April 2000

Science & Technology REVIEW

U.S. Department of Energy's
Lawrence Livermore
National Laboratory

Decoding Human Genome Nears Completion

Also in this issue:

- DOE Labs Collaborate on Revolutionary Particle Accelerator
- Remote Sensing Technologies Put to the Test
- Speckle Imaging Maps a Saturn Moon

About the Cover

The Joint Genome Institute, a collaboration of the Livermore, Berkeley, and Los Alamos national laboratories, will soon release the draft sequence of chromosomes 5, 16, and 19. This month's cover article, beginning on p. 4, focuses on the institute's accomplishments and its contributions to the Human Genome Project, a worldwide effort to map all human chromosomes. On the cover, Tijana Glavina removes a plate of purified cloned DNA fragments from a plate washer during an early step of the sequencing process. Also shown is a chromatogram of sequenced DNA.

Cover photography: Michael Anthony

About the Review

Lawrence Livermore National Laboratory is operated by the University of California for the Department of Energy. At Livermore, we focus science and technology on assuring our nation's security. We also apply that expertise to solve other important national problems in energy, bioscience, and the environment. *Science & Technology Review* is published 10 times a year to communicate, to a broad audience, the Laboratory's scientific and technological accomplishments in fulfilling its primary missions. The publication's goal is to help readers understand these accomplishments and appreciate their value to the individual citizen, the nation, and the world.

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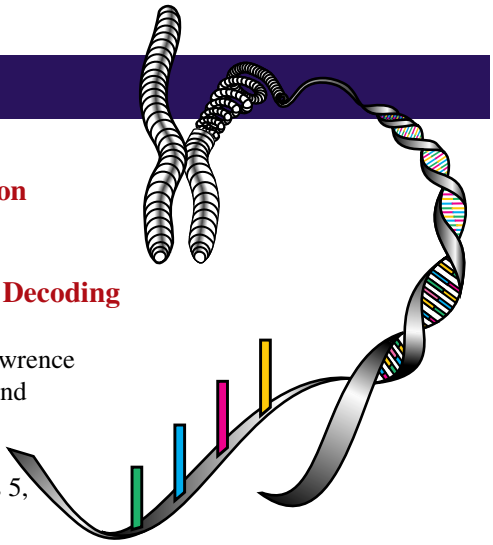

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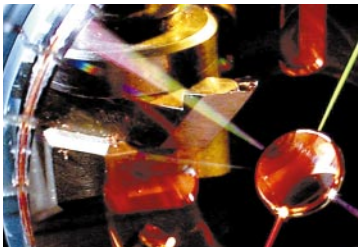

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Lab breaks own crystal-growing record

Lawrence Livermore researchers have produced the world's largest fast-growth crystal. Weighing 318 kilograms, the crystal bests the previous record of 295 kilograms, also achieved at Livermore using a variant of the rapid-growth crystal-growing technique developed at the Laboratory.

The pyramid-shaped KDP (potassium dihydrogen phosphate) crystal measures approximately 66 by 53 by 58 centimeters. It was grown in a record 52 days using the special Livermore technique, which delivered twice the yield originally projected.

The enormous crystal will be sliced into thin plates for use in the National Ignition Facility (NIF) currently under construction at the Laboratory. The crystal plates will be used to convert the laser's infrared light beams into ultraviolet light just before the beams strike laser targets. NIF will require as many as 600 crystal plates.

According to Ruth Hawley-Fedder, leader of the Livermore crystal-growing team, the latest rapid-growth technique "offers the possibility of producing even larger and higher quality crystals in the future. Our newest record-holder could have grown even larger, but we simply ran out of room in our growth tank."

Alan Burnham, deputy systems manager for NIF's final optics, notes, "Ruth and her team brought large-scale rapid-growth technology to the reliability needed to realize savings of millions of dollars for both construction and later operation of NIF."

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Lab technology images Neptune, Titan clearly

A research team led by Livermore's Claire Max recently used Hawaii's Keck II telescope to capture the clearest Earth-based images ever taken of Titan (Saturn's largest moon) and Neptune. Max's team, made up of scientists from Lawrence Livermore, the University of California at Berkeley and Los Angeles, and the Keck Observatory, revealed their successes at the annual meeting of the American Astronomical Society in Atlanta, Georgia, in mid-January.

The unprecedentedly clear images of the distant celestial bodies were captured in infrared light. They are among the first taken after Livermore researchers helped install adaptive optics technology, developed at Livermore, on Keck II, one of the twin telescopes that are the world's largest. Adaptive optics uses rapid mirror adjustments to remove Earth's atmospheric turbulence from what the telescope sees.

The images, which surpass even those possible using the Hubble Space Telescope, reveal giant Neptunian storms driven by prevailing winds of 1,800 kilometers per hour. Scientists are using information provided by the telescope to study the planet's storms and their evolution, a first step toward understanding Neptune's weather and climate.

The adaptive optics images of Titan reveal features that could be frozen land masses separated by cold hydrocarbon seas and lakes. They tell astronomers about the complex surface composition of the frigid Saturnine moon. Sunlight shining on Titan's nitrogen-rich atmosphere produces a deep orange haze that obscures Titan's surface. Keck's infrared detectors penetrate this haze to reveal surface details.

"Combining the power of Keck with adaptive optics is taking us to new worlds," says Max. "That's an extremely exciting prospect as we enter the next millennium."

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Researchers' theory tracks absorbed CO_2

In the January 2000 issue of *Science*, Laboratory climate scientists Kenneth Caldeira and Philip Duffy posit their solution to an old scientific mystery. Early computer models showed that large amounts of carbon dioxide (CO_2) from human activity are readily absorbed by the icy waters of the Antarctic (or Southern) Ocean south of Australia. These models are consistent with the general rule that colder water absorbs CO_2 more easily than warm water. Yet, sampling reveals that the Antarctic Ocean does not contain massive CO_2 reserves.

Caldeira and Duffy's study suggests not that the models are wrong but that the cold, CO_2-containing water moves deeper and deeper as it runs north from the point of absorption at 60° south latitude to the tropics (40° south latitude), explaining why the carbon is found so deep in the subtropical ocean. Furthermore, the warmer layers of water in the subtropical ocean push down on the colder, denser water layers, keeping them and the carbon they contain deep in the subtropical waters.

A problem arises as humans generate more CO_2. As the ocean absorbs more and more carbon dioxide, it becomes more acidic and therefore perhaps less efficient at carbon absorption. Not only is acid corrosive to calcium carbonate, an essential ingredient of shells and coral reefs, but acidity warms water, inhibiting its ability to absorb CO_2.

"The fear is that if you warm things up too much, more precipitation will make the surface of the Southern Ocean less dense," says Caldeira. "You may start shutting off the entrance of carbon dioxide into the ocean, and things would warm up a lot faster."

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Toward a Biological Revolution

MANY are predicting that the 21st century will be remembered for a revolution in biotechnology and medicine, a revolution made possible by the successful decoding of the complete human genome. In the next several years, as the locations for all of the genes that regulate life are pinpointed, huge advances may occur in the way that bioscientists and doctors develop more precise diagnostic tests, individualize drug therapies, and ameliorate and cure diseases. Gene therapy may replace current medical practices for some diseases. Work on unraveling the genomic structures of viruses and bacteria will lead to an understanding of infectious diseases and how they attack our own genetic material.

We at Lawrence Livermore are proud to be partners with Lawrence Berkeley and Los Alamos national laboratories in the Joint Genome Institute in Walnut Creek, California. The institute is funded by the Department of Energy's Office of Biological and Environmental Research. As described in the article beginning on p. 4, employees of all three laboratories are sequencing chromosomes 5, 16, and 19, which account for about 10 percent of our DNA. The institute is one of five centers around the country working with government-supported laboratories in France, Germany, Japan, and China to develop a map of the entire human genome.

Last fall, scientists in the U.S. and England completed the sequencing of chromosome 22, and preliminary maps for other chromosomes will begin appearing soon. A working draft of the 3 billion pieces of our DNA will be complete in 2001, with final sequencing to be done in 2003. The original schedule for completion was 2005, but recent radical advances in robotics and automation have pushed sequencing production to levels that no one could have dreamed of even a few years ago.

Livermore and other Department of Energy laboratories have been using their multidisciplinary capabilities to address biomedical research issues since the 1950s. Research on the effects of radiation on humans led naturally to an examination of its effects on our genes. DNA mapping began at Livermore in the late 1980s and expanded in 1990, when the Department of Energy formed a partnership with the National Institutes of Health for the Human Genome Project, the largest biological undertaking in history. Then in 1996, the Livermore, Berkeley, and Los Alamos national laboratories joined forces in the Joint Genome Institute to maximize their sequencing capabilities in an industrial-scale production facility. Since late 1998, in efficient laboratory and robotics areas, institute personnel have been generating and analyzing the genomic sequence 24 hours a day.

After the institute completes sequencing of chromosomes 5, 16, and 19, it will study the mouse, whose DNA is amazingly similar to our own. Examination of the similarities will help considerably in defining what is important in human genetic material.

If a biological revolution indeed comes to pass, it will be because the sequencing efforts at the Joint Genome Institute and elsewhere have provided life science researchers with the infrastructure they need to make important new discoveries. In the latter half of the 20th century, basic research at the Department of Energy laboratories supplied a comparable infrastructure for physics, computations, and material science. As we move into the 21st century, Livermore and its sister laboratories will continue doing what they do best—science in the national interest.

■ Jeff Wadsworth is Deputy Director for Science and Technology.

The Joint Genome Institute
Decoding the Human Genome

Oh, for a decoder ring! Divining the sequence of chromosomes 5, 16, and 19 is a 24-hour-a-day job at the Joint Genome Institute.

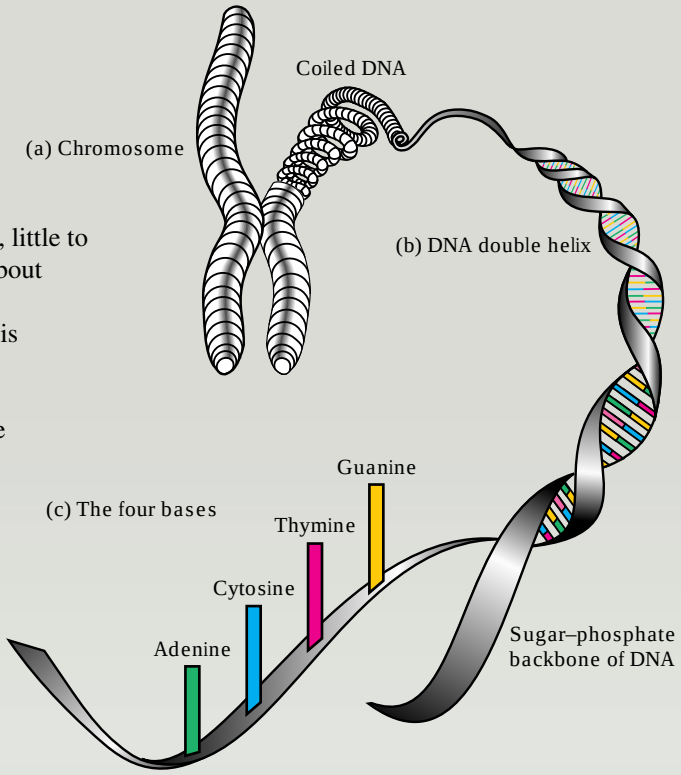
Tucked away in a light industrial park in Walnut Creek, California, about 35 miles north of Livermore, is the Joint Genome Institute (JGI), a collaboration of Lawrence Livermore, Lawrence Berkeley, and Los Alamos national laboratories funded by the Department of Energy's Office of Biological and Environmental Research. There, employees of the three institutions are working together to sequence human chromosomes 5, 16, and 19 for the worldwide Human Genome Project. This spring, the institute will announce the completion of the draft sequence of these three chromosomes, a year ahead of the schedule that was set just 18 months ago.

Sequencing is the process of decoding the 3 billion parts of our DNA, of determining the precise order of the four "bases"—adenine (A), thymine (T), guanine (G), and cytosine (C)—that comprise the entire human genetic code. By the end of 2001, the draft sequence for all 23 chromosomes will be finished, with some gaps and ambiguities still unresolved. The goal is a high-quality human DNA reference sequence by 2003. But even before the final sequence is complete, the draft sequence will be a valuable tool for researchers.

Sequencing our DNA is all about hunting genes. Each of our 100,000 genes is composed of a unique sequence of pairs of the four bases, called base pairs. Earlier research has shown that chromosome 19, for example, is home to the genes that govern lymphoid leukemia, myotonic dystrophy, diabetes mellitus, and a susceptibility to polio, along with about 2,000 others. More than 99 percent of the human DNA sequence is the same for everyone, but the variations in the remaining sequence can have huge implications. And at many places in the sequence, getting the sequence exactly right matters. A single misplaced base among the 3 billion base pairs may have lethal consequences.

Researchers know the approximate locations of genes that govern many medically important traits, but they don't know the exact location or the gene's sequence. For many other genes, their sequence (and often their location) are known, but nothing is known about what they do. And for the other tens of thousands of genes, nothing is known

Lawrence Livermore National Laboratory

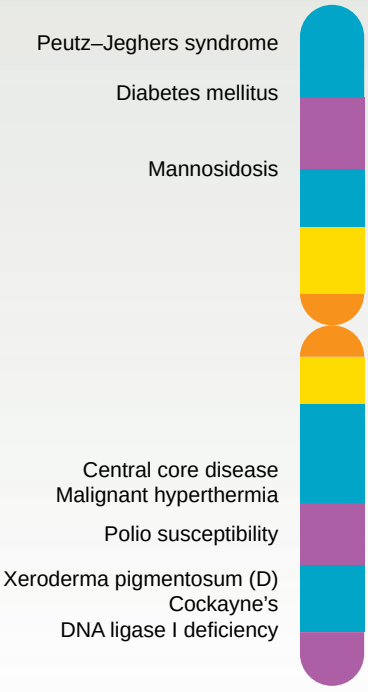


The basics of genetics. Each cell in the human body (except red blood cells) contains 23 pairs of chromosomes. Chromosomes are inherited: each parent contributes one chromosome per pair to their children. (a) Each chromosome is made up of a tightly coiled strand of DNA. The current research lies in the details of the DNA structure, which, in its uncoiled state, reveals (b) the familiar double helix shape. If we picture DNA as a twisted ladder, the sides, made of sugar and phosphate molecules, are connected by (c) rungs made of chemicals called bases. DNA has four, and only four, bases—adenine (A), thymine (T), guanine (G) and cytosine (C)—that form interlocking pairs. The order of the bases along the length of the ladder is called the DNA sequence. The hunt for genes is focused on reading the order of the bases for each DNA strand and determining which parts of the sequence constitute genes.

about their location, little to nothing is known about their sequence, and generally even less is known about their function. A goal of the Human Genome Project, the largest biological undertaking in history, is to locate all the genes on human DNA, determine their precise A, T, C, and G sequence, and then learn their function.

One of the problems in locating and sequencing genes is that among those 3 billion base pairs, only about 4 percent constitute DNA that matters to gene function. "And that 4 percent," says physicist Elbert Branscomb, director of the Joint Genome Institute, "is buried in a sea of junk—DNA whose function, if any, we do not yet understand. Furthermore, a gene does not come in a tidy package, all in one place. Pieces of a gene may be strung out along the DNA strand with lots of irrelevant DNA in between."

Even after a gene is precisely located on a chromosome and sequenced, researchers generally do not know what it does. They will usually need to determine what protein the gene produces and what those proteins do in the cell. Not only do genes and their proteins cause inheritable diseases, but they also determine how we look, how well our body metabolizes food or fights infection, and sometimes even



Research by organizations around the world had determined the location of numerous genes on chromosome 19 before Livermore began mapping it in 1987.

how we behave. In addition, some genes may become altered because of environmental factors, resulting in such maladies as heart disease, many cancers, and possibly some psychiatric disorders. For all of these genes, researchers want to determine how and why they change and what their altered proteins do to the body. For most genes, there are as yet no clear answers.

Completing the draft sequence of the human genome is just the beginning of a long, complicated chain of research events. The gene for cystic fibrosis, for example, was discovered more than four years ago. Although we are still a long way from "fixing" the cellular defect that causes this disease, unraveling the gene's secrets has allowed private industry to deal with a major symptom of the disease.

The Department of Energy is supporting the sequencing of other organisms as well. At other institutions, several viruses and bacteria have already been completely sequenced, as have such larger organisms as baker's yeast (*Saccharomyces cerevisiae*) and the roundworm (*Caenorhabditis elegans*). As part of DOE's Microbial Genome Program, numerous microbes are being sequenced that may be useful for remediation of toxic waste sites or understanding how microbes contribute to carbon sequestration and global warming. Other programs are responsible for sequencing such pathogens as anthrax and smallpox for a better understanding of ways to counter a biological terrorist attack. In addition, considerable work is under way on the mouse, about 85 percent of whose genes are identical to our own (see *S&TR*, December 1999, pp. 14–17). "The similarities indicate which parts of the genome must be really important," notes biochemist Trevor Hawkins, deputy director of the JGI. Comparative genomics—analyzing and comparing the genetic material of different species—is an important tool for studying evolution, the functions of genes, and inherited genes.

Branscomb says, "The goal of our large-scale sequencing work is to help lay down the infrastructure that allows biological scientists to answer questions as efficiently as possible. Genomic studies should soon reveal why some people are able to defend against the AIDS virus and others are not, for example.

"The genome is the basis of all life," he continues. "When we get sick with an infectious disease, what's going on is a war between two sets of genes—ours and those of the virus or bacteria. Someday the medical profession will have better ways to handle these diseases, thanks to work on the genome."

Energy Secretary Bill Richardson dedicated the Production Sequencing Facility of the Joint Genome Institute on April 19, 1999.

In a Production Mode

Livermore, Berkeley, and Los Alamos had been working on the Human Genome Project for several years when the three joined forces to form the JGI in 1996. The offices in Walnut Creek house the JGI's Production Sequencing Facility (PSF). Approximately 120 people work there, half of them in sequencing and the rest in research and development, organization of the vast amount of genetic information being amassed, and other tasks.

One usually thinks of DOE's national laboratories as research and development institutions and not as industrial-scale production facilities. But the JGI has changed that, at least for DNA sequencing. The PSF was formed because the R&D facilities at Livermore, Berkeley, and Los Alamos were not expandable or adequate for the large-scale production required to meet the demanding deadlines of the Human Genome Project. In contrast, the PSF offers large, open laboratory and robotics areas that allow for high efficiency and maximum production. Power and data connections are located overhead to minimize downtime during equipment changes or production line reconfigurations. Even large pieces of equipment are on wheels to facilitate quick changes.

Employees of the Livermore and Berkeley laboratories began moving into the Walnut Creek facility in December 1998, and Energy Secretary Bill Richardson dedicated it on April 19, 1999. Los Alamos employees live a

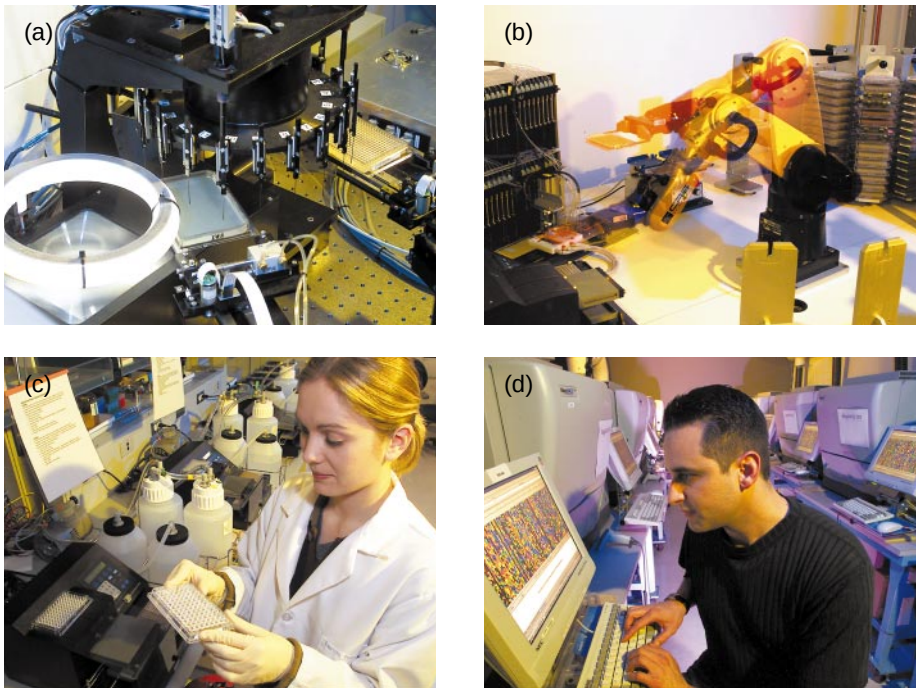
thousand miles from Walnut Creek, so some of their sequencing work continues at Los Alamos. Currently, the only Los Alamos employee at the PSF is Deputy Director Trevor Hawkins, who also serves as director of sequencing.

Some tasks of the Joint Genome Institute are still under way at Berkeley and Livermore until additional space is available at Walnut Creek. The microbial sequencing operation at Livermore led by Jane Lamerdin is, for example, scheduled to move to Walnut Creek in June when a new building opens.

In a highly automated process, the staff at Walnut Creek is identifying human DNA sequence 24 hours a day at a rate of about 10 million Phred-20 base pairs (bp) every day. (Phred 20 is a measurement of quality, indicating a 1 in 100 chance of any base pair being incorrectly identified.) Not so long ago, sequencing 40,000 bp was considered a worthy multiyear thesis project for a Ph.D. student.

Speeding up Sequencing

The sequencing process has many steps. It begins when the DNA to be sequenced is randomly sheared into



The sequencing process at the Joint Genome Institute (JGI) has numerous steps, four of which are shown here: (a) Colonies of cells containing human DNA are selected from a cell culture plate. (b) The CRS robot system places a DNA sample plate onto a plate washer for purification of the DNA. (c) Tijana Glavina, a JGI researcher, removes a plate of purified DNA from a plate washer. (d) Aaron Avila, a JGI research technician, reviews the sequencing data produced by one of JGI's 84 DNA capillary sequencers.

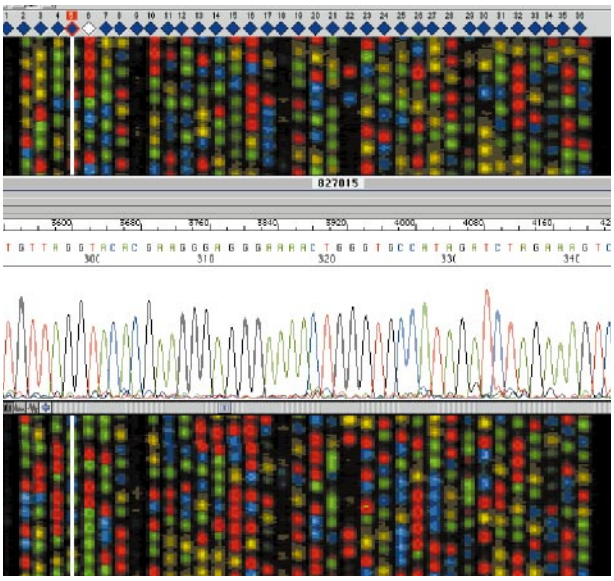
Why DOE and Genome Research?

The formation of the Joint Genome Institute was a logical outgrowth of the involvement of the national laboratories in the Human Genome Project and earlier work on human genetics. Decades ago, the U.S. Congress charged the Department of Energy's predecessor agencies (the Atomic Energy Commission and the Energy Research and Development Agency) with studying and analyzing the consequences of human genetic mutations, especially those caused by radiation and the chemical byproducts of nuclear energy production. A particular focus of research has been the attempt to detect tiny genetic mutations among the survivors of the Hiroshima and Nagasaki bombings and their descendants.

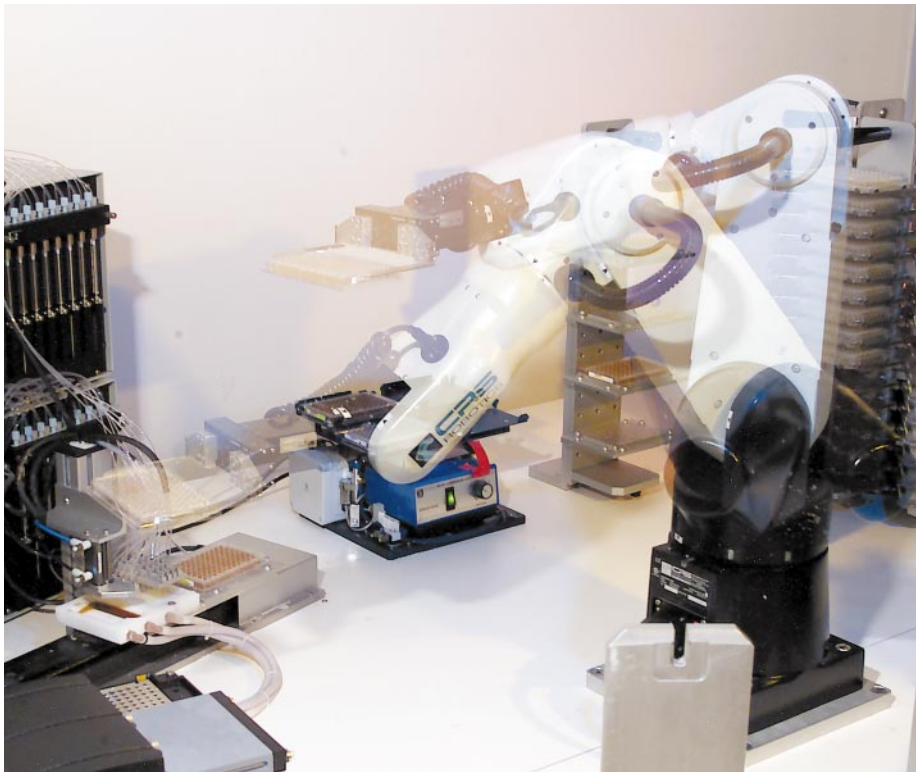
At Livermore, the first biomedical program was chartered in 1963 to study the radiation dose to humans from isotopes in the environment; a natural extension was to explore how radiation and chemicals interact with human genetic material to produce cancers, mutations, and other adverse effects. One Livermore project examined three genes on chromosome 19 that are involved in the repair of DNA damaged by radiation or chemicals.

From studies such as these grew the recognition that the best way to study genetic changes was to analyze the entire human genome to obtain a reference sequence. In 1986, DOE was the first federal agency to launch a major initiative to completely decipher the entire human genetic code. A year later, Livermore researchers began studying all of chromosome 19. In 1990, DOE joined forces with the National Institutes of Health, which had its own research under way, to kick off the Human Genome Project.

In 1994, DOE expanded its genomic research with the Microbial Genome Initiative to sequence the genomes of bacteria of likely interest in the areas of energy production and use, environmental remediation, and waste reduction. Such microbes live under extreme conditions of temperature and pressure and could be engineered for such practical purposes as waste control and environmental cleanup.



The four colors in this chromatogram represent the four bases that make up our DNA: green is adenine (A), blue is cytosine (C), yellow is guanine (G), and red is thymine (T). Each fragment of DNA differs from the next fragment by one base, and the dye indicates the terminal base of each fragment. The order of the colors indicates the order of the bases and hence the sequence of the DNA.



An automated platform centered around an articulated robot made by the robotics firm CRS is used to isolate DNA samples from cellular debris and purify them for sequencing. The Joint Genome Institute uses two of these robots, which, together, can process nearly 31,000 samples every day. Here, one of the CRS robots is placing one plate of 96 DNA samples onto a plate washer to remove cellular debris.

overlapping chunks of about 150,000 to 200,000 bp. Many clones or identical copies are made, which are then cut into smaller overlapping fragments of 2,000 to 4,000 bp and cloned again in a culture of *E. coli* bacteria. The DNA is then purified to remove all cellular debris.

Next, four nearly identical reactions are run in a plate with 96 tiny wells. During the reaction, an enzyme copies the input DNA to produce fragments that differ from one another by one base. Four fluorescent dyes are added to the mix. Each dye is attracted to one and only one base.

Next, in a process known as electrophoresis, an electric current is applied to the labeled fragments. Because the DNA itself has a negative charge, the many fragments migrate at different rates depending on their size: smaller ones move faster than larger ones. As the fragments migrate past a certain point, a scanning laser beam excites the dyes on the DNA fragments to indicate which base is on the end of each fragment. Then another group of labeled DNA fragments, one base longer than the previous group, passes the laser scanner, indicating the identity of that terminal base. The process continues with each set of fragments one base longer than the previous set. The fluorescent signals are captured and digitized, resulting in a four-color chromatogram showing peaks that represent each of the four DNA bases. At this point, the order of the colors is the order of the bases and therefore the sequence of the DNA.

About a year ago, the PSF replaced a labor-intensive and space-consumming electrophoresis process with a commercially developed, automated one. It employs machines with tiny capillary tubes that fit into the 96 wells and through which the samples pass as the laser scans them. Hawkins says, “If the time and labor savings weren’t

enough, the capillary machines also produce higher quality data and can read longer fragment lengths."

After the bases are read, computers reassemble the overlapping fragments into long continuous stretches of sequenced DNA that are analyzed for errors, gene-coding regions, and other characteristics. This process is repeated over and over for all of the chunks of DNA that make up a chromosome.

The front end of the operation, where the chunks of DNA are cut, involves the most skilled handwork. Virtually all other facets of the process have been automated, using robots such as the one shown on p. 8.

Molecular biologist Paul Predki manages the draft sequencing operation at the PSF. Paul Richardson, manager of research and development and also a molecular biologist, works with Predki's staff to find ways to improve the production process. Richardson and his team are on the lookout for ways to cut out steps, develop new materials, and increase automation. They are also working to reduce the volume of reagents used. A major development has been new plates with 384 wells, four times the capacity of the 96-well plates.

These changes in instrumentation and methodology, combined with a physical reorganization of laboratory operations more in line with an industrial production setting, have resulted in remarkable increases in the amount of DNA that can be sequenced. Production is measured in the number of lanes run through the capillary machines (or earlier through the gel plates). Production has increased spectacularly during the months that the JGI has been in operation. In January 1999, 113,000 lanes were run; in December 1999, 823,000 lanes were run.

Because of a continuing stream of improvements, the schedule for the Human Genome Project has been revamped several times. The goal now is for a finished, fully sequenced genome by 2003, two years earlier than originally planned.

Genomes of Microbes, Too

For the overall genomic effort, sequencing the genomes of microbes has both short-term and long-term benefits. In the short term, researchers such as Jane Lamerdin and her team are studying specific microbes that may be helpful in environmental remediation. Looking to the longer term, we will learn more about the microbial role in the overall "metabolism" of Earth. For an increasing number of microorganisms, microbiologists can proceed from a complete knowledge of an organism's genomic blueprint to its consequent activities and behaviors. "With our information, biologists will have a better understanding of how organisms interact and work together in a given environmental niche," says Lamerdin.

Microbes are thought to make up more than 60 percent of the Earth's biomass. They are found in every environment, thriving in extremes of heat, cold, radiation, pressure, salinity, acidity, and darkness, often where no other forms of life are found and where nutrients come only from inorganic matter.

It is precisely this ability to thrive in apparently bizarre environments that makes microbes potentially so

Ethical Concerns about Genomic Discoveries

Even before the formal beginning of the Human Genome Project in 1990, project managers, researchers, and lawmakers recognized that increasing knowledge about human biology and personal genetic information would raise a number of complex issues for individuals and society. In response to Congressional mandates for identifying and defining such issues and developing effective policies to address them, the Department of Energy and the National Institutes of Health have devoted 3 to 5 percent of their annual Human Genome Project budgets to studies of the project's ethical, legal, and social implications (ELSI).

Such implications include the ability to predict future illnesses well before any symptoms or medical therapies exist; the privacy and fair use of genetic information with respect to employers, insurers, direct marketers, banks, credit raters, law enforcement agencies, and others; the availability of genetic information in largely unprotected data banks; and the possible discriminatory misuse of genetic information. One possible misuse of the Human Genome Project is that genome research and the wide use of genetic screening could foster a new genetic underclass, leading to a host of new societal conflicts.

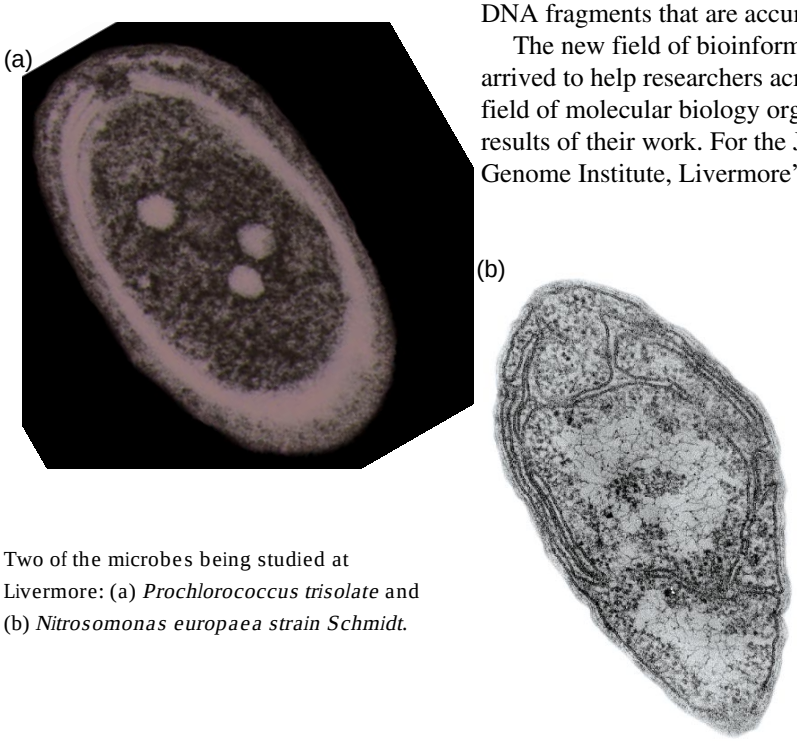
With these concerns in mind, the ELSI program emphasizes the privacy of genetic information, its safe and effective introduction into the clinical setting, fairness in its use, and professional and public education. One of DOE's major commitments is to the Human Genome Management Information System, which disseminates information on all aspects of genome research.

The ELSI program has become a model for others around the world and has led to the establishment of similar programs as part of other research activities.

The Gene Letter is a free, online quarterly newsletter on ethical, legal, and social issues in genetics for interested professionals and consumers. See www.genesage.com/geneletter/.

useful in environmental remediation. Of particular interest to DOE is the growing amount of excess carbon dioxide (CO_2) in the atmosphere and the role of microorganisms in global carbon sequestration. Lamerdin's team is sequencing five microorganisms that all use CO_2 as their sole carbon source (as opposed to an organic carbon source) and that are fairly common within their respective ecosystems. Two soil-dwelling microbes, *Nitrosomonas europaea* and *Rhodopseudomonas palustritis*, carry out chemical functions that make them possible candidates for use in the treatment of contaminated soil and water. This particular species of *Rhodopseudomonas* is also important in carbon cycling because it degrades and recycles components of wood, the most abundant polymer on Earth. A third terrestrial species of microbe being sequenced (*Nostoc punctiforme*) enters into symbiotic associations with fungi and lichens, relationships that are relevant to carbon cycling and sequestration in tundra.

The JGI is also sequencing two ubiquitous marine bacteria, *Prochlorococcus marinus* and *Synechococcus*. The former is intriguing because it has adapted to a wide range of light conditions at the various depths of its ocean habitat. It is also speculated to be the most abundant photosynthetic organism on the planet. In these microbes' genomes, researchers are looking for more information on the way they use CO_2 and nutrients in their environment to better understand their growth properties, which are often affected by global climate changes.



Two of the microbes being studied at Livermore: (a) *Prochlorococcus trisolate* and (b) *Nitrosomonas europaea strain Schmidt.*

All That Information!

What happens to the ever-expanding sequence data for all of the chromosomes in our DNA? Estimates are that if the sequence for the whole genome were printed out, it would fill 200 Manhattan-size telephone directories. And that does not count the annotation and additional data about specific genes and DNA fragments that are accumulating.

The new field of bioinformatics has arrived to help researchers across the field of molecular biology organize the results of their work. For the Joint Genome Institute, Livermore's Tom Slezak is responsible for the flood of data. Slezak, a computer scientist, has been working on the Human Genome Project for many years and notes, "The challenge is keeping up with the extraordinary rate of change and growing masses of information within the industry."

The institute participates in the most widely used database for genomic data, which is at the National Institutes of Health. The NIH's National Center for Biotechnology Information creates public databases, conducts research in computational biology, develops software tools for analyzing genome data, and disseminates biomedical information. GenBank is in partnership with two other major repositories, the European Molecular Biology Laboratory and the DNA Data Bank of Japan, to exchange data. Submissions to any one of them show up at the other two within a day, with consistent accession numbers. Last December, chromosome 22 made history as the first human chromosome to be completely sequenced and deposited in GenBank.

All parties recognize that continued investment in current and new databases and analytical tools is critical to the success of the Human Genome Project and to the future usefulness of the data it produces. These databases are already helping bioscientists in their quest to diagnose and treat disease.

After the Draft

By mid-2000 when the draft sequence is complete, work on finishing the sequence for chromosomes 5, 16, and 19 will shift to the Stanford Genome Center where the sequencing process will continue to fill in gaps. Stanford joined the JGI in October 1999.

Generating the draft sequence is requiring researchers to sequence each

piece of DNA about five times. Producing the highest quality sequence will require an additional two to five times so that each piece is sequenced seven to ten times. To ensure the highest level of confidence—and perhaps to uncover important individual differences—researchers may eventually sequence most biologically or medically important regions even more exhaustively. The error-rate goal for the finished sequence is 1 error in 10,000 bases.

Back in Walnut Creek, post-draft sequencing efforts will shift to the mouse, whose genome is remarkably similar to ours. There is an almost one-to-one correspondence between genes in the two species, although they sometimes occur in different places in the two genomes. The human genome is, of course, also nearly identical to that of chimpanzees, and it even shares many common elements with the genome of the lowly fruit fly. But the mouse, with its small size, high fertility rate, and experimental manipulability, offers great promise for studying the genetic causes and pathological progress of diseases. Studies of the mouse will also help us better understand the genetic role in disease susceptibility.

The JGI will continue collaborative sequencing work with researchers at other institutions. Various projects with scientists at Harvard, Yale, the Massachusetts Institute of Technology, Johns Hopkins, and University of California campuses at San Francisco and Davis involve in-depth sequencing of chromosomes 5, 16, and 19 as well as work on the mouse and other organisms to learn more about cancer, liver disease, autoimmune disorders, and other diseases. Tim Andriese, the institute's collaborative liaison, notes, "Producing sequence data for collaborators follows our primary goal—to provide the research community with essential sequence data."

Another focus of future work at the JGI is functional genomics, which, as its name implies, interprets the functions of human genes and other DNA sequences. This work requires that resources and strategies be developed for large-scale investigations across whole genomes. At the JGI, Edward Rubin manages this effort, which now involves several small pilot projects being carried out at many different DOE laboratories.

The ultimate goal of the work at the JGI and elsewhere is to develop a molecular-level understanding of how we develop from embryo to adult, what makes us work, and what causes things to go wrong. "Solving the genetic code of humans and other creatures is a huge, important quest," says Branscomb, "It will allow us to solve the mystery of mysteries: how does life work? Then we can really begin to address human suffering."

—Katie Walter

Key Words: bioinformatics, DNA, functional genomics, Human Genome Project, Joint Genome Institute (JGI), microbial genetics, mouse genome, sequencing.

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Also see the following Web sites:
- *The Joint Genome Institute, jgi.doe.gov/*
- *The Human Genome Project, www.ornl.gov/hgmis/*
- *The DOE's Human Genome News, www.ornl.gov/hgmis/publicat/hgn/hgn.html*

About the Scientist

ELBERT BRANSCOMB is the director of the Department of Energy's Joint Genome Institute (JGI), a collaboration of Lawrence Livermore, Lawrence Berkeley, and Los Alamos national laboratories responsible for the sequencing of human chromosomes 5, 16, and 19. Branscomb received his B.A. in physics from Reed College in 1957 and his Ph.D. in theoretical physics from Syracuse University in 1964. He joined Lawrence Livermore in 1964 as a theoretical physicist and became a senior biomedical scientist in 1969. In 1996, he became director of JGI.

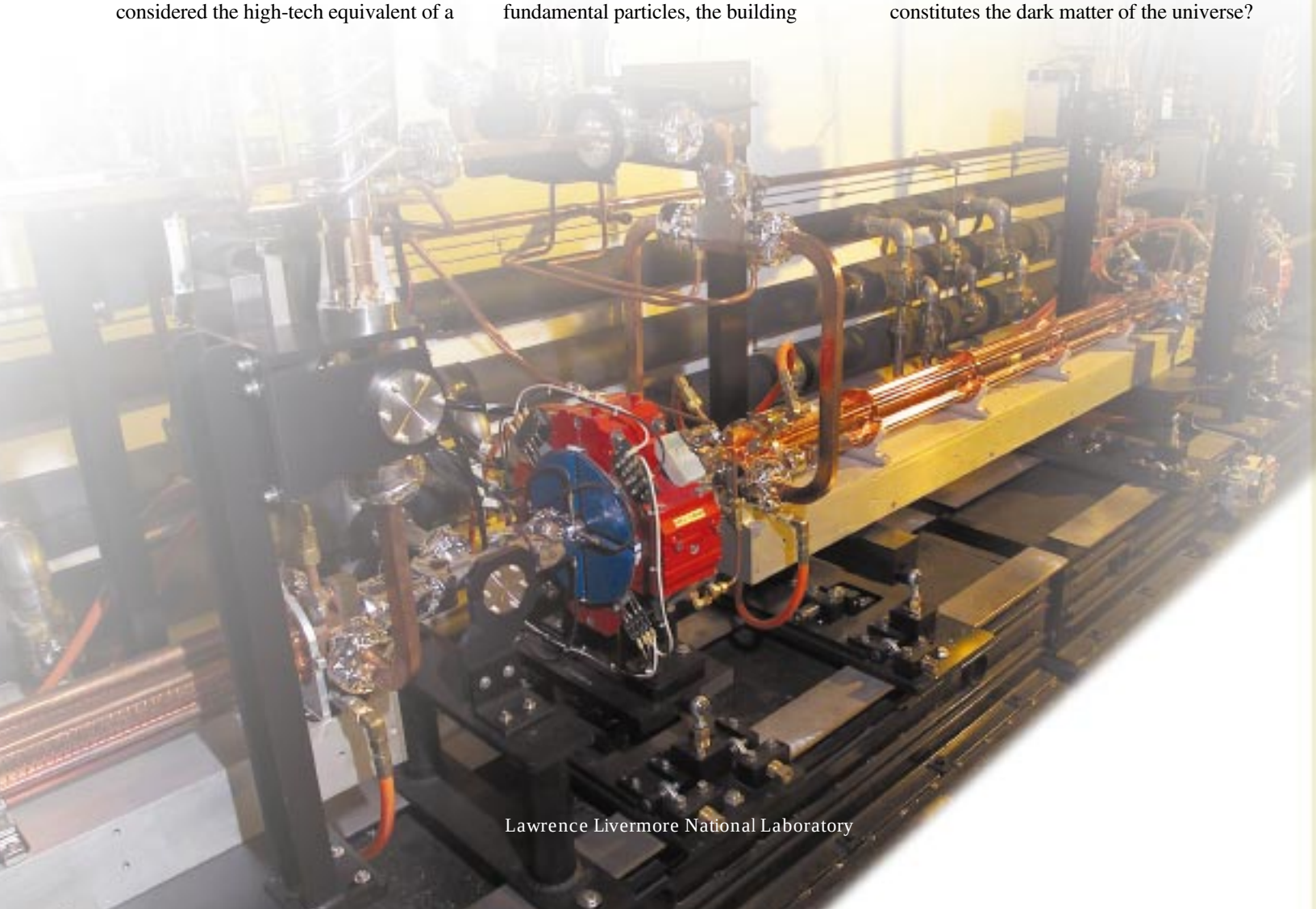
Branscomb's professional activities include being a member of the Editorial Board of the *Journal of Computational Biology* and of the National Cancer Institute's Cancer Genetics Working Group. From 1996 to 1998, he was a member of the Panel of Scientific Advisors for the National Institutes of Health–National Council of Human Genome Research's Pilot Project for Large-Scale Sequencing of the Human Genome. He is also the coauthor of numerous scholarly articles, primarily on scientific research related to the human genome.

The Next Accelerator for Revolutionizing Physics

The Next Linear Collider—Getting More Bang for the Buck in Particle Physics.

HIGH-energy physics has always been a frontier discipline in science, driving technological innovation and pushing the limits of what we know about the disparate but interconnected worlds of cosmology and elementary particles.

That being the case, the proposed Next Linear Collider (NLC) could be considered the high-tech equivalent of a frontier outpost—at the edge of a new world. The NLC is being developed by a collaboration of four Department of Energy national laboratories—Stanford Linear Accelerator Center (SLAC), Lawrence Livermore and Lawrence Berkeley national laboratories, and Fermi National Accelerator Laboratory (FNAL or Fermilab). It will accelerate fundamental particles, the building blocks of our universe, to energies in the teraelectronvolt (TeV) range—that's a trillion (10^{12}) electronvolts. Physicists believe that the NLC, and other extreme high-energy particle accelerators like it, will lead the way in answering some of the most fundamental questions of science: How do particles acquire mass? What is the structure of space–time? What constitutes the dark matter of the universe?



Lawrence Livermore National Laboratory

Conceptual drawing of the Next Linear Collider, housed in a tunnel approximately 30 kilometers long inside which are two opposing linear accelerators (linacs). Within each linac, the electrons (or positrons) are accelerated within thousands of copper accelerator structures, each made up of more than 200 precision-machined copper cells (see inset). Precision machining and alignment of the cells is crucial to keep the beam bunches sharp, small, and straight.

Karl van Bibber, who leads the Lawrence Livermore effort for the NLC collaboration, notes that each decade in the 20th century has had major discoveries in high-energy physics, while continually pushing the definition of "high energy" to ever-higher values. Physicists are almost certain that truly revolutionary discoveries will be made within the next 10 years.

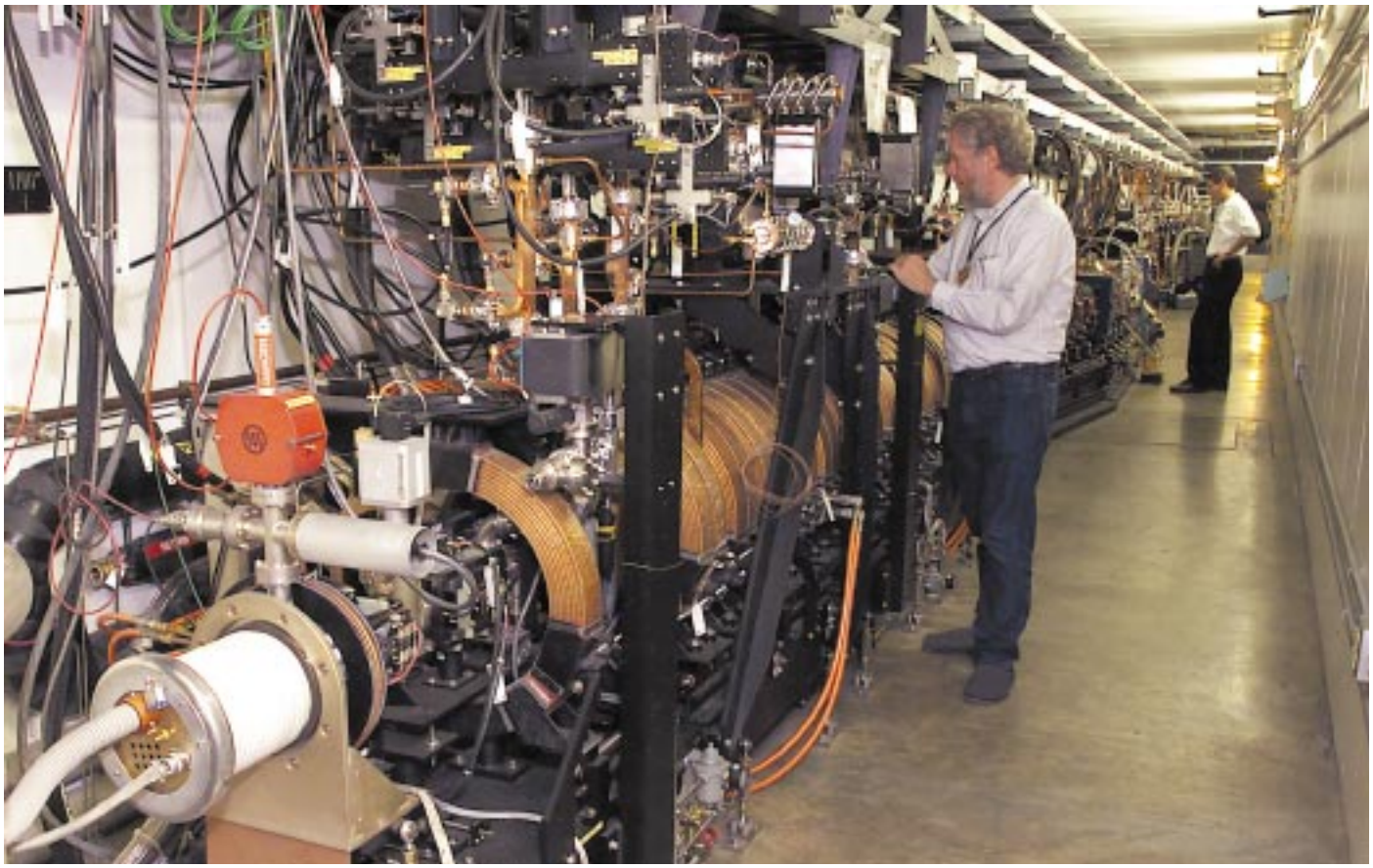
In the landscape of high-energy physics, three regions of intense activity center around major facilities: the European Laboratory for Particle Physics (commonly known by the acronym CERN from its former name) in Geneva, the Japanese High Energy Accelerator Research Organization (KEK) in Tsukuba, and Fermilab and SLAC in the U.S. Fermilab's 2-TeV Tevatron is now the highest energy machine in the world, but CERN's Large Hadron Collider will operate at 14 TeV once it is completed in 2005. Both of these machines are proton colliders and may well make the next discoveries in high-energy physics.

Van Bibber explains the proton collider process: "Colliding beams of protons is like smashing together two beanbags. You're looking for the rare events where two beans inside them will undergo a hard, pointlike collision." Because protons are made up of many quarks and gluons, new heavy particles will be created only if a single quark or gluon might collide with its counterpart in the other proton. Thus, only a small fraction of the protons' total energy goes into creating new heavy particles. The other constituents merely create a mess of background particles of no interest.

"Studying proton collisions is a high-background and low-statistics business," notes Van Bibber. "An electron–positron collision, in comparison, is often much more fruitful. Both the electron and the positron are pointlike fundamental objects, so when they collide, the total energy of both goes into creating new particles." As an example of the difference, a proton collider at CERN discovered the intermediate vector boson particles—the W^+, W^-, and Z^0—which are responsible for the weak interactions, including radioactive decay. After five years or so of operation, the total number of Z^0 events created was about 100. CERN's Large Electron–Positron collider created 12 million Z^0s and the Stanford Linear Collider created half a million spin-polarized Z^0s.

For more than a decade, a coordinated worldwide research and development program has worked toward developing a TeV-scale electron–positron linear collider. At present, two preconceptual design proposals may be the contenders for future construction: the NLC, on which the U.S. and Japan are working to a common baseline design, and the TeV Energy Superconducting Linear Accelerator (TESLA), a European effort centered at DESY (Deutsches Elektronen–Synchrotron), the German high-energy physics laboratory.

The NLC is an electron–positron linear collider designed to begin



The Next Linear Collider Test Accelerator consists of a modulator to convert ac line power into dc pulses and klystrons that are driven by the dc pulses to produce radiofrequency power. The test accelerator also includes pulse compressors that reformat the radiofrequency output into 300-megawatt, 300-nanosecond-long pulses and accelerator structures that then use those pulses to establish the electromagnetic wave on which electrons surf.

operation at 0.5 TeV and ultimately be scaled up to 1.5 TeV. It will be 30 kilometers long and dominated by two opposing linear accelerators, or linacs. Although the NLC is based on mature technology, it still faces the big challenge of cost reduction. As SLAC physicist Marc Ross says, "Our mantra is 'Make it cheaper, make it cheaper, make it cheaper.'"

Van Bibber notes that the elements driving up costs are the tunnel—digging a 30-kilometer tunnel will be expensive—and the linacs themselves. "Luckily, the linac is a repetitive system. You're increasing energy, but not the speed of the particles, because they're already close to the speed of light. So what increases is the relativistic mass, which means we can be repetitive in the linac subsystems."

The basic linac has a modulator that converts ac line power—the same power one gets from a wall plug—into dc pulses to drive the klystrons (oscillators) that produce 75 megawatts of peak radiofrequency power at 11.4 gigahertz. Pulse compressors then reformat this radiofrequency output into 300-megawatt, 300-nanosecond-long pulses. The pulses are delivered to the accelerator structures, which establish the traveling electromagnetic wave on which the electrons surf.

"We're trying to build the linac for under $1 billion, even for as low as half a billion. That means we must get the subsystems down to $100 million each. The modulators and accelerator structures are where we, at the Lab, are focusing our efforts," says van Bibber.

Modulating Power with Solid State

For the NLC, the modulator must be designed to keep costs down and still be efficient, reliable, and serviceable. Efficiency is a key criterion, notes Livermore engineer Ed Cook, who spearheads the effort to develop a modulator to fit the bill. "A 1-percent decrease in efficiency anywhere between the wall plug and the beam increases the required ac line power by a megawatt and adds a million dollars a

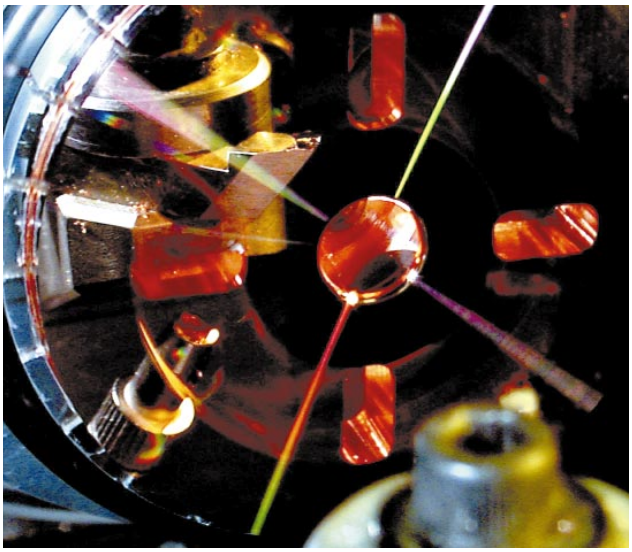
year to the operating costs." This small efficiency decrease would also have a ripple effect and increase the cost of components—from the modulator power supplies to the cooling systems required to remove the waste heat.

The new modulator for the NLC is based on solid-state technology that will provide significant improvement over previous equipment. Modulator efficiency is determined largely by the shape of the energy pulse produced. The ideal pulse shape is rectangular, because the energy in the pulse rise-time and fall-time is not usable. The waveform's rise and fall in old-style modulators (hydrogen thyratron-fired pulse-forming networks, a technology dating from the 1940s) were less than precipitous, so energy was wasted. The advent of high-voltage and high-current solid-state switches—similar to those used in modern rapid transit systems—has made it possible to generate the required voltage pulses more efficiently. The goal is to have a rise-time and fall-time of less than 200 nanoseconds and a usable interval of more than 1.5 microseconds.

Designed as a modular part, the solid-state modulator can be pulled out and replaced easily, keeping maintenance costs down. The near-term goal is to design and make a prototype of a 500-kilovolt, 2,000-ampere modulator that will drive eight klystrons. The NLC will need about 400 of these modulators to drive its 3,200 klystrons.

The modulator is in the prototyping phase. Late in 1999, Livermore demonstrated a single modulator cell, consisting of a solid-state switch, a capacitor, and a transformer core, and delivered a five-cell stack to SLAC for measurement. "Results were good," says Cook. "We were striving for 75-percent efficiency from the modulator, an improvement over the 60-percent efficiency of old-style modulators."

By spring this year, Bechtel Nevada—a key player on the Livermore team—will finish fabricating and assembling an additional 70 cells. Those, with the five already at SLAC, will comprise a complete modulator.



About 200 copper cells—each differing slightly in its interior dimensions—are contained in each of the long tube structures in which the electrons and positrons are accelerated. The cells must be diamond-turned to tight tolerances and then precisely stacked and bonded together.

Accelerating down the Line

The NLC also will require between 5,000 and 10,000 structures—long tubes in which the beam flies in the machine—to accelerate the separate bunches of electrons and positrons to the interaction region. Each structure has about 200 precision copper cells. Each cell differs slightly from the others in its interior dimensions, with fabrication and alignment tolerances at the micrometer level.

Livermore, KEK, and SLAC worked together to build a 1.8-meter prototype structure. Livermore's role was to develop a procedure for diamond-turning these cells to the required tolerance and to fabricate them. KEK stacked and diffusion-bonded the cells into a single copper structure, and SLAC completed and beam-tested the final assembly in June 1998.

"The structure is very unforgiving," notes engineer Jeff Klingmann, Livermore's contact for this work. "Each pulse contains 106 bunches of particles. The oscillating electromagnetic field pushes the bunches down the pipe at higher and higher energies. If one bunch wavers even a bit off center, it instigates an electrical field in its wake (a so-called wake field) that will affect the bunches following it and cause them to stray further off center. In short order, the beam fuzzes out and crashes into the cell walls. Our goals are to keep the beam very sharp, small, and straight and to develop a design that minimizes wake fields."

The prototyping work highlighted two needs that must be addressed before cells can be manufactured in the millions: researchers must minimize the amount of diamond-turned machining, which is an expensive and time-consuming process, and they must design a cell assembly procedure that is automatically immune to alignment errors.

Klingmann says, "Our proposed new mechanical design reduces diamond-turning by 80 percent because our materials scientist John Elmer came up with a design in which only those surfaces that need to be completely smooth for bonding need to be diamond-turned. Our design also has interlocking features so each cell is necessarily aligned to its neighbor."

The tolerances require precision machining and assembly, but cost pressures push the other way. As Elmer explains it, "The challenge is to make each one of these cells as cheap as a rollerskate wheel. We're looking at each step in the manufacturing and assembly process to cut costs. Casting in a vacuum means we get less porosity, but that costs $50 per cast. We need to get the cost down to $5." Elmer has also been examining cost-efficient ways to bond the cells together.

Improving Positron Targets

Creating beams of positrons turns out to be a difficult problem. As Livermore engineer Charlie Landram explains, "Positrons don't exist naturally. They're produced by crashing a high-energy electron beam onto a target—in this case, made of a tungsten–rhenium alloy. The result is a low-energy shower of electrons, gamma rays, and positrons. The positrons are captured and boosted in energy, then injected into a damping ring to cool the beam down, allowing it to be squeezed into a tiny cross-sectional area."

The targets that are planned for the NLC are similar to those currently being used at the Stanford Linear Collider, where a recently removed target showed damage more serious than expected. This postmortem discovery brought the NLC positron target issue to the fore, because the NLC target must produce more than 20 times the number of positrons and handle power about 10 times higher than Stanford's. Livermore scientists modeled the Stanford target using Monte Carlo particle codes and thermohydraulic models, while Los Alamos National Laboratory scientists evaluated the damaged target.

"All our calculations show us to be just below the critical heat flux, which means there is very little margin to avoid a burnout condition. We're looking at ways to keep future targets from reaching these fluxes under more extreme conditions," says Landram. "Right now, we're considering a target with a larger radius, which could accommodate the extra heat, and improved heat paths to the cooling tubes. We're still examining the damage to the Stanford Linear Collider target and considering the best ways to carry off the heat. We need a better handle on what the experiments are doing to the target so we don't encounter problems in the NLC."

One Success Encourages Another

The NLC builds on the success of the B Factory (see *S&TR*, January/February 1999, pp. 12–14, and *S&TR*, January/February 1997, pp. 4–13). Van Bibber says, "With the B Factory, the collaboration delivered on time and on budget. The machine now holds the world's record for electron–positron luminosity and is still improving. The DOE uses that three-lab partnership as a model for future major facility acquisitions."

These two projects are part of a long line of efforts that include the BaBar detector at SLAC, Brookhaven National Laboratory's PHENIX detector, proton radiography and the Scrounge-atron proton accelerator, the Rare Isotope Accelerator, the Spallation Neutron Source, the Accelerator Production of Tritium, and the Accelerator Transmutation of Waste. The B Factory and the NLC are just the latest accelerator science and technology efforts in which Lawrence Livermore has been involved. Whether performed within Livermore or in partnership with other laboratories in the U.S., this work leverages the Laboratory's strengths in accelerator physics, detectors, engineering, and physics to add value to the nation's accelerator efforts.

—Ann Parker

Key Words: accelerator structure, electron–positron linear collider, high-energy particle accelerator, Next Linear Collider (NLC), positron target, proton collider, solid-state modulator, Stanford Linear Accelerator Center (SLAC), Tevatron.

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About the Scientist

KARL VAN BIBBER is a graduate of the Massachusetts Institute of Technology with a B.S. in physics and mathematics and a Ph.D. in physics. He joined the Laboratory in 1985 as a senior physicist. Since July 1991, he has been group leader for High-Energy Physics and Accelerator Technology in the Physics Directorate. He was recently the project leader for Livermore's work on the B Factory at the Stanford Linear Accelerator Center and is currently the leader of Lawrence Livermore's contributions to the Next Linear Collider collaboration.

A Speckled Look at Saturn's Moon, Titan

THE stars and planets have fascinated human beings since time immemorial. Using the crude telescopes available at the time, the 17th century French astronomer Giovanni Domenico Cassini discovered the division in Saturn's rings and four of Saturn's moons—among them Titan, the largest.

Today, Titan holds particular fascination for astronomers. It is the only moon in the solar system with a thick nitrogen-dominated atmosphere, similar to Earth's, surrounding it. Also as on Earth, Titan's organic chemistry is driven by sunlight. Titan is several hundreds of degrees colder than Earth and has a methane-rich atmosphere, but its chemistry seems in some ways to be like that of Earth before life appeared.

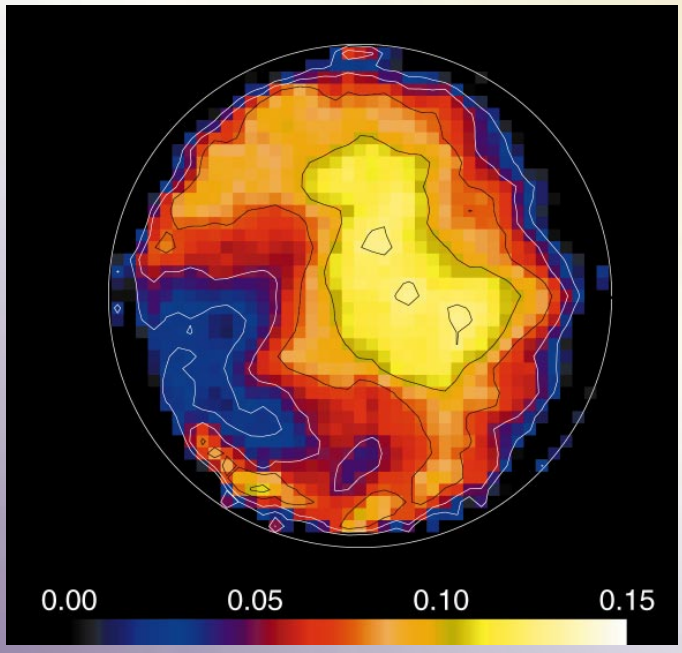
Although imaging methods have improved enormously since Cassini's day, Titan is still difficult to see. Ultraviolet light changes atmospheric methane gases into a thick, smoglike haze that sits in the upper atmosphere. Imaging techniques that use visible light cannot penetrate this haze. When the Voyager spacecraft flew by Titan and took photographs with a telescope that used visible light, the resulting photos showed only a bright blob.

Infrared light can partially penetrate the smog. But Titan is so far away that conventional infrared telescopes on Earth also see only a blob because the image is blurred by Earth's atmosphere. The Hubble Space Telescope uses infrared light, but it lacks sufficient resolution to see much detail. Even with these deficiencies, both Hubble and ground-based studies have shown that Titan has a complex surface.

Hungry for more information about Titan and other celestial bodies, Livermore scientists adapted speckle interferometry, an imaging technique developed during the 1980s, for astronomical use. Until recently, speckle interferometry at Hawaii's 10-meter Keck I telescope gave the world the best look at this mysterious planetary moon.

Scientists have suspected for some time that Titan may have liquid seas formed by ethane that has "rained out" of the atmosphere to produce reservoirs of liquid hydrocarbons. Livermore astrophysicists Claire Max and Bruce Macintosh believe that the extraordinarily dark, unreflective area in the lower left corner of the image below could well be an oily, black ocean of hydrocarbon. Brighter, more reflective patches appear to be continents of ice and rock.

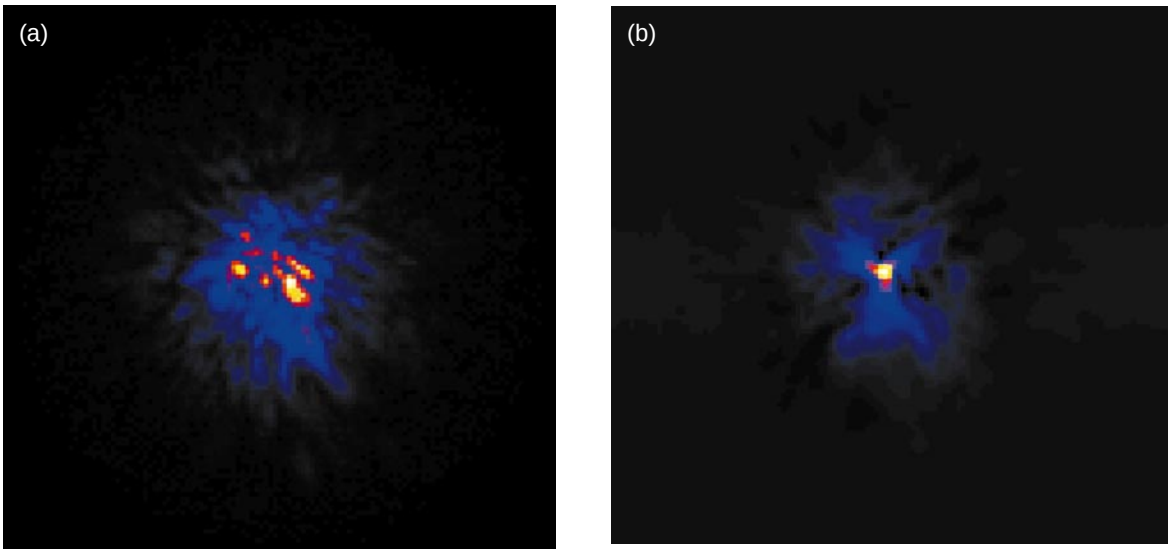
"If Titan does have a sea, it is the only other one in the solar system besides those on Earth, and we would like to know what is going on there," says Macintosh. "Titan seems to be similar to Earth 4 billion years ago, before life formed. Although Titan is too cold for life as we know it, it could be a laboratory for the processes that occurred here on our own planet."



The 2-micrometer albedo (reflectance) of Titan from the Keck I telescope speckle images.

Reflecting the Surface Only

Traditional astronomical imaging uses long exposures to gather as much light as possible into a single image. Because of Earth's atmosphere, that method often results in a fuzzy image for objects that are small or far away. In speckle imaging, several hundred pictures with short exposures are taken to freeze Earth's atmospheric turbulence. The pictures of Titan are taken using specific infrared wavelengths that are transparent "windows" through the methane spectrum, or haze. At wavelengths of 1.9 to 2.1 micrometers, scientists can more easily observe photons reflecting from Titan's surface, and thus the pictures have more contrast than would be possible at other wavelengths.



A complex computer algorithm combines (a) the interference patterns from 100 specklegrams taken over a 90-second period into (b) a single speckle image.

Each exposure of about 100 milliseconds produces a specklegram, which is the pattern caused by the interference of light rays as they travel through Earth's atmosphere. As shown above, a complex computer algorithm combines the interference patterns from 100 specklegrams taken over a 90-second period into a single final image.

These composite images can then be used to measure the reflectance, or albedo, of Titan's surface. Livermore astrophysicist Seran Gibbard adapted a radiative transfer model to separate reflectance data of Titan's atmosphere from those of its surface so scientists can map surface features only. Albedo measurements range from 0 to 1, with 0 being black and totally unreflective and 1 being white. The dark area on Titan that scientists believe may be a hydrocarbon sea has an albedo of nearly zero. The brightest, ice- or rock-like continental area has an albedo of 0.15.

Using speckle imaging, the Livermore team has mapped both of Titan's hemispheres, one of which is shown in the figure on p. 17.

Probing Titan

For several years, speckle imaging has been the best way to view small, distant celestial objects such as Titan. But better ways have been developed. Constructing a final image using speckle imaging takes considerable time on both the telescope and the computer. A faster method that produces almost immediate results is adaptive optics, which allows telescope mirrors to compensate directly for the distortions generated by Earth's atmosphere. An adaptive optics system has been installed at the Keck observatory and has recently produced even clearer images of Titan. (See p. 2 of this issue and *S&TR*, July/August 1999, pp. 12–19.) Spectroscopic data obtained using adaptive optics will also help improve models of Titan's atmosphere.

In late 2004, the most detailed information yet about Titan will begin to arrive on Earth from another source altogether. The spacecraft Cassini, which blasted off in October 1997, will begin to orbit Saturn to learn more about its famous rings, its magnetosphere, and its moons, Titan in particular. The primary contributors to the Cassini program are NASA, the European Space Agency, and the Italian Space Agency.

In November 2004, Cassini will drop a probe called Huygens (named for a Dutch physicist and astronomer) into Titan's upper atmosphere. As it breaks through the cloud deck, a camera will capture pictures of the Titan panorama. Other instruments will measure the organic chemistry of Titan's atmosphere as the probe descends to Titan's surface on the rubber duck–shaped continent visible in the figure on p. 17. Designed by the European Space Agency, Huygens can both bounce and float, so it is prepared for whatever surface it finds. But Huygens will only send information for a few hours because it must operate on batteries. Titan's haze is too thick for solar power. Cassini will continue to orbit Saturn and Titan for years, sending data back to information-hungry, Earth-bound scientists.

—Katie Walter

Key Words: adaptive optics, Saturn, speckle imaging, Titan.

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Remote Sensor Test Range
Proving Ground for Tomorrow's Sensing Technologies

IT'S 1:30 on an August afternoon at Frenchman Flat at the Nevada Test Site. The temperature outside is sweltering. The wind, which blew erratically that morning, has settled down to a steady southwest to northeast, clocking in at 24 kilometers per hour. Dust and grit whip through the heated air, coating clothes and skin. Metallic surfaces burn when touched with a bare hand.

It's perfect weather.

Perfect, that is, for open-air tests at the Remote Sensor Test Range (RSTR). The RSTR, operated jointly by Lawrence Livermore and Bechtel Nevada, is the proving ground for nascent remote-sensing technologies developed by the Department of Energy's national laboratories. Five laboratories conduct experiments at the range: Lawrence Livermore, Los Alamos, Sandia, Pacific Northwest, and Brookhaven.

Home on the Range

The range had its genesis in 1984 when DOE was looking into the pros and cons of liquefied natural gas as a possible energy source. Needing more information about the safety aspects of this gas, DOE developed a site for large-scale chemical releases at Frenchman Flat at the Nevada Test Site. Through 1988, DOE and Lawrence Livermore conducted a series of large-scale tests at this site, including tests of ammonia and nitrogen tetroxide spills and releases of hydrogen fluoride.

By 1994, interest in remote-sensing technology had increased to the point that a site was needed to test these technologies on open-air gas releases. The spill test facility, now called the HAZMAT Spill Center, was chosen as the best site. "There were several critical elements in its favor," explains Lawrence Livermore physicist Henry Goldwire, project leader for the RSTR. "Frenchman Flat is isolated from populated areas and has unusually stable weather, particularly wind patterns." The Laboratory's RSTR group and Bechtel Nevada joined up to improve the site's communications, site power, and chemical release mechanisms.

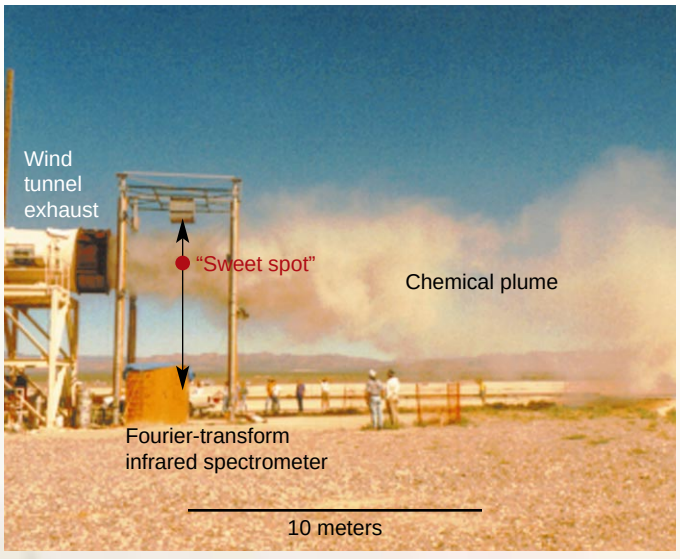
In developing the range, the Livermore team, then headed by Dennis Slaughter, sat down with sensor developers to discuss what kind of sources would be best for field tests. As Goldwire notes, "You can't just open a gas canister on the ground, let the gas escape, and point your instrument at it. If you do, you can't control the release or verify your results. In other words, you have no 'ground truth.'"

The RSTR group developed a reliable and verifiable chemical release system based on a wind tunnel originally built in 1987 for hydrogen fluoride tests. In addition, two stack sources were developed later that more closely imitate the conditions under which chemicals must be sensed. Ultimately, the sensors will be used in aircraft, but as tested at the RSTR, they are not usually flyable systems.

Wind-Tunnel Truth

In the wind-tunnel-based source designed by Lawrence Livermore engineer Steve Yakuma, test chemicals are injected into the tunnel, atomized, and mixed with ambient air before being released horizontally at high velocity (about 1,540 cubic meters per minute).

The wind tunnel provides a calibrated and well-characterized, 2-meter-diameter chemical plume at which



The range's wind tunnel exhaust plume creates an open air gas calibration cell target for remote sensors. The point at which most sensors aim is called the sweet spot.

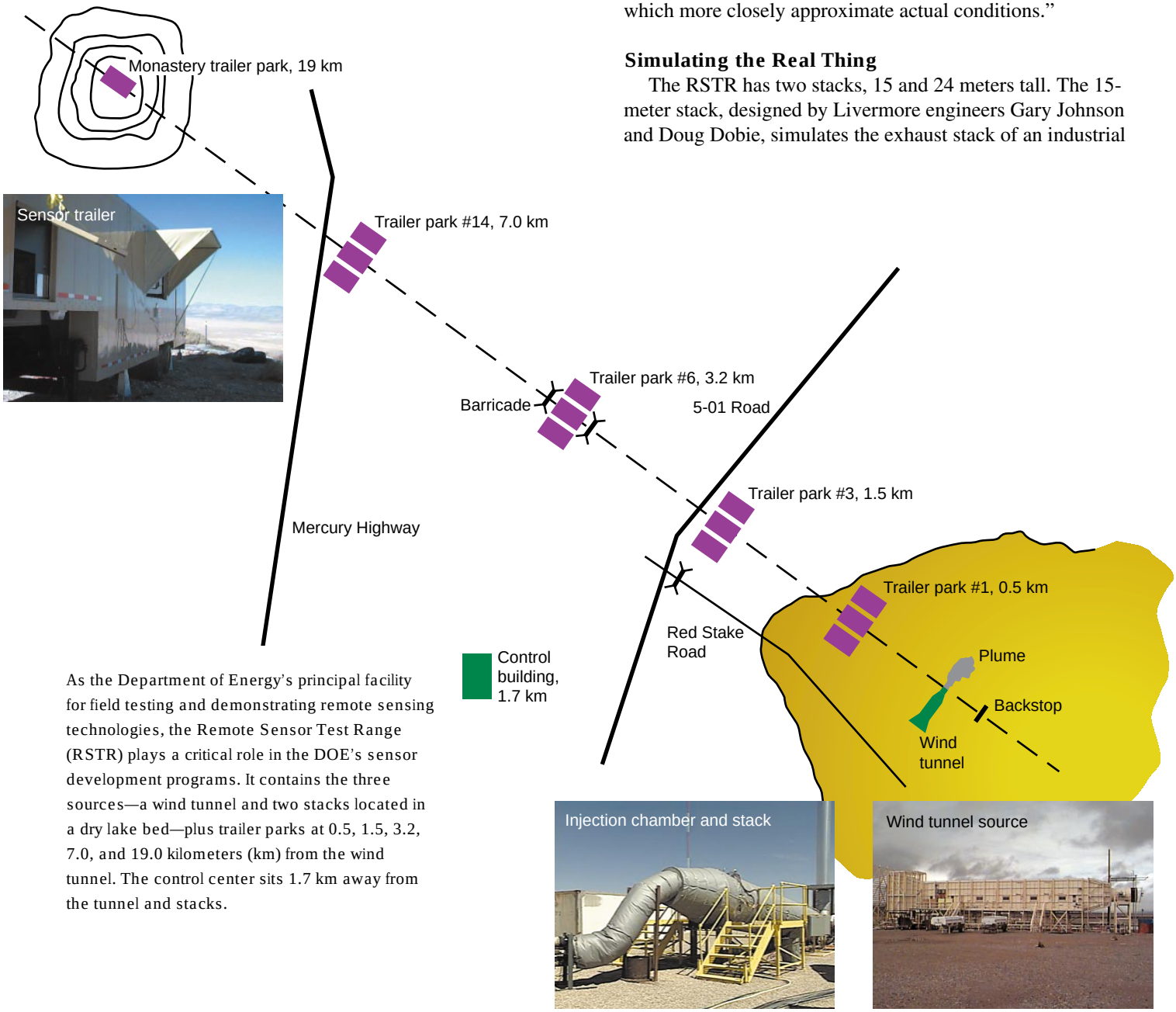
developers can aim their remote-sensing instruments. Plume concentrations of up to four gases can be independently controlled over a range of 1 to 1,000 parts per million. The concentration is determined by measuring the mass flow of the chemical as well as the airflow through the wind tunnel and taking the ratio of the two. "The system is expertly operated and maintained by mechanical technicians Jack Robson and Tom Schaffer. We've not had a single day lost to source failure in our five years of operation," notes Goldwire.

Diagnostics include infrared gas sensors inside the wind tunnel and a Fourier-transform infrared (FTIR) spectrometer at the exit to the wind tunnel. These diagnostics provide important backup data that validate the wind tunnel's performance and provide the ground truth against which sensor developers can compare their results.

"The wind tunnel was designed to be a research tool," Goldwire said. "It's a place where sensor developers can prove their technologies. Technologies that are further along the development path can be tested on our stack sources, which more closely approximate actual conditions."

Simulating the Real Thing

The RSTR has two stacks, 15 and 24 meters tall. The 15-meter stack, designed by Livermore engineers Gary Johnson and Doug Dobie, simulates the exhaust stack of an industrial



As the Department of Energy's principal facility for field testing and demonstrating remote sensing technologies, the Remote Sensor Test Range (RSTR) plays a critical role in the DOE's sensor development programs. It contains the three sources—a wind tunnel and two stacks located in a dry lake bed—plus trailer parks at 0.5, 1.5, 3.2, 7.0, and 19.0 kilometers (km) from the wind tunnel. The control center sits 1.7 km away from the tunnel and stacks.

facility. It can independently control and release up to six chemicals at a time. "Start carts" (the kind used to warm up jet engines) produce a 200°C air stream that projects and evaporates the injected chemicals. The stack provides realistic scenarios as the chemicals exit the stack and are whipped about by the wind. In addition, the stack can handle a wider range of chemicals than the wind tunnel source, including some that are highly toxic or have high boiling points. The stack releases the chemicals into a 0.56-meter-diameter plume of fully mixed, heated air and chemicals. Chemical concentrations can vary from 10 to more than 8,000 parts per million.

The stack also has an FTIR to provide ground truth that developers can check against their sensor results. Goldwire notes that the source flow data, together with FTIR data provided by Livermore chemist August Droege, have withstood all challenges from the users.

Preparing and Delivering on Test Day

Planning for each test series begins in January. The sensor developers present their needs; Goldwire—with guidance from DOE—helps set priorities. "Over the years, the users have learned to work together, negotiate, and do a little horse trading at the table," says Goldwire. "They've also found out they can piggyback on each other's experiments." It takes about 20 weeks to plan and prepare for the annual 4- to 6-week series of tests—not surprising, considering the complex nature of the tests and the wide range of chemicals involved. For example, in the Mountain Lion test series of 1998, five groups from three national laboratories fielded sensor systems from two trailer parks and from four types of aircraft. During that test series, a team of 16 operators—eight from the RSTR group and eight from Bechtel Nevada—loaded and released 108 chemicals in 21 test days, with an average of five chemicals per day.

Days are planned to use every minute of testing time to maximum effectiveness. "We try to match the chemicals to the source," explained Goldwire. "For instance, a chemical's physical state and boiling point determine the types and sizes of nozzles used to inject the chemical into the heated air. Acids and bases use different systems. Between runs, we purge the systems with nitrogen. In 24 hours, we can clean up after the previous tests, change out all sources and chemicals, and be ready for the next day's test." Tests are usually conducted for four to five hours each afternoon and occasionally in the early evenings.

For the 21 test days of Mountain Lion, 56 releases were performed with the wind tunnel system and 50 with the two stacks. Plume concentrations varied from 1 to 8,000 parts per million. The data-acquisition systems recorded about 250 channels of data and controlled about 600 system components.

Annual Tests at the Remote Sensor Test Range.

Year/Series	Chemicals	Number of Tests	Hazards
1994 Iguana	11	26	Toxic, flammable
1995 Jack Rabbit	17	20	Toxic, flammable
1996 Kitfox	~30	30	Toxic, flammable
1997 Lynx	~30	4	Toxic, flammable
1998 Mountain Lion	~30	21	Toxic, flammable
1999 Nighthawk	~30	10	Toxic, flammable

"A major factor in our success, year after year, is the dedicated team supporting the range," says Goldwire, "Key individuals have been with the range from its inception." Weather, however, can sometimes preempt the carefully prepared schedule. In Mountain Lion, for instance, four days were lost to El Niño storms.

In addition to the requests put in by users, the Livermore–Bechtel Nevada team ran three-scenario days for the Mountain Lion test series. These scenario days are essentially final exams, in which sensor developers pit their technologies against unknown (to them) releases of chemicals and mixtures. "If a new technology passes these tests, there's a good chance it will be viewed positively for further development by the sponsor," said Goldwire.

Travis White from Lawrence Livermore's Engineering Department praises the test range and its personnel. "The Livermore and Bechtel Nevada teams do an outstanding job," says Travis, a three-year veteran user of the RSTR. "For people like me, the range provides a scientific and methodical way to evaluate technologies and to test concepts. It's a unique capability, unparalleled anywhere else in the nation."

—Ann Parker

Key Words: chemical release testing, Frenchman Flat, HAZMAT Spill Center, Mountain Lion test series, Nevada Test Site, Remote Sensor Test Range (RSTR), remote sensing.

For more information contact Henry Goldwire, Jr. (925) 423-0160 (goldwire1@llnl.gov).

Patents and Awards

Each month in this space we report on the patents issued to and/or the awards received by Laboratory employees. Our goal is to showcase the distinguished scientific and technical achievements of our employees as well as to indicate the scale and scope of the work done at the Laboratory.

Patents

Patent issued to	Patent title, number, and date of issue	Summary of disclosure
David M. Sanders Derek E. Decker	**Method and Apparatus for Fabrication of High-Gradient Insulators with Parallel Surface Conductors Spaced Less Than One Millimeter Apart** U.S. Patent 5,955,221 September 21, 1999	A process using optical patterns and lithographic techniques to embed parallel and evenly spaced conductors in the nonplanar surfaces of an insulator to produce high-gradient insulators. The approach increases the size to which high-gradient insulating structures can be fabricated and improves the performance of those insulators by reducing the scale of the parallel, alternating insulator/conductor lines on the insulator's surface. This fabrication approach also substantially decreases the cost of producing high-gradient insulators.
Paul R. Coronado John F. Poco	**Flexible Aerogel Composite for Mechanical Stability and Process of Fabrication** U.S. Patent 5,973,015 October 26, 1999	A flexible aerogel and process of fabrication. An aerogel solution is mixed with fibers in a mold and allowed to gel. The gel is then processed by supercritical extraction or air drying to produce a flexible aerogel formed to the shape of the mold. The flexible aerogel has excellent thermal and acoustic properties and can be used in numerous applications, such as for energy absorption and for temperature and acoustic insulation, especially in the contours of aircraft and where space is limited. The flexible aerogel may be of an inorganic (silica) or organic (carbon) type, containing fibers of same.
Jordin T. Kare	**Method and Apparatus for Reducing Range Ambiguity in Synthetic Aperture Radar** U.S. Patent 5,973,634 October 26, 1999	A modified synthetic aperture radar system with reduced sensitivity to range ambiguities. It uses secondary receiver channels to detect the range-ambiguous signals and subtract them from the signal received by the main channel. Both desired and range-ambiguous signals are detected by a main receiver and by one or more identical secondary receivers. All receivers are connected to a common antenna with two or more feed systems offset in elevation. The output of the secondary receiver(s) is then subtracted from the main receiver output in such a way as to cancel the ambiguous signals while only slightly attenuating the desired signal and slightly increasing the noise in the main channel. Thus, output of secondary receiver(s) does not significantly affect the desired signal. The subtraction may be done in real time, or outputs of the receivers may be recorded separately and combined during signal processing.
Charles R. Carrigan John J. Nitao	**Electro-Osmotic Infusion for Joule Heating Soil Remediation Techniques** U.S. Patent 5,975,799 November 2, 1999	A method of using electro-osmotic infusion of groundwater or chemically tailored electrolyte to enhance, maintain, or recondition electrical conductivity during joule-heating remediation. Induced flows can be used to infuse electrolyte with enhanced ionic conductivity into the vicinity of the electrodes, maintain the local saturation of near-electrode regions, and resaturate a partially dried-out zone with groundwater. Electro-osmotic infusion can also tailor the conductivity throughout the target layer by infusing chemically modified or heated electrolyte to improve conductivity contrast of the interior. Periodic polarity reversals will prevent large pH changes at the electrodes. This infusion method can be used to condition the electrical conductivity of the soil, particularly low-permeability soil, before and during the heating operation. Electro-osmotic infusion is carried out by locating one or more electrodes adjacent to the heating electrodes and applying a dc potential between two or more electrodes. Depending on the polarities of the electrodes, the induced flow will be toward the heating electrodes or away from them. In addition, electrodes carrying a dc potential may be located throughout the target area to tailor its conductivity.

Patent issued to	Patent title, number, and date of issue	Summary of disclosure
James C. Davidson Joseph W. Balch	**Microinjector Sample Delivery System for Charged Molecules** U.S. Patent 5,980,713 November 9, 1999	A microinjector sample delivery system for charged molecules. The injector is used for collecting and delivering controlled amounts of charged molecule samples for subsequent analysis. The injector delivery system can be scaled to large numbers (greater than 96) for sample delivery to massively parallel high-throughput analysis systems. The essence of the injector system is an electric-field-controllable loading tip that includes a section of porous material. By applying the appropriate polarity bias potential to the injector tip, charged molecules will migrate into porous material, and by reversing the polarity bias potential, the molecules are ejected or forced away from the tip. The invention has application for uptake of charged biological molecules (for example, proteins, nucleic acids, polymers, for delivery to analytical systems and for use in automated sample delivery systems.
Richard A. Van Konynenburg Joseph C. Farmer	**Means for Limiting and Ameliorating Electrode Shorting** U.S. Patent 5,980,718 November 9, 1999	A fuse and filter arrangement for limiting and ameliorating electrode shorting in capacitive deionization water purification systems that use, for example, carbon aerogel. This arrangement limits and ameliorates the effects of conducting particles or debonded carbon aerogel in shorting the electrodes of a system such as a capacitive deionization water purification system. This limiting and amelioration are important because of the small interelectrode spacing and the finite possibility of debonding or fragmentation of carbon aerogel in a large system. The fuse and filter arrangement electrically protects the entire system from shutting down if a single pair of electrodes is shorted and mechanically prevents a conduction particle from migrating through the electrode stack and shorting the series of electrode pairs in sequence. It also limits the amount of energy released in a shorting event. The arrangement consists of a set of circuit breakers or fuses with one fuse or breaker in the power line connected to one electrode of each electrode pair as well as a set of screens or filters in the water flow channels between each set of electrode pairs.
Brian D. Andresen Fred S. Miller	**Ultratrace Detector for Hand-Held Gas Chromatography** U.S. Patent 5,980,832 November 9, 1999	An ultratrace detector system for handheld chromatography. The system has high sensitivity to emissions generated during production of weapons, biological compounds, and drugs. The system is insensitive to water, air, helium, argon, oxygen, and carbon dioxide. It is composed of a handheld capillary gas chromatograph (GC), an insulated heated redox chamber, a detection chamber, and a vapor trap. The system may, for example, use gas-phase redox reactions and spectral absorption of mercury vapor. The GC initially separates compounds that percolate through a bed of heated mercuric oxide (HgO) in a silica (or other metal) aerogel, which acts as an insulator. Compounds easily oxidized by HgO liberate atomic mercury, which subsequently passes through a detection chamber. This chamber includes a detector cell (such as quartz) illuminated with a 254-nanometer ultraviolet mercury discharge lamp that generates the exact mercury absorption bands used to detect the liberated mercury atoms. Atomic mercury, which strongly absorbs 254-nanometer energy, is therefore a specific signal for reducing compounds eluting from the capillary GC, whereafter it is trapped in, for example, a silicon-aerogel trap.

Awards

Laboratory scientists **Anne Happel, Christine Hartmann Siantar, Bill Nellis,** and **Mordy Rosen** were recently honored with the first-ever **Edward Teller Fellowship** awards. The Director's Office initiated the Teller fellowships to honor one of the Laboratory's most distinguished founders. The fellowships recognize and promote the scientific accomplishments of recipients, all of whom have made pioneering advances in their fields of expertise. They also provide fellows with the flexibility to expand their research or explore new areas of scientific inquiry.

Anne Happel of the Laboratory's Environmental Restoration Division was honored for her outstanding scientific accomplishments in studying environmental contaminants, particularly methyl tertiary-butyl ether (MTBE), in California's groundwater. Her widely recognized research has examined the extent of MTBE contamination in the state's groundwater and the behavior of the compound at leaking underground-fuel-tank sites. Currently, she is developing a Geographical Information System for California that will be used to assess the threat posed by MTBE leaking from tanks to groundwater resources.

With the fellowship, she plans to expand her analysis to other areas of the United States as well as continue to serve on federal Environmental Protection Agency policy panels.

Christine Hartmann Siantar, principal investigator for the PEREGRINE radiation dose calculation program in the Physics Directorate, was honored for her "unique and exemplary record of important scientific discoveries and leadership in the PEREGRINE Program." Her previous honors include an R&D 100 Award in 1999, the Department of Energy's Young Independent Scientist Award in 1996, and the Presidential Early Career Award for Scientists and Engineers in 1996.

With her Edward Teller Fellowship, she intends to study how radiation damages DNA.

Bill Nellis, who codiscovered a method for achieving metallized fluid hydrogen, was recognized for his excellent, long-standing contributions to and influence on the field of shock physics. Most noteworthy, according to his award, are his "innovative research efforts in the use of impact-generated shocks to measure the properties of dense, warm molecular and atomic fluids." He is a fellow of the American Physical Society, has published 166 papers, and holds five patents. All of his work at the Laboratory has involved shock compression of solids, liquids, and aerogels.

The award enabled him to work as a visiting fellow at Trinity College, Oxford University, from mid-February through mid-March 2000. He also plans to start a book on fluids at high pressures and temperatures.

Mordy Rosen, a former division leader in the Defense and Nuclear Technologies Directorate and now the division's chief scientist, was cited for his "long-standing scientific excellence not only at LLNL for over 20 years, but also for [his] contributions at UC Berkeley and UC Davis." His honors and awards include being a centennial lecturer of the American Physical Society in 1999, an American Physical Society fellow, and one of the top 100 innovators named by *Science Digest* in 1985 for his work on x-ray lasers. He has cowritten nearly 300 publications.

Rosen intends to use his fellowship to enhance the science base of DOE's Stockpile Stewardship Program. In particular, he plans to study radiation transport in complex geometries and present a more technically rigorous case than those previously made for the use of aboveground experimental facilities such as the National Ignition Facility. In addition, Rosen plans to develop and teach a course in high-energy-density physics.

Abstracts

The Joint Genome Institute: Decoding the Human Genome

This spring, the Joint Genome Institute, a collaboration of Lawrence Livermore, Lawrence Berkeley, and Los Alamos national laboratories, will announce the completion of the draft sequence of chromosomes 5, 16, and 19 in the human genome. Decoding these chromosomes, which constitute about 10 percent of human DNA, gives researchers a valuable tool for locating our 100,000 genes and determining their function. Work is also under way to sequence the DNA of several microbes that may be useful for remediating toxic waste sites or understanding how microbes contribute to carbon sequestration and global warming. After the institute's work on human DNA is complete, work will begin on the mouse, about 85 percent of whose genes are identical to those in humans.

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The Next Accelerator for Revolutionizing Physics

Lawrence Livermore has joined forces with three other Department of Energy laboratories—Stanford Linear Accelerator Center, Lawrence Berkeley National Laboratory, and Fermi National Accelerator Laboratory—to design the proposed Next Linear Collider (NLC). Scientists believe that this electron–positron collider, which will operate in the teraelectronvolt (trillion-electronvolt) range, and other extreme high-energy particle accelerators like it will help answer some of the most fundamental questions in cosmology and elementary particle physics. Currently in the preconceptual design stage, the NLC is being designed to operate ultimately at 1.5 teraelectronvolts. The big challenge is to build this 30-kilometer-long collider for under $1 billion using mature technologies. Lawrence Livermore is contributing its expertise and innovations to the design of the accelerator modulators, which convert ac line power into dc pulses; the accelerator structures, which accelerate beams of electrons and positrons to the interaction region; and the high-power positron targets, which create the positron beams.

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Hunting Down the "Signatures" of Biological Weapons

Livermore scientists are developing biological "signatures"—bits of telltale DNA that can detect and identify toxins and virulent organisms—for use against biological warfare.

Also in April

- *Developed for national security, laser isotope separation is also proving useful in energy, medicine, astronomy, and industry.*
- *An imaging catheter makes surgical fixes less invasive, safer, and more effective.*
- *JanUSP, the world's brightest laser, enables new regimes of research in plasma physics.*

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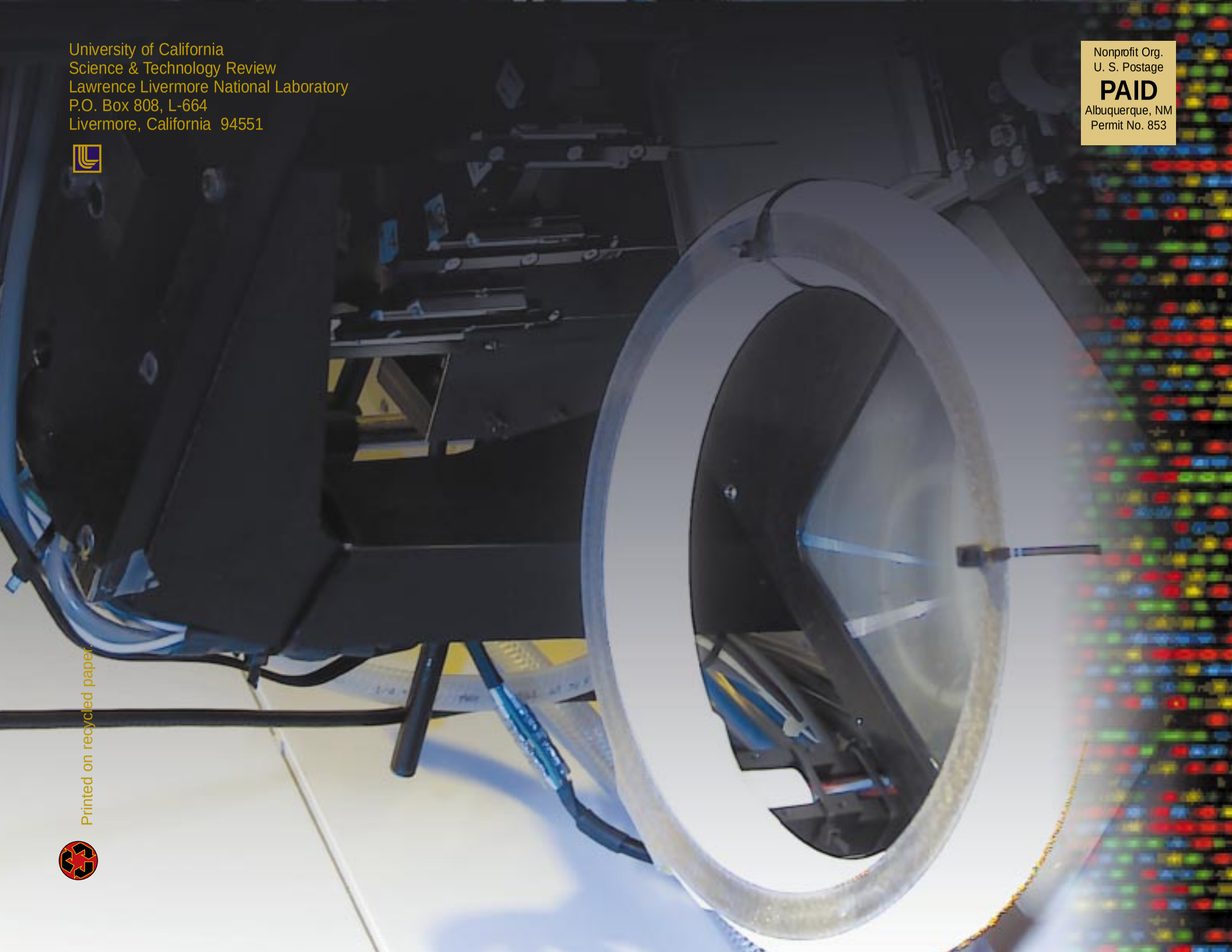

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