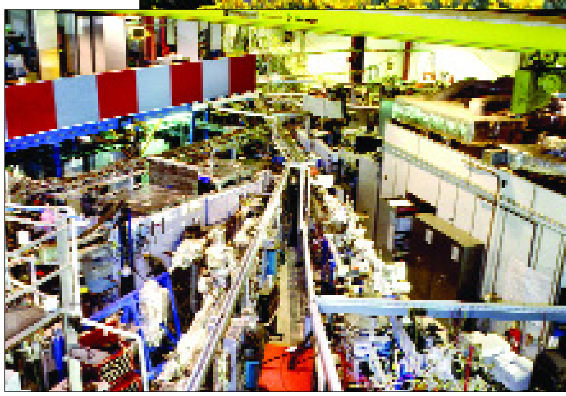
Lost Experiment Was Headed for X-ray Analysis

More than 80 scientific experiments were lost in the Space Shuttle Columbia disaster in February, including a protein crystal growth experiment that might have helped in the development of cancer drugs and disease-resistant plants.



The Canadian Space Agency has funded protein crystal growth research at the Brookhaven National Laboratory's synchrotron facility *(above and left)*. One such experiment was lost in the Space Shuttle Columbia disaster.

Canadian researchers are working with Brookhaven National Laboratory's National Synchrotron Light Source (NSLS) in Upton, N.Y., to study crystals the growth of which may be disturbed by Earth's gravity. In microgravity, the crystals aren't as susceptible to disturbances such as convection, said Jurgen Sygusch, a biochemist at the University of Montreal and one of the researchers who would have studied the now-lost crystals. "The undisturbed protein concentration gradient acts as a mass filter so that fewer impurities get into the crystal."

Once such crystals are returned to Earth, the crystals are irradiated by an X-ray beam, which produces diffraction patterns that are characterized by spots. The diffracted spots are registered on a CCD detector and the images are downloaded into a computer. This process reveals three-dimensional structural information about the protein, Sygusch said. It could show which drugs bind to which HIV proteins, for example, whereas on Earth, "we might not see the exact shape of the drug. The closer we get to improved resolution, the sharper the image," and the faster effective drugs make it to market, he said.

Scientists from around the world visit the Brookhaven light source facility every day, said Anand Saxena, who manages one of the six beam lines there. The facility is one of about a dozen in the world that provide an extremely intense beam of photons at wavelengths ranging from ultraviolet to hard X-ray. "Crystals are hard to grow and they are extremely small. If you have one that's over 0.1 mm, then it's a big crystal," Saxena said.

Determining the structure of a protein molecule, with its many thousands of atoms, requires bombarding the crystal with a monochromatic beam of X-rays and then analyzing the thousands of reflections emanating from the crystal, Saxena said.

Before synchrotrons

Before the advent of synchrotron sources, work of this kind was done with rotating anode X-ray generators, which are similar to X-ray machines used in doctors' offices, Saxena said. The intensity of photon beams in synchrotron sources is much greater than in X-ray generators; crystals are kept cold by a stream of air at 100-degrees Kelvin to prevent them from disintegrating under the intense beam.

"There is another important advantage of X-rays generated from a synchrotron source," Saxena said. "While X-rays from a rotating anode source are essentially monochromatic, a synchrotron source produces a wide band of energies from which a suitable wavelength is produced. This feature is important because it allows diffraction data collection at a desired wavelength, which in turn helps in determining the phases of reflections, a step that is crucial for analyzing the structure of the molecule."

Use of synchrotrons by the biological community has increased rapidly over the past decade. Initially designed for physicists, biology-based researchers such as Sygusch now are the single largest group of synchrotron users, Saxena said.

The research continues

Canada has sent crystals on more than a dozen space flights. The crystals selected to travel on Columbia were expected to show promising results, Sygusch said. "The scientific loss is going to be very difficult to assess, but it could be huge," he said.

Canada will continue growing protein crystals in microgravity, and interferometry could play a critical role in determining which proteins are good candidates for the program, Sygusch said. His team is hoping to acquire a miniature Michelson interferometer. "If we could use optical means for measuring the protein concentration gradients, we could have a criteria for flying a particular protein or not," he said.

Robert Sweet, a Brookhaven researcher and collaborator on the protein crystal growth program, said he hopes such experiments eventually don't involve manned missions such as Columbia.

"It costs so much to put people up there, and this puts a remarkable budget limit on experiments in space. Nearly everything we do… can be automated."

Shedding Light On the Brain Before Birth

Flashes of light are being used to detect brain activity in fetuses, thanks to a new device developed by a team from the University of Arkansas for Medical Sciences. The hope is that the technology could be used to detect and prevent fetal brain damage. It is thought to be the first magnetoencephalography (MEG) study of fetuses using light, not sound.

"At birth, a brain structurally may look normal, and a child may have a number of problems we see manifested later," said Giovanna Spinella, a pediatric neurologist and program director at the National Institutes of Health, which supported this research. "If we can tap into that black box of fetal development, we can begin to understand early physiological issues in brain development."

The SQUID Array for Reproductive Assessment, or SARA, detects tiny fluctuations in magnetic fields corresponding to electrical activity in the body. SQUID stands for Superconducting Quantum Interference Device. Other techniques, including magnetic resonance imagery (MRI) have been used to study fetuses for auditory responses, said Hari Eswaran, a member of the Arkansas team. In an MRI, however, the woman sits in a magnetic field; SARA records magnetic fields coming *from* the body. "This device is sort of the opposite of an MRI," Eswaran said.

The new SARA device uses sensors to collect information from pregnant women about fetal brain activity.

The system includes 151 sensors that are arranged in a concave array. The woman leans forward against the array, allowing the sensors to receive signals from the entire abdomen. A 7.7 m-long fiber optic cable, laid across the abdomen, releases red light at a wavelength of 690 nm. "The peak illumination … measured over a 33 ms duration light pulse was 8800 lux," according to an article in *The Lancet* that described the research. "The light pulse was considered safe for the fetus, since it was of short duration, contained no short wavelength radiation, and had an intensity much lower than sunlight on a bright day (about 100,000 lux)."

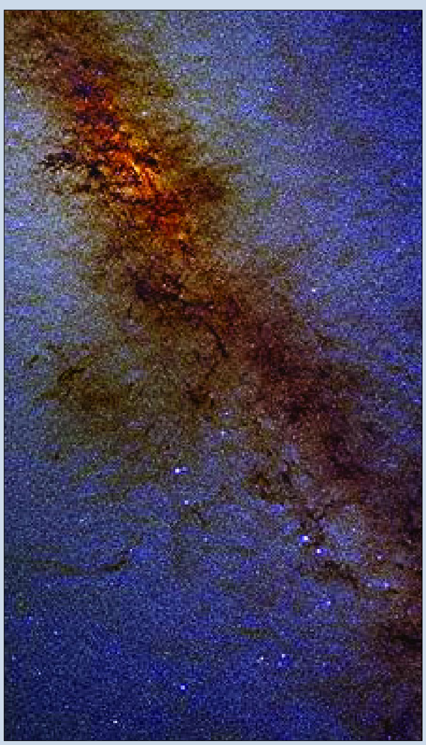
The team excluded from the initial study those fetuses that were positioned further than 3 cm away from the mothers' skin as well as those whose heads were facing down. Ten fetuses (28- to 36- weeks gestational age) were chosen for the study.

Four of the 10 fetuses initially tested with SARA had measurable brain responses to the light; researchers don't know why the six others did not respond, but they have said the fetuses could have been asleep or facing away from the light. Each session lasts for six minutes and includes 180 flashes; a spatial-filter-based null-projection algorithm helps weed out interfering maternal and fetal heart signals.

Researchers have used the device most recently to study fetuses already diagnosed by ultrasound as having various brain abnormalities.

"[This] opens a window for us to explore the frontier of fetal life," said the NIH's Spinella. "We now have another tool, and only time will say how powerful a tool it is."

DID YOU KNOW?



Using twin infrared telescopes, a team of astronomers has released a map of the entire sky, including millions of once-elusive stars and galaxies. The project, Two Micron All-Sky Survey (2Mass), was led by the University of Massachusetts, Amherst, with support from the National Aeronautics and Space Administration and the National Science Foundation. For more than three years, astronomers collected data from telescopes in Chile and in Arizona and produced two major catalogs. Sky studies have been done using other parts of the electromagnetic spectrum. But with infrared light, "you can see farther, and you can see the structure of the galaxy better," said Martin Weinberg, an Amherst astronomer. Visit http://www.ipac.caltech.edu/2mass/ to access the 2MASS products and images.

This infrared view of 10 million stars, revealing the center of our Milky Way galaxy, is one of many images available through the 2Mass sky analysis.

Articles in "Scatterings" are written by Kim Douglass, assistant managing editor of *Optics & Photonics News*. Do you have a story idea? Write her at kdougl@osa.org.