Increase in protein analysis pushes demand for synchrotron operators

From biology to physics, synchrotrons offer a bright future to users and specialists alike, says Helen Gavaghan.


ESRF

Light touch: synchrotron facilities, such as the one based in Grenoble, are in demand from structural biologists because they can reveal the full structures of proteins.

"If I were a young scientist now, I would want to work with synchrotrons. The technical developments of these machines are extremely exciting and there is much virgin territory." So says Giorgio Margaritondo, chair of the European Round Table for Synchrotron Radiation and Free Electron Laser, and a professor at the Swiss Federal Institute for Technology in Lausanne.

Synchrotrons are extremely versatile tools. They produce radiation across a broad range of wavelengths, allowing scientists to discern the atomic structure and behaviour of a variety of materials. As a user, Margaritondo might visit a synchrotron facility once or, if he were lucky, twice a year. Analysis of the data collected during such a visit could well keep a research team busy for the whole year.

At the same time as reaping the immediate rewards of their experiments, says Margaritondo, scientists are identifying new ways of exploiting synchrotron beams. It is this territory that Margaritondo thinks thousands of scientists from many disciplines will find exciting.

During the past decade there has been an explosion of interest in synchrotron radiation and its uses. Accelerator physicists, beamline scientists and engineers have developed a deeper understanding of the phenomenon and how it can be manipulated.

But even as scientists are finding new uses for existing facilities, and fresh ways to squeeze more performance from them, new facilities are being built and even newer technologies are being proposed. So rapidly has the technology developed, says Margaritondo, that users from all disciplines and those operating the machines are scrambling to keep up with what the ever-advancing facilities have to offer.

Inside a synchrotron

At Daresbury, home to Britain's current national synchrotron facility, some 270 people work directly on the synchrotron with another 140 employed in computing, engineering and instrumentation design and support. These numbers are typical for synchrotron facilities worldwide.

With the construction of the new synchrotron facilities in Britain and France — known as Diamond and Soleil, respectively — plus plans to add beamlines at Daresbury and keep the facility running until 2007, there will be exciting jobs to be had in the development and operation of these instruments. And in Britain, the government has announced several new projects in the north-east, including a proton synchrotron for medical applications and a fourth-generation free-electron laser light source.

The thousands of users queuing for beam time at synchrotrons would be lost without the accelerator physicists, beam scientists and engineers who provide expert support. And these staff members often undertake research projects themselves.

Synchrotrons are a uniquely multidisciplinary environment, says Susan Smith, a senior accelerator physicist at Daresbury. Smith has a degree in physics and maths from the University of Glasgow and did graduate work on free-electron lasers before joining Daresbury in 1985. In the past few years, her time has been split between providing support for Daresbury's synchrotron radiation source, doing generic accelerator studies and working on new light sources.

Rob Lewis has designed and worked with detectors since 1979 for the radiation source at Daresbury. He is now heading a science team to develop medical imaging as part of the proposed proton synchrotron to be based at the same site. Lewis has a degree in physics, a PhD in X-ray astronomy and postdoc experience in the same field. He says that he has seen quite a lot of people with his academic background, and an experimental rather than theoretical inclination, move as he has done towards medical physics.

Understanding synchrotron radiation or particle accelerators in depth is not a prerequisite for the work, says Lewis. When he

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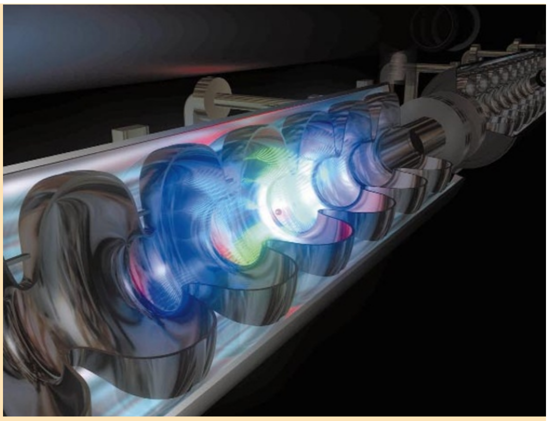
What is a synchrotron?



TESLA

Ironically, synchrotron radiation, although now greatly in demand, was a bane in the life of high-energy physicists working with particle accelerators. This is because the radiation represents a loss of energy.

In particle accelerators, charged particles travel millions of times round a doughnut-shaped ring containing a vacuum. Strategically placed magnets confine the particles to their circular path. The strength of the magnetic field must change as the particles accelerate, in order to keep them on course. Because this change must be synchronized with the energy gain associated with increasing the particles' speed, the radiation emitted acquired the name synchrotron radiation.

Particle accelerators are designed to compensate for the energy loss, but once scientists saw that synchrotron radiation might be useful, machines were built specifically to produce it — the 'second-generation' facilities. In these systems, the particle beams are confined in a 'storage ring' and siphoned off in a controlled manner along a beamline.

Instruments in the beamlines, such as monochromators, determine the frequencies available for a particular class of experiments — perhaps probing for fault lines or impurities in a material, or X-ray diffraction to determine a protein structure.

As accelerator physicists learned more about synchrotron radiation, they designed magnets engineered with precise proportions to increase the energy and brightness in a beam and so expand its potential range of applications. Instead of squeezing these 'insertion devices' into synchrotrons as an afterthought, 'third-generation' synchrotrons are specially designed with the devices in mind. One such facility, the Swiss Light Source, is scheduled to come online this August in Villigen, and Diamond and Soleil are planned for later this decade in Britain and France.

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joined Daresbury he knew nothing about the subject. Like Smith and others who join synchrotron facilities around the world, he learned to apply his knowledge of physics to the subject once he had got the job.

Typically, when scientists such as Lewis join national synchrotron facilities they become part of a team that deals with a class of experiments, such as protein crystallography. They are likely to be physicists, chemists or engineers by background. "Anything from 80% upwards of your time is supporting the users. You need to understand what they want to achieve and to liaise with them about what the equipment can do," Lewis says. "There is a real dearth of people who can fill this middle ground."

Beam-time shortage

Although the next generation of machines (see 'What is a synchrotron?', above) will mean there are more beamlines available, competition among users for beam time is, and will continue to be, acute, says Guy Le Lay, a professor at the University of Provence and member of the European Round Table for Synchrotrons and Free Electron Laser. "Obviously some competition — perhaps 150% over-subscription — is healthy," says Margaritondo, who chairs the round table, "but beamlines currently are between 200% and 300% oversubscribed and the situation for protein crystallography is even worse."

Given that opportunities are now opening up for biologists to learn about the proteins that the sequencing of the human genome tells them the body is producing, the pressure is not surprising and it will not ease up. But it is not only the biologists that are clamouring for time on synchrotron beamlines. The X-rays produced in synchrotron facilities are used by chemists, materials scientists and physicists alike.

Jörgen Albertsson, professor of inorganic chemistry at Chalmers University of Technology in Sweden, says that it can be hard to compete successfully against the protein crystallographers for beam time. Although the construction of Diamond and Soleil will ease this situation, users and providers of synchrotron radiation need to find ways to exploit both the second- and third-generation facilities more effectively.

In particular, the beamlines at these synchrotrons need better detectors, which offers fresh opportunities for beamline scientists and engineers. "In many cases it's not brightness that limits experiments, but how fast the detectors can record," says Lewis. Margaritondo agrees that there is a need for a major international push to develop better detectors.

But even as the third-generation facilities spring into operation around the world, the European Round Table for Synchrotron Radiation and Free Electron Laser is pondering the next step. There are two options: design a synchrotron at the limit of what physics allows or move to an alternative technology — free-electron lasers — that could surpass even the most advanced synchrotron.

One possibility could be for the European Synchrotron Research Facility based in Grenoble to develop the 'ultimate' synchrotron. Meanwhile, TESLA, a German proposal for a free-electron laser that can produce high-energy X-rays, would also be developed with international collaboration. "I sense a consensus developing that we should develop both," says Margaritondo.

So, whether as a user developing new techniques to exploit beamlines, as an accelerator physicist, beamline scientist or engineer, the job prospects at synchrotron facilities are bright for some time to come. And it is hard to imagine that in a decade or so any branch of science will not have some need of synchrotrons. ■

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Synchrotron radiation facilities

http://www.src.wisc.edu/links/sr_sources.html

European Synchrotron Research Facility

http://www.esrf.fr

European Round Table for Synchrotron Radiation and Free Electron Laser

http://www.elettra.trieste.it/sites/roundtable

Automated for the people

Without new synchrotrons, US structural genomics may depend on automating existing facilities to meet its goals. But without an influx of interested physicists and engineers — and the funding to support them — speeding up the process of discerning a protein's three-dimensional structure may prove difficult.

The automated gene sequencer revolutionized genomics. But no single machine, by itself, will greatly speed up structural biology. Working out a protein's structure is a more complex process, with many more stages, says Peter Kuhn, assistant professor at the Stanford Synchrotron Radiation Laboratory.

The protein must be purified, crystallized, mounted in the beamline, probed by the light, then reconstructed by computer. Potential bottlenecks occur at every stage — and each stage may need different combinations of expertise to speed it up. For example, automating sample mounting in the beamline requires engineering skills, whereas finding and centring the sample within the beam needs computational skills.

Different US groups are working on separate stages of this problem. For example, Stanford is in the nascent stages of automating sample mounting. Once individual steps have been automated, systems engineers will need to evaluate how the entire process fits together, Kuhn says.

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