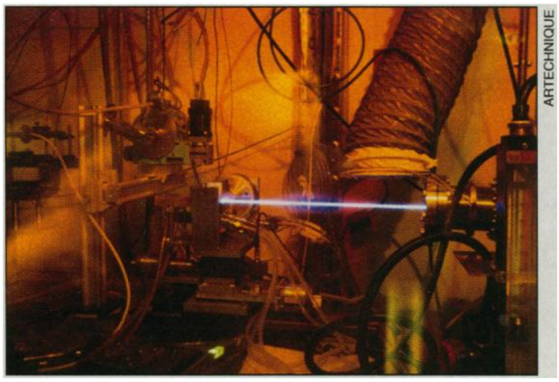
BIG PHYSICS

Europe's New X-ray Source Beams With Confidence

Scientists, administrators, and government representatives from 12 European countries, including France's science minister, François Fillon, gathered in Grenoble last week to pat themselves on the back. They had good reason: They were there for the official opening of the European Synchrotron Radiation Facility (ESRF), a $600-million particle accelerator, built on time and on budget, that is now the world's largest and brightest source of x-ray light. Indeed, the quality and power of ESRF's x-ray beams are far better than even the machine's designers had expected—so much so that much of the optics, detectors, and data-handling equipment in the experimental beamlines is struggling to keep up. Says Burton Richter, director of the Stanford Linear Accelerator Center: "ESRF is the model of how to set up an international project."



Seeing the light. Synchrotron light from ESRF. The facility is the world's brightest x-ray source.

Visiting scientists got a taste of ESRF's capabilities in early September when some of the beamlines were opened to outsiders for the first time. Already, researchers have used the intense x-ray beams to open a unique window on the behavior of oxygen under immense pressure, decipher the structure of a protein, and probe the atomic layering of diamond. "I have worked with several synchrotron sources, and only as a user do you appreciate the tremendous advantages of this source and the high level of organization that allows us to do first-class experiments," says Friso van der Veen of the FOM-Institute in Amsterdam, the Netherlands. Researchers like van der Veen are the vanguard of an army of academic and industrial researchers: By the time all the beamlines are complete—a total of 40 are planned—up to 2500 visiting scientists per year will use the facility.

It's a far cry from the days when synchrotron radiation "was looked on as a pest," notes British physicist Andy Fitch, who now works at ESRF. When particle accelerators were first developed, synchrotron radiation—which is generated when charged particles are forced into a circular path by a magnetic field—was primarily viewed by the machines' designers as an annoying energy drain. But scientists such as solid-state physicists, crystallographers, and molecular biologists saw this intense source of x-rays not as a waste but as a promising tool for probing the inner structure of matter. These researchers became known in the 1960s as "big-science squatters," as they installed themselves around obsolete particle accelerators.

In the 1970s, they got their own "second-generation" machines—electron accelerators designed specifically to shed x-rays—such as those at Brookhaven National Laboratory in the United States and Daresbury Laboratory in the United Kingdom. Now, these facilities are being surpassed by third-generation machines like ESRF: powerful synchrotrons that produce much more intense and precise beams. ESRF, a 6-gigaelectron-volt (GeV) accelerator, is the first of this new breed. It will hold pride of place for a couple of years, until the 7-GeV Advanced Photon Source (APS) starts up at Argonne National Laboratory in Illinois in 1996, followed in 1998 by SPring-8, an 8-GeV machine now under construction at Harima Science Garden City in Japan.

ESRF went relatively smoothly from the start. Construction began in 1988, and the building to house the synchrotron was completed 6 months ahead of schedule in September 1991 (*Science*, 8 November 1991, p. 794). The 844-meter-long electron storage ring was completed in February 1992, and by the end of 1992 it was already performing better than the original specifications.

Scientists credit the success of the project to a mixture of good staff, good advisers, and stable funding. In particular, says Richter, the international agreement to set up the ESRF was "a model for the future," as it got all 12 countries on board from the start and guaranteed funding of $600 million for the first 10 years of the project, to 1998. But the project has also benefited greatly from technological advances in creating and handling intense x-ray beams.

The beams themselves derive much of their power and precision from devices known as undulators and wigglers. These "insertion devices," positioned at straight sections of the ring between its 64 bending magnets, consist of a succession of magnets with alternating polarity. The rapidly changing fields force the electrons to wiggle, and the synchrotron radiation they produce becomes intensified in the direction of the electron beam because the photons radiated in that direction by each wiggle add up.

Because x-rays cannot be diverted or focused with conventional mirrors or lenses, researchers have to rely on carefully constructed diffracting crystals and mirrors that deflect x-ray beams at very small angles. And these optical devices have long been a limiting factor: "A few years ago, we believed that, even if the machine performed as expected, the optics would prevent us from fully exploiting the quality of the beam," says ESRF Director General Yves Petroff.

A pioneering achievement at ESRF has, however, greatly improved the ability to cope with the beam's power. ESRF physicists have developed a diamond monochromator, which uses the crystal lattice of a single-crystal diamond to select a narrow frequency band of the x-ray beam. Diamond was chosen because it buckles less when hot and is a far better heat conductor than silicon, the material traditionally used for diffracting x-rays. As a result, the monochromator can be cooled with water instead of liquid nitrogen. Says Keith Moffat of the University of Chicago, who is planning experiments for the APS: "Using diamonds is a technique that is very new; it was certainly not available when we began planning our beamlines at the APS."

These technical advances have resulted in x-ray fluxes that are pushing the limits of detectors and outstripping researchers' ability to handle the data they produce. "There is an urgent need to increase the pace of development over a wide range of detector technologies," says John Morse, head of the detector group at ESRF. "We are now moving on to ... systems that produce many tens, even hundreds of megabytes per second of data ... and the whole problem of data collection becomes a major issue." A typical example is the biocrystallography station: Although a sample may be exposed to x-rays for only 1 or 2 seconds, the detector needs 3 minutes to produce an image. "This beamline produces 2 gigabytes of data per day, of which 99% represents dead time," says Soichi Wakatsuki, a beamline specialist. And the problem will get worse: "The next generation of detectors will generate something like 50 times as much data," says Wakatsuki.

If there is any real concern about ESRF's future, however, it stems not from detector capabilities but from a more mundane problem: a wobbly floor. During tests in 1991 it was discovered that the floor under the beamlines was unstable. The flaw was repaired by injecting a mixture of epoxy and cement under the concrete floor slabs, but some worry that this solution will not be permanent. Physicist Michael Hart of Manchester University, United Kingdom, who is a member of the ESRF Review Committee for Methods and Instrumentation, says: "I have seen the floor at SPring-8; I have seen the floor at APS, and the one at ESRF is not only very thin; there isn't any steel in it." Petroff rejects such criticisms, however. "We run vibration experiments regularly. After 2 years we don't see any difference. I think the problem is solved for the moment."

Certainly, researchers who have been putting the machine through its paces are optimistic. A total of 12 beamlines are now in use, and the first 2-week run for visiting scientists, which began on 1 September, has produced several "firsts." Beamline specialist Daniel Häusermann has just finished an experiment with Yuichi Akahama from the Himegi Institute of Technology in Japan. "We could show that at a pressure of 900,000 atmospheres oxygen changes from a molecular crystal structure to a metallic crystal structure, a process called molecular metalization, and this is something that has never been done before." Akahama is returning home "a very happy man," says Häusermann.

Louise Johnson of the Laboratory of Molecular Biophysics in Oxford successfully determined the structure of a protein involved in cell-cycle control called $p13^{suc1}$, reports Wakatsuki. Van der Veen and Willem Jan Huisman, also of the FOM-Institute in Amsterdam, probed the outer atomic layer of diamond by recording the interference pattern produced by the intense x-ray beam. "The technique is not really new, but it is the first time that such an experiment can be performed on such an important prototype structure as diamond," says van der Veen.

These capabilities are expected to attract researchers to Grenoble in droves. Indeed, just as in high-energy physics, synchrotron radiation researchers have formed something of a traveling circus, continually migrating to the best current machine, then moving on to transfer knowledge and techniques to another facility. For example, Wakatsuki, who after his tenure at ESRF will possibly go on to SPring-8, says that "in Europe, the extraction and handling of scientific data is more advanced than in Japan. I am learning quite a lot." Adds Moffat: "It is a trading situation. I am strongly in favor of that; I think that is the way these facilities should be run."

–Alexander Hellemans

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HUMAN EMBRYO RESEARCH

Grant Applications Pile Up at NIH

When Congress and President Bill Clinton lifted a 15-year ban last year on federal support for research using human embryos, grant applications quickly began arriving at the National Institutes of Health (NIH). More than 70 researchers have already submitted proposals for studies ranging from the development of new fertilization technologies to basic research on early gene activation, says National Institute of Child Health and Human Development Director Duane Alexander. Last week, scientists who would like to get started on these projects got some welcome news when a panel of lawyers, ethicists, and scientists endorsed the lifting of the moratorium and laid out guidelines on what types of research are ethically permissible. However, it could be many months before any of these proposals are funded.

The panel's recommendations, described earlier in these pages (*Science*, 19 August, p. 1024), are just the first step in a long process of public consultation established by NIH Director Harold Varmus to determine how NIH should traverse this ethical minefield. Varmus will take the matter up at his next advisory council meeting, on 1 and 2 December, and he has invited the public to submit "substantive" comments.

To judge by the experience of the panel, there will be no shortage of comment on the research proposals. Steven Muller, president emeritus of Johns Hopkins University, who chaired the review, noted last week that the panel had become the target of organized letter campaigns by opponents of embryo research. NIH has received more than 30,000 pieces of mail; Muller said he has received "hundreds" himself. Relieved that the panel's job was done, Muller gave the group a pat on the back, saying, "We have stood the heat ... we have stayed in the kitchen, and we have completed the task ... striking a balance among divergent interests."

MARK HUGHES

Green light. Three-day-old embryo. Panel said research using early embryos is acceptable.

The recommendations are detailed and complex. The Muller panel members voted to encourage the use of "spare" embryos in research. These are fertilized eggs that both donors have specifically offered for research; they are stored in fertility clinics. Ethicist Ronald Green of Dartmouth College, a panel member, explained that the panel judged the moral status of such minute embryos to be greater than that of a "mass of cells," but less than that of an infant, child, or adult. To the extent that patients may benefit from "well-justified research" using such embryos, the panel decided that it should go forward "within a framework of stringent guidelines." The panel agreed that under limited circumstances, NIH grantees might also be allowed to create "research embryos" in the lab, if necessary, to validate the conclusions of research based on donated embryos. Panel members hoped these changes in policy would remove the shackles from an important area of science.

But some observers—including panel member R. Alta Charo, law professor at the University of Wisconsin, Madison—were disappointed that the panel's recommendations would impose a layer of federal red tape on the field. Charo dissented from a section calling for the creation of a new "ad hoc advisory panel" at NIH with a 3-year lifetime. This ad hoc group would report directly to the NIH director and monitor compliance with general guidelines on a case-by-case basis, ensuring that researchers are scientifically qualified, that studies promise "significant scientific or clinical benefit," and that research cannot be "otherwise accomplished by using animals or unfertilized gametes." One Clinton Administration official, speaking anonymously, echoed Charo's dissatisfaction, saying the advisory panel had produced a jumble of detailed and confusing guidelines. This aide regretted that not even one area of embryo research had been exempted from red tape.

But the panel appears to have steered a middle course through the minefield, as another dissenter—Georgetown University law professor Patricia King, co-chair for policy—filed a dissent leaning in the opposite direction. King specifically opposed allowing new embryos to be created in the lab for purposes other than very narrowly limited research, defined as studies related directly to human health "when the information needed cannot be obtained in any other manner." She disagreed with the recommendation that next-of-kin should be able to donate a woman's ova for research, and she argued that women undergoing fertility treatment may be too vulnerable to make an independent judgment about the research use of their donated ova.

The ball is now firmly in Varmus's court. "If and when guidelines are put in place," Varmus said last week, NIH will ensure that embryo research projects are in full compliance with them. That clause—"if and when"—may send a chill through some of the 70 researchers whose grant proposals are now awaiting NIH's attention.

–Eliot Marshall