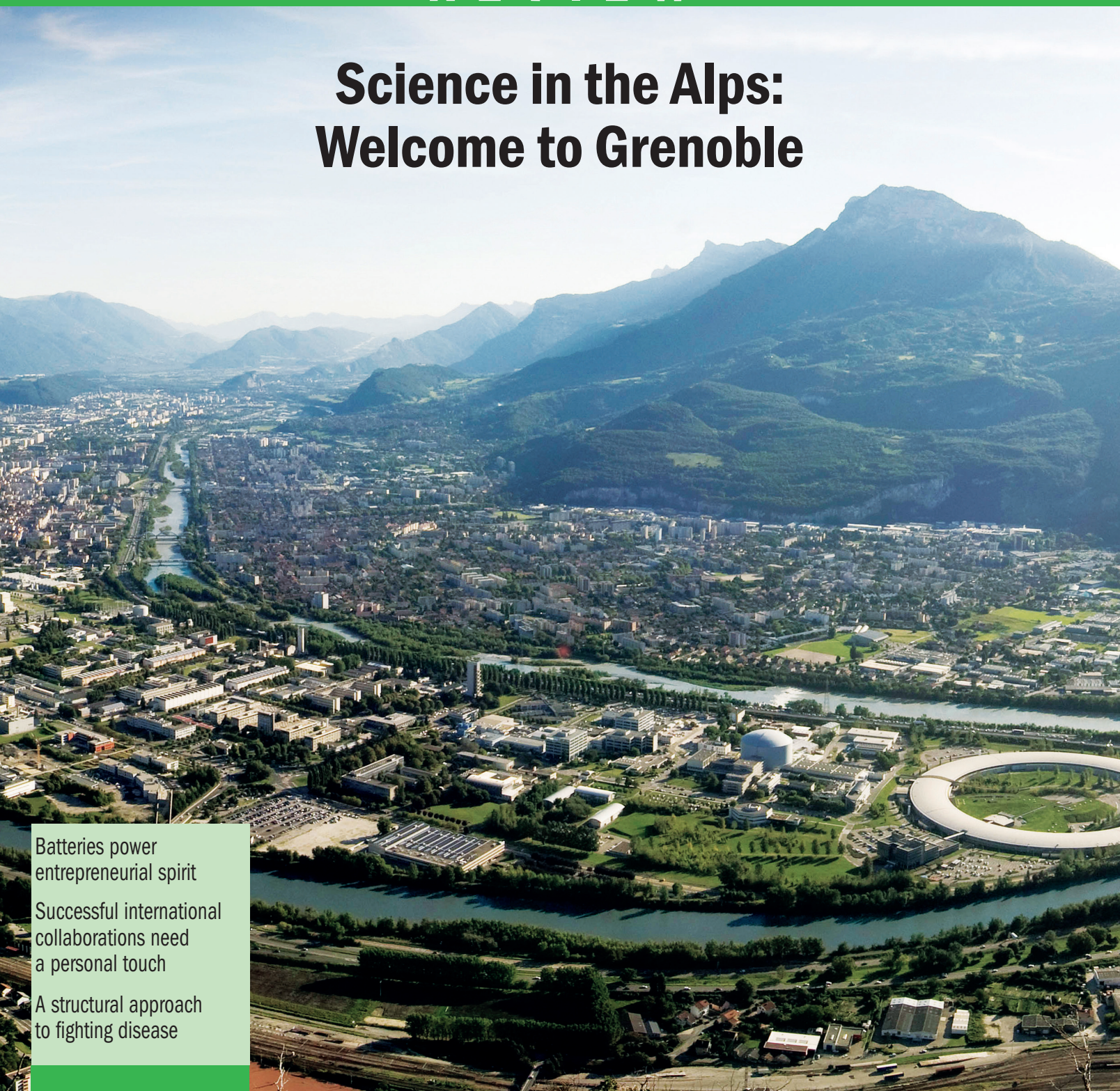
Spring 2015

GIANT REVIEW

Science in the Alps: Welcome to Grenoble



Batteries power entrepreneurial spirit

Successful international collaborations need a personal touch

A structural approach to fighting disease

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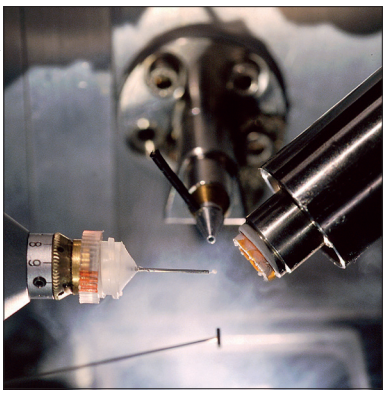

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On the cover
The French city of Grenoble is a major centre for science and innovation (Jean-Marie Francillon, Ville de Grenoble)

Editor Hamish Johnston
Production Editor Louise Nancekievill

Managing Editor Susan Curtis
Advertisement Production Mark Trimnell
Diagram Artist Alison Tovey
Art Director Andrew Giaquinto

GIANT Review Editor-in-Chief Stéphane Siebert
GIANT Review Editorial Board Emmanuelle Bensaude, Giovanna Cicognani, David Fraboulet, Anne Giraudel, Michael Krisch, Yassine Lakhnech, Vincent Mangematin and Olivier Métais

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Welcome to the GIANT Review

Nudging up close to the Alps, the French city of Grenoble has become a world-class centre for science and innovation. Now, in a bold move to drive the technological breakthroughs of the future, eight international institutions within the city have come together to form the GIANT innovation Campus. They include three top-tier academic centres – the Grenoble Ecole de Management, the University Joseph Fourier, and the Grenoble Institute of Technology – as well as major European facilities in the shape of the ESRF light source, the ILL neutron source, and the European Laboratory for Molecular Biology. Completing the picture are two major research organizations in France, the National Centre for Scientific Research (CNRS) and the Alternative Energies and Atomic Energy Commission (CEA).

This pilot issue of the *GIANT Review* offers just a brief snapshot of some of the initiatives that are already making a difference, whether in education, research, or managing innovation. And, as Mohammad Nasiruddin reminds us on p18, let's not forget that Grenoble is a fantastic place to live and work. Read on to find out why.
Hamish Johnston, Editor

Features

Strong research and industry links drive innovation in Grenoble

Rechargable-battery pioneer **Rachid Yazami** tells Hamish Johnston why Grenoble is a world-class centre for the development of new technologies

Terran Rang

Charged with innovation: Rachid Yazami, who studied at the Grenoble Institute of Technology, plays a key role in making Grenoble a leader in technology development and commercialization.

Billions of people worldwide who use mobile phones, tablets and other portable devices can thank Rachid Yazami for his crucial role in developing the rechargeable batteries that make these portable technologies possible. Yazami was born in Fez, Morocco, and studied at the Grenoble Institute of Technology (Grenoble INP), where he gained an MS in electrochemistry and a PhD for the study of graphite compounds for use in lithium batteries. It was while doing his PhD research in 1980 that Yazami invented the graphite anode, which is used in most mobile-phone batteries produced today.

After finishing his PhD, Yazami joined CNRS in Grenoble, where he is currently research director. At CNRS he continued to develop graphite anode technologies and also invented the graphite fluoride cathode electrode. This technology has been commercialized by the US-based company Contour Energy Systems, which was founded by Yazami.

Yazami spent 10 years at the California Institute of Technology (Caltech) where he co-founded a CNRS-Caltech joint laboratory to develop new materials for energy storage. He is currently a visiting professor at the School of Materials Science & Engineering of Nanyang Technological University (NTU) in Singapore, and he is also director of battery programs at NTU's Energy Research Institute. He also runs a Singapore-based company called KVI Pte Ltd, which creates new technologies for managing battery systems.

What makes the city of Grenoble unique as a centre for science and technology?

Grenoble has perhaps the highest concentration of institutions dedicated to scientific and technological education and research in the world. For many decades Grenoble has gained international recognition for the excellence in innovation of its research centres, especially in high-energy physics, electronics, computer science and biology/medicine. This unique environment supported by excellent business-management schools has stimulated entrepreneurial activity in the high-tech, high-risk and high-added-value areas. As a result, many start-up companies have chosen to locate in Grenoble, and the city's concentration of know-how has led to their rapid growth.

Grenoble offers a breadth of opportunities for those large- and small-sized companies who seek to develop cutting-edge technologies for the future

Grenoble offers a breadth of opportunities for those large- and small-sized companies who seek to develop cutting-edge technologies for the future. Only a handful of places in the world offer such a stimulating environment for high-speed growth. I would strongly advise both entrepreneurs and investors to consider Grenoble as their place of business because of its international status and its dynamism.

Why are networks such as GIANT essential for economic and scientific success?

The GIANT campus is an efficient tool linking all of Grenoble's research, education and industry institutions and companies to promote innovation and create economic wealth. It provides excellent support to those who wish to move between research and entrepreneurship within the Grenoble ecosystem. With eight prestigious Grenoble institutions under its banner, GIANT plays a major role in linking people from different backgrounds so they can share information, exchange experience, stimulate networks and promote economic development.

Why does Grenoble excel in battery research and development?

Grenoble excels in creating new battery technologies because it combines strong research cultures in both materials science and electrochemical science. Exceptional researchers in these two disciplines rarely meet in the same place at the same time and their presence in Grenoble allowed pioneering work to be done on polymer electrolytes and electrode materials.

The École Nationale Supérieure de Physique, Électronique et Matériaux and its predecessor the École Nationale Supérieure d'Électrochimie et d'Électrométallurgie de Grenoble (ENSEEG) have a long history of excellence in electrochemical science and technology, including the development of batteries.

The work on graphite-based cathode materials for rechargeable batteries started in the mid-1970s and was led by Michel Armand and Philippe Touzain. This was followed by my work on graphite anodes in the late 1970s and early 1980s, under Touzain. Then in 1996, the two research labs that led these efforts at ENSEEG merged to create the the Laboratoire d'Electrochimie et de Physicochimie des Matériaux et des Interfaces (LEPMI), which remains a leader in the development of electrochemical energy storage. Moreover, Grenoble CNRS labs and CEA-Liten have been covering a wide range of research and development activities in lithium batteries from fundamental to applied science.

I would strongly advise both entrepreneurs and investors to consider Grenoble as their place of business

What are some of the most exciting battery technologies that have been or are being developed in Grenoble?

There are more than 370 peer-reviewed scientific papers on lithium batteries alone involving Grenoble universities and labs, and this accounts for 16% of French publications in the area. CNRS labs and CEA-Liten labs are leading the efforts, especially in the electric-mobility and stationary energy-storage applications. Perhaps the most promising research area is combining new lithium-battery chemistries and fuel-cell technologies such as the lithium-air and lithium-sulphur batteries.

What is your vision of the future for science and technology in Grenoble?

Grenoble has a long tradition in innovative technologies. It has kept international excellence and competitiveness in many areas of future development. I see Grenoble as the leading European city in science and technology for the 21st century.

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Centre for biology: Grenoble is home to the Institut de Biologie Structurale, which offers state-of-the-art facilities for studying biological molecules.

GIANT scientists take a structural approach to fighting disease

To win a fight, you need to know your enemy. This is exactly what scientists at GIANT are doing, by studying the shape and role of proteins involved in deadly diseases such as malaria, HIV and influenza. **Hamish Johnston** asks experts in structural biology why they chose to work in Grenoble and looks at some of their recent successes in the fight against disease

HIV, cancer, influenza and malaria blight the lives of millions of people worldwide, and developing effective cures and treatments is the aim of many scientists working at GIANT.

Much of this research effort focuses on understanding how drug molecules bind to proteins associated with a particular disease. In some cancers, for example, the work is leading to the development of new drugs that stop mutated genes from being expressed. In the case of communicable diseases such as influenza and malaria, research at GIANT is helping pharmaceutical companies to develop drugs that stop infectious agents from reproducing within human cells.

Some of this work is done at the Grenoble Outstation of the European Molecular Biology Laboratory (EMBL), where German biologist Daniel Panne heads a group that studies the structure of proteins involved in regulating gene expression. Panne completed his PhD at the University of Basel and worked at Harvard University before joining EMBL in 2007.

Key facts

- GIANT structural biologists have world-class experimental facilities on their doorstep
- These tools help scientists understand how drug molecules bind to disease-related proteins
- Structural studies in Grenoble have led to anti-influenza compounds being developed by the pharmaceutical giant Roche
- Automated beamlines at ESRF can collect diffraction data from 240 different samples in one batch
- Scientists at ILL have made rapid advances in using neutrons to study protein structures

State-of-the-art facilities

Panne came to Grenoble because, uniquely for a structural biologist, the city offers access to sources of both X-rays (at the European Synchrotron Radiation Facility, ESRF) and neutrons (at the Institut Laue-Langevin, ILL). Also close at hand are the state-of-the-art suites for electron microscopy and nuclear magnetic resonance (NMR) at Grenoble's Institut de Biologie Structurale (IBS), which is operated in partnership with the Université Joseph Fourier (UJF) the French Alternative Energies and Atomic Energy Commission (CEA) and the

National Centre for Scientific Research (CNRS). Furthermore, the proximity of so many research institutes, universities and a teaching hospital makes GIANT a fertile ground for collaborations.

Panne is interested in how drugs – or drug fragments – bind to certain proteins involved in cancer. In a collaboration with biologist Saadi Khochbin at UJF, Panne studies a protein called p300, which plays an important role in the regulation of gene expression.

Khochbin and Panne are trying to understand p300's role in a rare cancer called NUT midline carcinoma, which is often resistant to treatment and has an average survival from diagnosis of less than one year. This cancer occurs when a mutation causes the NUT gene to fuse with another gene, causing the normally silent NUT to be expressed. Khochbin and colleagues showed that the fused NUT gene traps p300, thus preventing p300 from regulating gene expression and causing healthy cells to become cancerous.

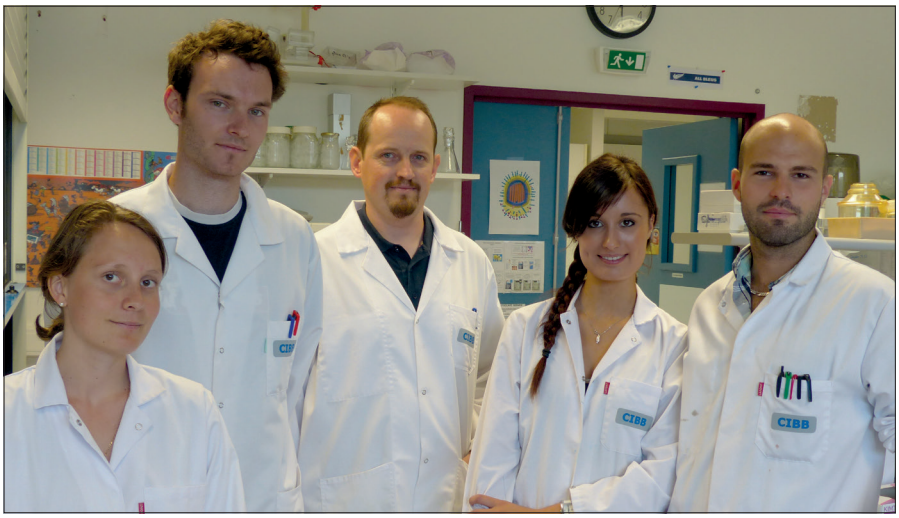
Khochbin and Panne want to know how p300 binding to NUT switches on the gene's expression. The ultimate goal is to find a drug molecule to stop p300 from binding to NUT, thus preventing the cell from becoming cancerous. This could provide a highly targeted treatment against NUT midline carcinoma and avoid the nasty side effects associated with more generic chemotherapy.

From hospital to beamline

This cancer research is a great example of what makes Grenoble unique in terms of research opportunities. While studying tumour cells from a patient at the University Hospital of Grenoble, Khochbin first discovered that p300 was trapped in foci. Then he was able to work with Panne to study the structure of p300 and understand how it interacted with NUT.

The binding of proteins is at the heart of just about every biological process, and knowing exactly how proteins and drugs bind to each other can help find better treatments. "Structural biology is founded on the principle that the structure of a particular protein is linked to its function," explains Stephen Cusack, who has been head of the EMBL in Grenoble since 1989.

Cusack is also founder and co-ordinator of a European project called FLUPHARM, which is developing drugs for treating influenza. FLUPHARM focuses on a protein complex called polymerase, which is essential for the flu virus to multiply once it enters a human cell. The original idea was to identify structural differences in polymerase that could explain why flu viruses are usually species-specific – one virus may be deadly for birds but relatively harmless for humans while another has the opposite effect.



Fighting disease: Thibaut Crépin (centre) and his team use X-rays, neutrons, electrons and NMR to study biological molecules that play an important role in a variety of diseases.

Structural biology is founded on the principle that the structure of a particular protein is intimately linked to its function
Stephen Cusack, EMBL

Using the beamlines at the ESRF, Cusack and colleagues were able to determine the structures of polymerase fragments that are essential to its function. "We showed that if you could stop these parts from working, then the polymerase was essentially dead," he explains. This discovery happened around the time of the 2009 H1N1 influenza pandemic, which in 2010 prompted the European Commission to fund a consortium of 12 research labs and drug companies across Europe – including GIANT members EMBL, CNRS and UJF, where a team of biologists led by Rob Ruigrok works on FLUPHARM.

Cusack and his FLUPHARM colleagues began looking for candidate drugs that bind to the polymerase and stop it from working. An important technique used by the team is "co-crystallization", whereby candidate drug molecules are bound to polymerase molecules and crystallized as a pair. X-ray diffraction is then used to study the contacts between the drug and the polymerase, and work out which molecules are best at blocking the polymerase.

The primary aim of FLUPHARM is to get drug candidates to the pre-clinical stage, while the Swiss drug company Roche Pharmaceuticals takes care of the drug-development aspects of the project. This is crucial, according to Cusack, because only a major pharmaceutical company like Roche has the resources to develop candidate molecules into fully fledged drugs.

Recent breakthrough

Meanwhile, Cusack and colleagues have recently managed to determine the structure of the entire polymerase complex, rather than just fragments. This new information will further fuel the development of anti-influenza drugs.

Thibaut Crépin, who works for GIANT member CNRS and is based in Rob Ruigrok's group, is also involved in FLUPHARM. Crépin completed his PhD in biochemistry at Ecole Polytechnique in Paris before coming to Grenoble to work with Stephen Cusack. Like Panne, he puts Grenoble's success at characterizing protein structures down to the access that its scientists have to ESRF and other

world-class facilities.

"If I have a crystal that needs urgent analysis, my proximity to the ESRF beamlines means I can use odd spare hours and, with luck, get things done quickly," says Crépin. If he wasn't in Grenoble it could take weeks or even months to get time at the ESRF. "So it's clear that we have an ideal position here," he says. His team also uses neutrons at ILL to look at the dynamics of proteins in solution, and studies the polymerase structure in collaboration with a group at IBS with expertise in using the institute's electron microscopes and NMR facilities.

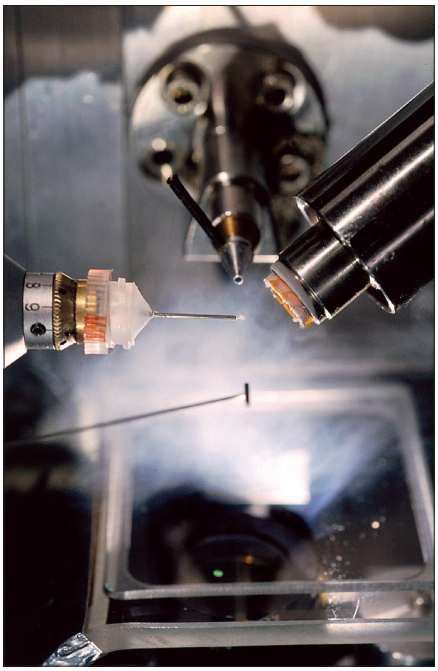
Improving antimalarial drugs

GIANT scientists are also using the might of structural biology in the fight against malaria, a disease that kills about one million people worldwide every year. The chemist Andres Palencia, who did a PhD at the University of Granada before joining Stephen Cusack's group at EMBL in 2008, has teamed up with Mohamed-Ali Hakimi of UJF and a pharmaceutical company to search for drug molecules that bind to malaria proteins, but not to the human equivalent. The ultimate goal is to boost the potency and/or selectivity of novel antimalarial compounds. However, this is no easy task because malaria and human proteins are very similar, even more so than human and bacterial proteins.

Palencia and colleagues are looking at novel compounds that are effective against malaria, but have no adverse effect on human cells. "We have found that some compounds have excellent activity, but we don't know why; that's what the structural studies will try to explain," he adds. He has also looked at similar compounds that are effective against drug-resistant bacteria. This work, which started in 2008 in collaboration with Californian company Anacor, has already yielded a novel compound now in clinical trials that represents the first antibiotic in more than 30 years to offer a truly different mechanism to kill harmful bacteria.

Better detectors, faster computers

Much of the structural work carried out by GIANT's structural biologists is performed at the ESRF, where the synchrotron's structural biology group leader is Gordon Leonard. When he first arrived at ESRF in 1996, the technique of anomalous dispersion – a technique that makes it more straightforward to solve the crystal structures of proteins using X-ray crystallography – was relatively new. At first experiments were long and complicated, and it would take months to determine the structure of a protein. Now, thanks to advances that include better detectors and faster computers, a structure can be determined in as little as 10 minutes. It is these improvements that allow scientists to study the binding of many different drug candidates, making drug-discovery projects like FLUPHARM possible.



Denis Morel/ESRF

Tiny crystal: A crystalline protein sample ready for analysis in the X-ray beam at the ESRF.

When I arrived here I realized that I was surrounded by experts. You could see there was a scientific melting pot of people and techniques; it's a great position to be in
Matthew Blakeley, ILL

Now that data collection and processing are no longer bottlenecks, Leonard and colleagues at ESRF and EMBL have created "high-throughput" automated beamlines that can handle as many as 240 samples in one batch. As well as speeding up the analysis process, these beamlines can be controlled remotely over the internet. This, according to Leonard, is particularly popular with industrial users, who will typically send 100 samples to ESRF and then make their measurements remotely.

ESRF is not the only GIANT major facility to be involved in structural biology. The neutron beams produced by ILL are an important complement to X-rays because they can map the locations of hydrogen atoms in proteins – atoms that are virtually invisible to X-rays. However, structural biologists have been slow to adopt neutron crystallography because it historically required much larger crystals than X-ray techniques – and large crystals can be extremely difficult to grow.

But this is changing thanks to Matthew Blakeley and colleagues at ILL, who have made rapid advances in neutron protein crystallography to allow the use of much smaller crystals. In 2013, Blakeley teamed up with researchers in the US and UK to show how a clinical drug used as part of HIV treatment binds to its target enzyme HIV-1 protease through hydrogen bonding. Importantly, the study revealed potential ways to improve the binding of the drug, as well as ways to improve drug resistance.

New neutron techniques

This year, Blakeley and collaborators from the UK and Germany have performed the first successful experiments to determine the structure of a cryo-trapped enzyme intermediate using neutrons. This exciting development, which was published in *Science*, provides important information towards deciphering the catalytic pathways of enzymes.

Blakeley arrived in Grenoble in 2000 as an ILL/University of Manchester PhD student and has been here ever since. "I was initially attracted to Grenoble to live in another country, learn how to speak French and to go skiing, which was a big pull for me," he explains. "When I arrived here I also realized that I was surrounded by experts. You could see there was a scientific melting pot of people and techniques; it's a great position to be in." It is this mixture of state-of-the-art structural biology infrastructure, human expertise and partnerships with pharmaceutical industries that makes GIANT a unique environment to develop tomorrow's drugs.

International collaborations benefit from a personal approach

Collaborations that cross multiple borders, languages and time zones are a mainstay of modern business and science. **Bart Chollet** of Grenoble Ecole de Management and **Emmanuelle Bensaude**, co-ordinator of a project spanning 12 organizations, share their tips for success with Hamish Johnston

If you are involved in a collaborative project today there is a very good chance that it will be international; stretching across borders, time zones, languages and customs. So how do you make sure that you and your colleagues who are spread across the world understand each other and work towards the same goal?

The person to ask is Bart Chollet, who studies cooperative projects at the Grenoble Ecole de Management (GEM) and has devoted much of his career trying to answer that very question. "International collaboration is the prevailing mode of innovation in business," he says. "Long-distance projects are widespread, but not much studied," he adds, which is why he has undertaken a controlled study of the reasons that some collaborative projects thrive and others fail.

Chollet joined forces with Leslie DeChurch of the Georgia Institute of Technology, Steve Zaccaro of the George Mason University and others to simulate collaborations between people in France and the US that lasted 6–8 weeks. Each subject kept a log of their communications with colleagues, and the researchers could also monitor the conference-call system and project-management software to see how the project was progressing. The success or failure of the collaboration was also evaluated by looking at the quality of the end product – a solution to the problem of declining fish stocks in the North Atlantic.

According to Chollet, the study revealed that subjects found it extremely difficult to remain objective about the contributions of their distant collaborators without knowing about their colleagues' professional and personal circumstances. A classic example would be a person – let's call them Alice – making an urgent e-mail request to a distant colleague, Bob. Alice doesn't know that it's a holiday in Bob's country and interprets his silence as a lack of commitment to the collaboration. Bob, on the other hand, thinks that Alice is being unreasonable by asking him to do something on his day off.

iStockphoto/Robert Churchill

Breaking the ice: A face-to-face meeting is the best way to start an international collaboration.

The trick is to start any virtual meeting with what is on the mind of each person
Bart Chollet, Grenoble Ecole de Management

Building relationships

Of course such conflicts could be avoided by better formal communication between teams, but Chollet believes that there is a more effective informal way of communicating important issues such as team-member absences. This involves building strong relationships between team members so that people understand the constraints and conditions that their colleagues are working under.

The best way to achieve this, according to Chollet, is to devote the first team meeting of the project to developing a "charter" that defines how the collaboration will be run. In the discussions that ensue, all parties should get a very good first impression of the working environments and working styles of their distant colleagues. Chollet cautions that while many think that such a meeting is "a boring waste of time", research says otherwise.

While this initial meeting is important, discussing local circumstances must be done on an ongoing basis. "The trick is to start any virtual meeting with what is on the mind of each person," he explains. In the case of Alice and Bob, for example, Bob might mention that he is rushing to finish his tasks early this week because Friday is a holiday – and in an informal way, Alice has gained important information about her colleague's work situation.

Emmanuelle Bensaude of the Grenoble Outstation of the European Molecular Biology Laboratory has first-hand experience of coordinating an international collaboration. She agrees wholeheartedly with Chollet's emphasis on initial face-to-face interaction. Bensaude is project manager of FLUPHARM, which is a pharmaceutical research and development collaboration with 12 partner organizations based in six countries across Europe. These partners include EMBL Grenoble, along with another GIANT member the Université Joseph Fourier.

Bensaude believes that it is extremely important to begin a collaboration with an in-person "kick-off" meeting that all key members attend. She says that this meeting should be informal and mostly social, which allows team members to build a rapport. She points out that while business people tend to understand the benefits of establishing personal relationships with colleagues, scientists tend to focus on facts and goals, and sometimes don't appreciate the importance of social contacts in a professional collaboration.

Meeting people

Annual in-person meetings are also very important according to Bensaude. Partner organizations should take turns hosting the annual meetings, Bensaude says, because this will ensure that all partners will feel that they are deeply involved with the collaboration. As well as providing collaborators with important insights into the working environment of the host, hosting a meeting gives an organization the opportunity to demonstrate its commitment to the collaboration by being a genial host and providing team members with good hospitality.

Indeed, she believes that the venue is an extremely important factor in the success of any meeting. "It must be comfortable and have good food," she says. "Scrimping on these things is a false economy." Bensaude adds that organizers should not be tempted to cram as much as possible into the day, but include long breaks for food and comfort. As well as easing the strain on delegates, plentiful breaks also encourage important personal interaction between group members. Indeed, an opening "icebreaker" session in which delegates play a simple game such as charades is essential to ensure that people know and are comfortable with each other.

In-person meetings are also a good time to ensure that all participants are happy with the collaboration. "Conflict is normal," Bensaude says, adding that "speaking face-to-face is a very good way of diffusing conflict".

While she believes that such face-to-face meetings should be held at least once a year, Bensaude also thinks it is important to begin remote meetings with a brief discussion of what is on collaborators' minds. This, she says, is important for maintaining an ongoing rapport within the group.

Language is often an important issue in remote collaborations, especially when members are in different countries. English is the working language of FLUPHARM and Bensaude believes that it is very important to ensure that all members are able to express their concerns regardless of their confidence in the language. If a participant is not comfortable with expressing a concern in English, Bensaude will speak to them before the meeting and then raise the issue on their behalf.

Indeed, Bensaude believes that it is essential for the collaboration co-ordinator to interact with all participants before meetings to ensure that members feel valued and encouraged to contribute during meetings.

International collaborations can also be affected by cultural differences and misunderstandings, and Bensaude has learned a few ways to mitigate problems that could arise. In scientific collaborations such as FLUPHARM, Bensaude says that the high mobility of scientists can be used to overcome this problem. If a Spanish organization is struggling to understand how things are done at a German institute, for example, there is a very good chance that there is a Spaniard at the German institute who could act as an "ambassador" between the two parties and minimize cultural misunderstandings.

So the secret to a successful remote collaboration is contact and communication. Participants should ideally first meet each other in person and should most definitely gain a good understanding of their colleagues' working styles and environments. Once a rapport is established in an initial face-to-face meeting, annual in-person meetings are needed to draw out the concerns of members. Finally, a few minutes of personal chit-chat at the beginning of a telephone or video conference can provide team members with valuable insights into how their distant colleagues work.

Tips for a successful international collaboration

- Individuals must understand the professional and personal circumstances of their distant collaborators
- The first meeting should involve the creation of a "charter" that defines how the collaboration will be run
- Annual face-to-face meetings hosted in turn by different member organizations ensures that all collaborators feel valued
- The collaboration's co-ordinator should interact with all participants before a meeting to ensure that their concerns are aired
- A few minutes of informal chit-chat before a meeting can provide valuable insights into how distant colleagues work

Conflict is normal. Speaking face-to-face is a very good way of diffusing conflict
Emmanuelle Bensaude, Grenoble Outstation of the European Molecular Biology Laboratory

Grenoble institutes rise to the challenges of big data

Organizations of all kinds generate vast quantities of data, and putting all of this information to good use is becoming a crucial challenge for businesses and researchers alike. **Hamish Johnston** speaks to "big data" experts in Grenoble to find out how they are helping organizations to get the most out of the information they generate

iStock

Processing power: Big data offers new possibilities to both business and science.

An important challenge facing many companies is how to make the move from using customer data for marketing purposes to using it for operational purposes
Renaud Cornu-Emieux, Grenoble Ecole de Management

Collecting, processing and analysing large quantities of data is no longer the preserve of government statisticians or scientists working in fields such as genomics and particle physics. Today, more and more companies around the world rely on the analysis of constant streams of data describing their operations, customers and suppliers. Within the scientific realm, technological breakthroughs in instrumentation and automation mean that researchers who previously worked with small amounts of data find themselves having to manage large amounts of information. In addition, the trend towards the open sharing of data in the sciences means that research facilities are having to archive and transfer more information than ever.

In Grenoble, the business challenges and opportunities associated with "big data" are being addressed by a new Master's degree in the subject being offered jointly by the Grenoble Ecole de Management (GEM) and the Grenoble Institute of Technology (Grenoble INP). GEM's Renaud Cornu-Emieux played an important role in creating the programme and he explains that it brings together GEM's expertise in information-technology management with the mathematics, statistics and computer science know-how of Grenoble INP.

An important challenge facing many companies at the moment, according to Cornu-Emieux, is how to "make the move from using customer data for marketing purposes to using it for operational purposes". Making this transition requires employees with the correct set of skills, but experts at Gartner point out that of the estimated 4.4 million big-data specialists needed in 2015, only about one-third of vacancies will be filled.

The programme is accredited by the Conférence des Grandes Ecoles (CGE) of France and is currently supported by 19 companies – including Oracle, IBM, Michelin and Euro Disney – that operate in a diverse range of business areas.

"Students coming from a business-school background will benefit from the technical expertise that the enginering school brings to the course," explains Cornu-Emieux, "whereas those with engineering degrees will benefit from exposure to GEM's expertise in business." He adds, "the goal is to mix engineering and business students so they can learn from each other". To ensure that all students get the most out of the course, the business students that are selected have a strong mathematics background.

An important goal of the course is to produce people that can help organizations avoid the common problems that stem from the development of big-data applications without any technical input – or when applications are developed without consulting the business side of the organization. The course currently has two modules with one focusing on the management of architectural issues surrounding big data and the other examining the value of big data. As well as looking at the technical and business challenges facing companies that use big

data, the course also considers the ethics of managing and exploiting information.

The course began in September with 12 students and Cornu-Emieux says that the goal is to get enrolment up to about 40–50 students per year. All of the current students have engineering backgrounds, but the plan is to include business students in the 2015 intake.

Pierre Jayet

Senior students at GEM: The Grenoble Ecole de Management and the Grenoble Institute of Technology have teamed-up to offer a Master's degree in big data.

Science institutes tackle big data

The amount of data that scientists have to deal with is also increasing rapidly thanks to innovations in instrumentation, automation and information-storage technologies. Two international labs in Grenoble – the Institut Laue-Langevin (ILL) and the European Synchrotron Radiation Facility (ESRF) – are at the forefront of the drive to improve how these data are acquired, analysed and shared within the scientific community.

ILL has 38 scientific instruments that use neutrons supplied by the facility's nuclear reactor. It is home to 480 staff and hosts about 2000 visiting researchers every year, and the lab provides data-archiving and data-analysis services for its users.

ILL has also had an open data policy since 2011, whereby data are normally made available to the wider scientific community three years after they are obtained. According to Jean-François Perrin, who runs ILL's computing services department, data sharing encourages scientific collaboration and also ensures that research done at ILL can be scrutinized more easily so its quality will be higher. "It is very important to allow independent scientists to try to repeat the results of data analysis of other scientists and this requires access to the raw data," he explains.

The three-year grace period ensures that the scientists who plan, build and operate experiments at ILL have the opportunity to be the first to publish their results. "If the data were to be made available immediately, our researchers would not be happy, because it could allow scientists not involved in an experiment to beat them to a discovery," explains Perrin. He believes that three years is a good middle ground between the interests of ILL users and the interests of the wider scientific community. "In general, scientists don't want others to have free access to their data, but still appreciate having access to the data of others – so it is possible to reach a compromise."

Perrin points out that storing data is nothing new at ILL and that all raw data produced by the many experiments running there have been archived since 1973. Does Perrin think this has been valuable? "Yes, for the people who have done the research," he says, but he points out that many of these data are not particularly useful to other scientists because of a lack of metadata. This is crucial information that describes how the experiment was performed, including all of the relevant parameters from the instrument. Without this metadata, the raw data becomes impossible to interpret, and so ILL's open data policy also includes the retention and provision of metadata.

In the past, experiments at ILL have not been very data intensive compared with research done at other large facilities – particularly at particle-physics labs. However, this changed dramatically in 2012 when a particle-physics experiment called EXILL began producing about 35 TByte of data per run. This was more data than had been produced in a year by all of the other instruments at ILL combined.

Then in 2014 the ILL computer team began storing and processing data from another particle-physics experiment called STEREO, which is looking for sterile neutrinos that could be produced in the reactor core. This experiment produces a whopping 10 TByte of data per month, which is further challenging Perrin and colleagues.

Dealing with these data has been a challenge for Perrin's team and required the deployment of new hardware and software systems. One issue the team had to address is that most ILL users do not have sufficient computing resources at their home institutions to analyse the raw data. Indeed, even if they did have powerful enough computers, transferring the raw data over the internet would not be practical.

ILL's computing team has solved this problem by having the researchers store and analyse the data at ILL. As a result, providing local computing facilities and support to researchers is becoming an increasing problem as quantities of data increase. "Because ILL works with researchers ranging from particle physicists to medical doctors, we have to be sensitive to the fact that different users have very different support for analysing data at their home institutes," explains Perrin. "Typically, particle physicists tend to have a high level of support, while medical doctors tend not to."

Rudolf Dimper, head of the Technical Infrastructure Division at ESRF, agrees that for many synchrotron users, the management and analysis of large amounts of data is becoming a bigger challenge: "ESRF has about 6000–7000 visiting

scientists each year, who are currently expected to take their data and leave." Some of these scientists will be working on experiments that generate 20 TByte of data in 3–4 days of running – with some instruments producing 750 high-resolution images per second. "This amount of information cannot be transferred over the internet," explains Dimper, adding "it would take weeks to download it to hard drives that would then be transported back to the visitor's institution".

While some researchers are comfortable with information processing, many scientists that use ESRF don't have the high-level IT skills required to deal with large quantities of data. "We have a mixed group of users including chemists, biologists and material scientists," he explains. "They all have different data cultures, or no data culture," he says.

"We need to help visiting scientists deal with their data," explains Dimper. "Data analysis is a major barrier for future experiments at ESRF and if we find ourselves unable to deal with it, we could hit a wall." Improved data-management systems will be a fundamental part of future upgrades to ESRF, and Dimper believes that the best solution involves leaving the raw data at ESRF, where it can be reduced and then sent via the internet to the scientist's home institute. ESRF is currently part of a European consortium of synchrotron and neutron facilities that propose to develop a platform for achieving this. "The objective of this proposal is to develop, implement and demonstrate a science-driven data reduction and analysis platform for existing and future facilities," he explains.

We have a mixed group of users including chemists, biologists and material scientists. They all have different data cultures, or no data culture
Rudolf Dimper, head of Technical Infrastructure Division at ESRF

An international approach is important because most of the visiting scientists at ESRF and ILL make use of other large facilities in Europe, or sometimes worldwide. "This means that our users want similar data-storage and analysis processes at all the facilities they use," explains Dimper. "There is a huge variation in how ESRF data are processed, which currently involves several hundred different data-analysis programs developed by our scientists. In theory we could reduce the number of programs," he says, "but in practical terms this will not happen." One possible way forward, says Dimper, is to make existing programs available to new users, which would at least cut down on duplication in the future.

In an era when a large corporation can have to deal with amounts of data comparable to those of a research laboratory, it is very important that scientists, engineers and business people all work together to develop new ways of using this information. Both the Master's degree in big data and the efforts made at ESRF and ILL to streamline, standardize and improve data processes are important steps in that direction.

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HERCULES brings students to Grenoble's scientific facilities

Grenoble is famous around the world for its major scientific facilities and the city's scientists are committed to teaching the next generation of researchers how to make best use of the cutting-edge laboratories. The *GIANT Review* speaks to scientists and students at the HERCULES school, which gives students from across Europe and beyond practical experience using Grenoble's Institut Laue-Langevin and European Synchrotron Radiation Facility

Every year thousands of scientists from around the world travel to Grenoble to use the city's two major scientific facilities: the Institut Laue-Langevin (ILL) and the European Synchrotron Radiation Facility (ESRF). These visitors come from a broad range of disciplines including physics, chemistry, materials science, biology, engineering and medicine, and they all want to get the most out of their time using these world-class facilities.

That's why nearly 25 years ago the physicist Claire Schlenker of the Grenoble Institute of Technology (Grenoble INP) and the materials scientist Jean-René Regnard of the Université Joseph Fourier (UJF) and the French Alternative Energies and Atomic Energy Commission (CEA) started the Higher European Research Course for Users of Large Experimental Systems (HERCULES) to train future users of Europe's synchrotron and neutron sources.

Today, HERCULES is still organized jointly by Grenoble INP and UJF and its main annual event is a month-long school that involves about 75 participants, 50–60 lecturers and about 100 instrument scientists that run practical sessions and tutorials. About 80% of the participants are PhD students – who get academic credit for completing the course – and the rest are postdocs.

The school gives young scientists the chance to spend four weeks in Grenoble learning about the latest neutron and synchrotron techniques, and, most importantly, gives them the chance to make real measurements using advanced instruments in both facilities. In addition, students spend a week at research facilities outside of Grenoble and currently have the choice of going to the Paul Scherrer

Serge Claisse

Hands-on experience: HERCULES students spend 40% of their time in practical sessions.

Key facts

- HERCULES is a month-long school for young researchers who use synchrotron and neutron facilities
- Participants make use of the Institut Laue-Langevin and the European Synchrotron Radiation Facility in Grenoble, as well as the Laboratoire Léon Brillouin and SOLEIL near Paris, and the Paul Scherrer Institute in Switzerland
- It began in 1990 and its annual intake of 75 postgraduates and postdocs get hands-on experience using state-of-the-art facilities
- HERCULES also runs two one-week courses per year on special topics of interest to synchrotron and neutron users
- In 2015 a special three-week course will be held in Taiwan to celebrate the 25th anniversary of HERCULES

The lectures change every year and they follow the evolution of scientific techniques. We are getting European researchers ready to use the facilities of the future
Jean-René Regnard, co-founder of HERCULES

Institute (PSI) in Switzerland – which offers both neutrons and synchrotron light – or to Saint-Aubin near Paris, which is home to the SOLEIL synchrotron run jointly by CEA and the National Centre for Scientific Research (CNRS) and nearby Saclay where the CEA's Laboratoire Léon Brillouin neutron source is located.

Students spend about 40% of their time on the course in practical sessions that make use of these world-class facilities. The hands-on nature of the programme establishes good working relationships between the next-generation users and the staff scientists who run the facilities. "HERCULES is an excellent opportunity to speak to PhD students about the benefits of neutrons, as well as X-rays, for high-resolution structural studies of macromolecules," says ILL staff scientist Matthew Blakeley. "Since the students are from all over the world, the school allows me to update a large audience on the current status and developments of neutron macromolecular crystallography to a wide audience – some of whom may decide to include the use of neutrons in their own research."

Blakeley also says that the school is popular with young scientists at ILL: "The PhD students I have supervised at the ILL have all attended the course and found it extremely useful in learning about the large array of techniques available with X-rays and neutrons."

An important goal of the school is to give participants the technical knowledge and confidence needed to use neutron and synchrotron instrumentation. Regnard explains: "Each student does up to 15 practical exercises and everybody uses neutrons and synchrotrons, and by the end of the school all participants know how to use both facilities."

Serge Claisse

Work and play: HERCULES students enjoy a day out in the mountains surrounding Grenoble.

I found taking part in HERCULES very inspiring and challenging, and I learned all sorts of techniques beyond what I was using in my PhD
Vincent Favre-Nicolin, director of HERCULES

Inspiring and challenging

That spirit is embodied in Vincent Favre-Nicolin, currently director of HERCULES and also a graduate of the school. Favre-Nicolin, who is based at the UJF and CEA, studies nanostructures using synchrotron light at ESRF. He attended the school in 1997 when he was doing his PhD. He says "I found it very inspiring and challenging, and I learned all sorts of techniques beyond what I was using in my PhD." This, he believes, proved very useful in his later career: "If I had not done HERCULES, I would not have had as many ideas for future research," he says.

Valerio Cerantola is a PhD student at the Bavarian Research Institute of Experimental Geochemistry and Geophysics (BGI) at the University of Bayreuth and is one of the latest HERCULES graduates, having attended in 2014. He joined the school to gain a better understanding of how to use ESRF in his research into the properties of matter at high pressures and high temperatures. The Italian geoscientist had been doing experiments at ESRF for several months and saw the course as an ideal way to learn more about the capabilities of the facility. "At HERCULES I used beamlines and techniques that I had never used before," he explains.

Cerantola also says that the course is set up so that participants spend a lot of time together and does a very good job of fostering a community of young researchers, adding that he still interacts with many people on his course. This is something that rings true with Favre-Nicolin, who explains: "One of the goals of HERCULES is to create a community and we know that participants stay in contact once the school has finished."

While many HERCULES students are primarily interested in using one facility, Daniel Mazzone chose to attend the 2014 school precisely because it covered both synchrotron and neutron techniques. Mazzone is doing a PhD in physics at ETH Zurich in Switzerland and he currently makes use of both techniques at PSI to study the interplay between superconductivity and magnetism in unconventional metals. He says that the practical sessions gave him a very good idea of how to use neutrons and synchrotron radiation to his advantage.

International flavour

Although HERCULES is focused primarily on educating young European researchers, it also reflects the international nature of neutron and synchrotron science by hosting some students from outside Europe. In 2010 HERCULES took this one step further to celebrate its 20th anniversary by holding its first event outside the continent at the Brazilian Synchrotron Light Laboratory (LNLS) in Campinas.

2015 marks 25 years of HERCULES and this will be celebrated with a special

three-week school in Taiwan. Called "Neutron and Synchrotron Radiation for Physics and Chemistry of Condensed Matter and Biomolecular Structure and Dynamics", the school will be held at Taiwan's National Synchrotron Radiation Research Center, southwest of Taipei.

Regnard explains that HERCULES has been co-operating with scientists in Taiwan for 12 years to bring about the international school. Indeed, Taiwan has been regularly sending six students a year to attend the HERCULES course in Europe.

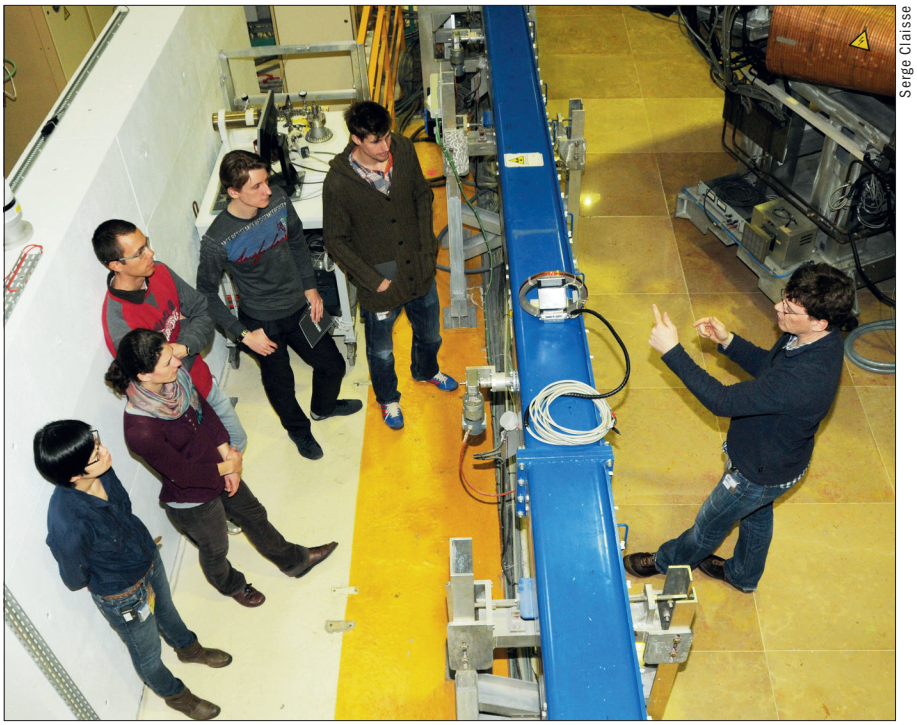
The Taiwan school is expected to attract about 50–60 students from all over the Asia-Pacific region and perhaps some from as far away as the Americas. Because there is no suitable neutron source in Taiwan, HERCULES plans to do practical exercises remotely at Australia's OPAL reactor on the outskirts of Sydney. OPAL already has a strong connection with Taiwanese scientists, who have built and now operate a spectrometer at the facility. As well as broadening the scope of the Taiwan school, the remote exercises could influence how HERCULES operates in Europe. "This will be an important test of whether remote practicals can play a role in HERCULES," says Favre-Nicolin.

Favre-Nicolin and colleagues are also planning to expand HERCULES' activities within Europe. "Encouraging the networking of participants with Europe's large facilities is an essential aspect of the course, and is supported by the European Union through several projects (CALIPSO, NMI3 and Biostruct-X)," explains Favre-Nicolin. In addition to the Saclay and PSI sessions, HERCULES is currently in discussions with several labs across Europe to see if more facilities could join in this aspect of the course.

Securing a legacy

The broad range of skills and knowledge in synchrotron and neutron physics has built up over the decades in Europe, and thanks to the efforts of the organizers and instructors on HERCULES, and the enthusiasm of its students, this legacy looks secure for the future.

HERCULES also runs specialized one-week courses in Grenoble during the spring and autumn. These cover specialized "hot topics" such as the use of neutrons and synchrotron radiation for the development of new energy technologies like solar cells, batteries and fuel cells. Other subjects covered include magnetism, genomics, and the preservation of cultural and historical objects. These courses normally have about 20 participants, and lectures, practical measurements and tutorials are run by the same number of local scientists.



Serge Claisse

School trip: HERCULES students study a neutron beamline at Institut Laue-Langevin.

HERCULES is set up so that participants spend a lot of time together and it does a very good job of fostering a community of young researchers
Valerio Cerantola, BGI/University of Bayreuth

While most HERCULES participants are PhD students and postdocs, some are from industry. To meet their needs, HERCULES has held one special course for industrial users of neutron and synchrotron facilities. Running for three days to suit the schedules of those working in industry, Favre-Nicolin says that the event was a success and that HERCULES is looking into running further industrial courses.

In addition to ensuring that young scientists develop the skills, another major aim of HERCULES is to create a network of scientists in Europe with skills in neutron and synchrotron sciences that they can pass on to others. This emphasis on the future means that HERCULES also informs its students about new synchrotron and neutron beamlines, and facilities that are currently being built. These include the European Spallation Source (ESS) neutron facility that is being built in Sweden and should welcome its first users in about 10 years.

Facilities of the future

"The lectures change every year and they follow the evolution of scientific techniques," explains Regnard. "We are getting European researchers ready to use the facilities of the future."

Thanks to HERCULES, Europe is already home to a legion of researchers who will be able to get the most out of new facilities as well as ongoing upgrades to existing facilities such as ESRF and ILL. If the enthusiasm of its directors, lecturers and students is anything to go by, the number of scientists and engineers using neutrons and synchrotron radiation to solve a wide range of problems will continue to grow and grow.

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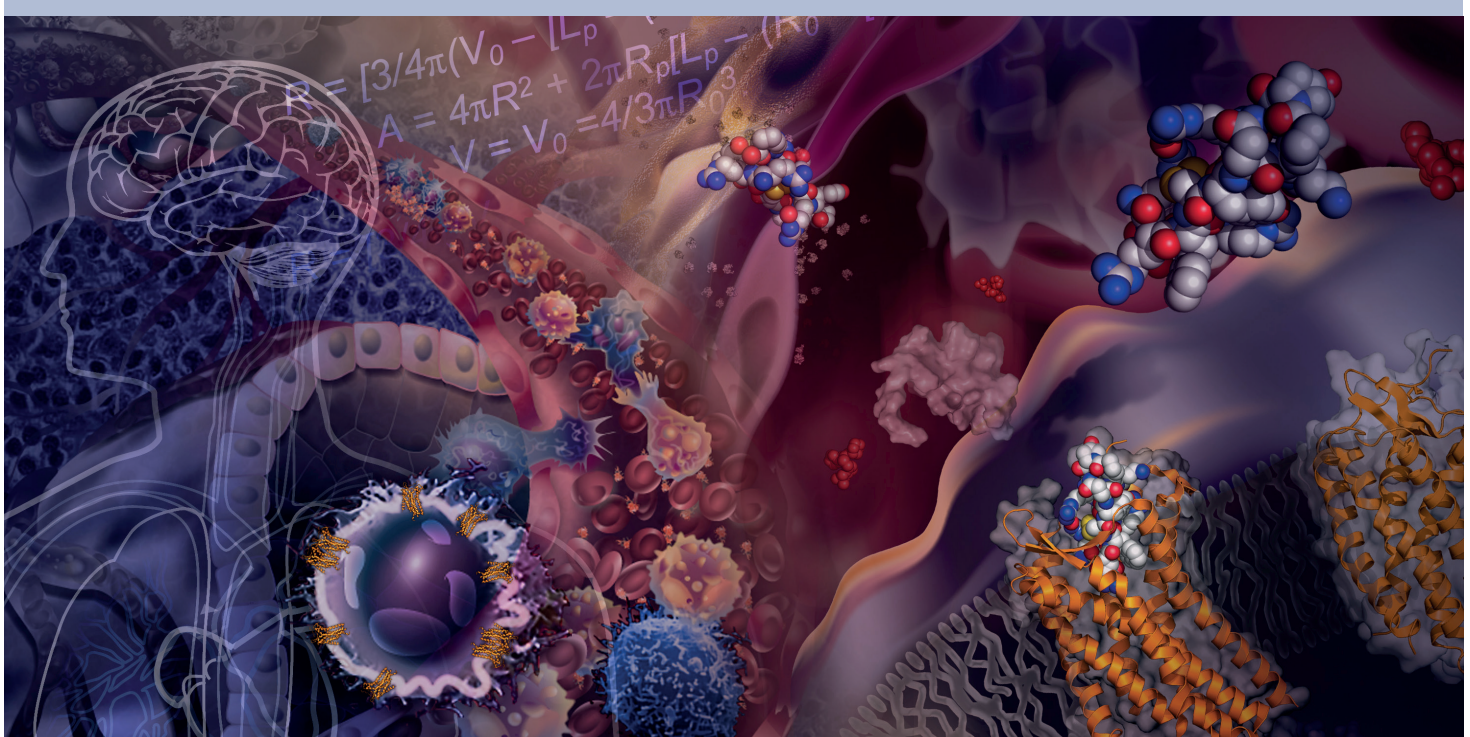

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Grenoble researchers create a solid solution for energy storage

New battery technologies for electric vehicles and power grids are emerging from award-winning research in Grenoble

The lithium-ion batteries used in mobile phones pack large amounts of energy into small and lightweight packages and should be ideal for use in electric vehicles and other energy-intensive applications. However, there are significant challenges that must be overcome before low-cost and safe lithium-ion batteries can be mass-produced for these applications.

Batteries for electric vehicles must be able to store about 30,000 times the amount of energy contained within a mobile-phone battery. Applications for storing excess energy in an electricity grid need capacities equivalent to millions of mobile phones. Developing large batteries for such applications is an important goal of a research team in Grenoble led by Renaud Bouchet, who is Professor of Electrochemistry and Materials Science at the Grenoble Institute of Technology (Grenoble INP) and researcher at the Laboratory of Electrochemistry, Physics and Chemistry of Materials (LEPMI.)

Bouchet won the 2014 EDF Pulse Science and Electricity Award for developing a new family of electrolytes for lithium-ion batteries that should be able to store large amounts of energy. The €150,000 grant will help Bouchet's team to develop the "lithium metal polymer" battery, which Bouchet describes as "a real breakthrough in terms of safety, cost and improved energy density".

A standard mobile phone battery contains a liquid electrolyte that is flammable. This is not a problem for smaller batteries, however, liquid electrolytes become a safety issue for larger batteries that are used in vehicles and grid storage. All batteries will heat up when used. While this heat flows easily out of small batteries, it is more difficult to remove heat from larger batteries. The build-up of heat can cause a runaway effect in the battery, which further boosts the temperature of the device and can ultimately result in a fire.

On solid ground: Renaud Bouchet describes the lithium metal polymer battery as "a real breakthrough in terms of safety, cost and improved energy density".

Bouchet and colleagues have developed a solid polymer electrolyte that does not burn and is also good at conducting lithium ions – which is the primary role of the electrolyte. The team took a "block co-polymer" approach whereby the solid electrolyte comprises a regular structure of two components (or blocks), one having the desired ion conductivity while the other is resistant to heat.

While very high temperatures can cause problems in lithium-ion batteries, polymer electrolytes still need to be operated at slightly elevated temperatures. Bouchet and colleagues have already managed to use the block co-polymer approach to create a polymer electrolyte that functions at 60 °C, which is 20° cooler than other polymer electrolytes. He believes that the operating temperature can be further reduced to 40 °C. Another important feature of the team's battery technology is that it uses a pure lithium electrode, resulting in a large boost in the energy density of the device.

The polymer electrolyte is also very good at suppressing "dendritic growth" on the electrodes. These are hair-like structures that shorten the lifetime of the battery. "Our electrolyte should be able to stand more than 1000 charge and discharge cycles," says Bouchet, which is on par with conventional batteries.

Bouchet's team is working with the French battery maker Blue Solutions to develop solid electrolytes for electric vehicles. Today, 10% of the cost of a vehicle battery is the safety system that prevents the battery from discharging too quickly and catching fire. When safer batteries based on polymer electrodes become available, Bouchet says that safety costs will drop significantly. Furthermore, manufacturing costs – which account for 20% of the price of a battery – will be cheaper. Much of the morphological analysis of the polymer is done using the European Synchrotron Radiation Facility (ESRF) in Grenoble.

Bouchet is currently putting together a laboratory that can investigate all of the steps in the chain from characterizing materials to evaluating functioning batteries. This new chapter in the long history of energy-storage innovation in Grenoble will keep the city at the forefront of developing batteries for large-scale energy storage.

More power to battery research

- Key to improving battery performance is understanding how lithium ions move through the electrodes, and neutron diffraction techniques available at the Institue Laue-Langevin offer researchers a great way to "see" what's happening inside the electrode materials.
- The Laboratory for Innovation in New Energy Technologies and Nanomaterials (LITEN), part of the CEA, is developing battery technologies ranging from new chemical formulations to complete energy-storage systems. The aim is to enhance performance and safety while also reducing cost, working with automotive and battery manufacturers to ensure an efficient transfer to industry.

River walks, mountain hikes and a passion for language processing

Computer science PhD student **Mohammad Nasiruddin** tells Hamish Johnston about life in Grenoble

Mohammad Nasiruddin is a second-year PhD student at Grenoble's Université Joseph Fourier. He is completing his thesis on natural language processing in the Study Group for Machine Translation and Automated Processing of Languages and Speech (GETALP) at the university's Laboratory of Informatics of Grenoble. As well as working on his PhD, Nasiruddin is also involved in GIANT's Junior Scientist and Industry Annual Meeting (JSIam) and the GIANT Student Network.

Nasiruddin grew up in Narayanganj, a city in Bangladesh near the capital city Dhaka. He studied computer science in Dhaka, where he became interested in developing speech-recognition technologies for Bangla, which is spoken by more than 200 million people.

Alexandrine Sadoul/CEA

Talking the talk: Mohammad Nasiruddin is a PhD student in Grenoble, researching natural language processing.

What first brought you to Grenoble?

The city has a large community of foreign students and foreign researchers, so as someone from Bangladesh it looked like a welcoming place to do my PhD. Grenoble is internationally renowned for the excellence of its scientific research, and many R&D labs of international companies are located in the city. There are good collaborative relations between the academic, research and business communities here.

What do you like most about the city?

There are three mountain ranges on my doorstep and lots of opportunities for hiking and climbing in summer, and skiing in winter. There is also a lot to do in the city. You can take a cable car from the city centre up to the Bastille, which is a fortress on cliffs overlooking Grenoble. The Palace of the Parliament of Dauphiné, the Museum of Grenoble and the Archaeological Museum of Saint-Laurent are all great places to learn about the history of the city.

If I have one complaint about Grenoble, it is the cold winters. There are days of snow almost every year and sometimes winter stays for a long time.

What do you do in your leisure time?

Like most PhD students I don't really have much spare time, but when I have an hour or two I like to walk along the Isère river and enjoy the fresh air. When I do have the time, I like to trek in the surrounding mountains, with the route up Moucherotte being my favourite. Although the ascent is difficult and the round trip takes nearly an entire day, Moucherotte gives the best views of Grenoble. The city also has easy access to the Robert lakes and Lake Achard in the nearby Dauphiné Alps. These are great places to visit on hot summer days, to swim or just to admire the landscape.

Why did you choose GETALP?

I wanted to get a PhD from a reputed international research lab in natural language processing and/or computational linguistics. GETALP is one of the pioneers in this field, having more than 50 years of research experience. I contacted some members of GETALP when I was looking for a PhD position and when they offered it to me I did not think twice about taking it. Personally, I would like to thank the French Ministry of Higher Education and Research, the members of our lab and the selection jury for making it possible for me to do a PhD with funding here in Grenoble.

What are your plans for the future after your PhD?

I would like to broaden my knowledge and research experience by finding a postdoctoral research position here in France or in the USA, Canada, Australia, the UK or Germany. Then, I will look for a permanent position abroad, or I will go back to Bangladesh to join a university as an assistant professor or start my own business.

Wherever I go and whatever I do, I intend to continue my research into natural language processing and share my knowledge for the betterment of humanity.

What's happening in Mohammad Nasiruddin's Grenoble?

Museum of Grenoble: Insights into how the museum has built its collection over the past decade is the subject of an exhibition running from 7 May to 30 August 2015. On display will a wide range of objects from ancient works of art to pieces by contemporary artists such as Philippe Cognée. For more details see **www.museedegrenoble.fr**.

Alpine lakes: Lake Achard is also a great place to visit in the winter, when visitors can reach it via the many snowshoeing trails that criss-cross the region. For the more adventurous, there is scuba diving under the ice in the Robert lakes. For more information see the Chamrousse resort website at **www.chamrousse.com**.

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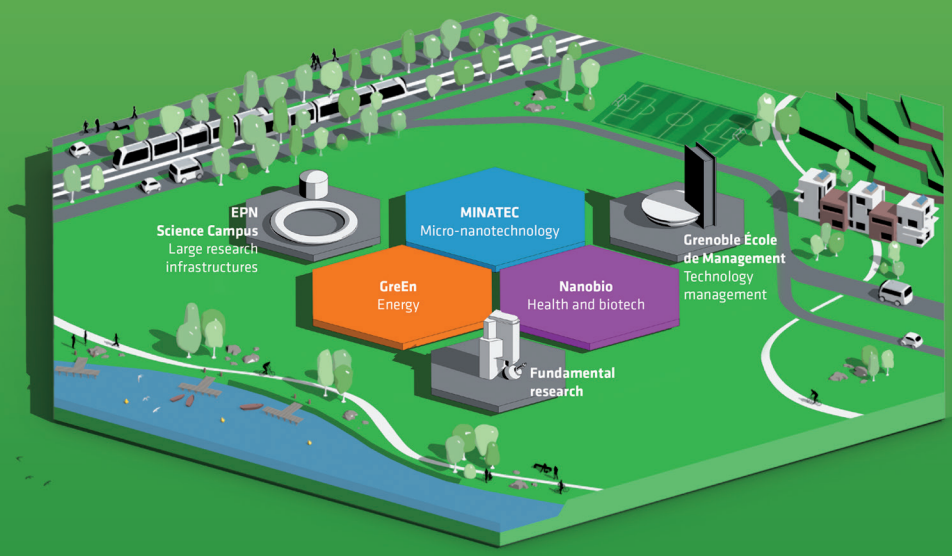

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