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LOS ALAMOS NATIONAL LABORATORY
WHERE SCIENCE MAKES A DIFFERENCE

DATELINE
LOS ALAMOS

LOS ALAMOS DEVICE UNCOVERS SECRETS TO HOW THE BRAIN FUNCTIONS

MAGNETIC FIELDS AROUND THE BRAIN COULD HOLD CLUES TO ALZHEIMER'S, SCHIZOPHRENIA

A neurosurgeon treating a patient with a brain tumor often faces a difficult choice. On one hand, surgically removing the tumor relieves symptoms almost immediately; on the other hand, depending on the tumor's location, surgery can permanently damage sensory, motor, or cognitive functions to the extent that the patient's quality of life is diminished.

A helmet-like device under development at Los Alamos since 1982 has the goal of making it possible to map brain function so precisely that the surgeon will be able to perform an incision with minimal loss of function. The device, known as the biomagnetometer, measures the extremely

→ The biomagnetometer developed at Los Alamos is an advanced diagnostic tool for studying neurological and psychological disorders. At right is a similar device currently being used at the Veterans Affairs Medical Center in Albuquerque, N.M.

weak magnetic fields generated by brain activity and is scheduled for completion this year. An alternate version of the instrument is currently being used at the Albuquerque Veterans Affairs Hospital in a clinical program initiated by Los Alamos National Laboratory.

The biomagnetometer already shows great promise as a tool for mapping brain function. Techniques exist for imaging brain structure and some types of brain function; however, the Los Alamos biomagnetometer will give researchers a noninvasive and economical way of looking at more dynamic brain processes — those that happen within a thousandth of a second.

The brain is an enormously complex organ made up of billions of nerve cells, or neurons, each having tens to hundreds of thousands of connections to other neurons.

Neurons in sensory regions of the brain are activated in response to external stimuli like sight or sound, and when that happens, they produce an electric current that generates a minuscule magnetic field. By measuring and analyzing those fields, scientists can determine which areas of the brain perform a particular function.

Magnetoencephalography, or MEG, is the measurement of the magnetic fields associated with biological systems like the brain and the heart.

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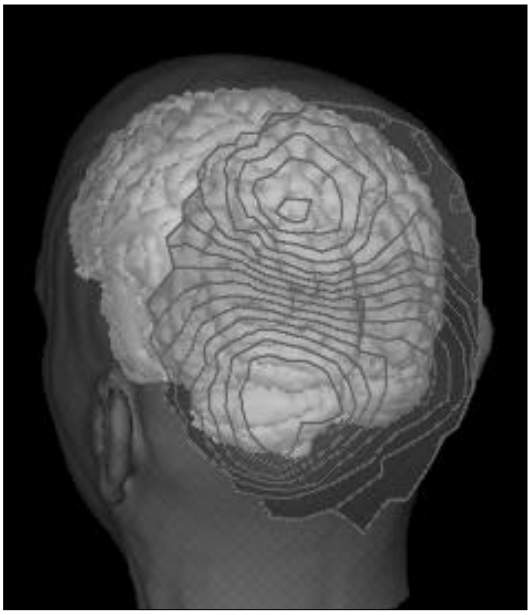
MEG holds great promise for studying neurological and psychiatric disorders, but to convert the technology into a practical diagnostic tool such as the biomagnetometer, the researchers needed to find a way to detect and isolate neuromagnetic signals more than one billion times smaller than Earth's magnetic field.

Applying quantum mechanics, the branch of physics that describes the nature of particles at the atomic and nuclear levels in terms of waves, to superconducting materials led to the development of the Superconducting Quantum Interference Device, or SQUID, in the 1960s. Simply put, SQUIDs detect weak biomagnetic fields by converting them into easily measured voltages.



Because all kinds of things from ceiling lights to Earth's iron core create magnetic fields, interference from ambient magnetic fields is a real problem when trying to isolate the signals emanating from the brain.

To eliminate interference, researchers came up with a tool called a gradiometer: a 3-inch tube with a set of superconducting coils wound in opposite directions. Any magnetic field induces electrical current in the two coils.

A gradiometer placed against the head can distinguish between distant magnetic fields and the ones coming from the nearby brain because the opposing coils effectively cancel out the current coming from a faraway source.

Laboratories currently working with MEG rely on two-coil gradiometers and specially constructed rooms to block out external magnetic fields. Because the two coils must be aligned exactly, gradiometers can cost several thousand dollars each to make, and it takes more than 100 of these to map the entire brain at once. In addition, it costs about half a million dollars to electromagnetically shield a room.

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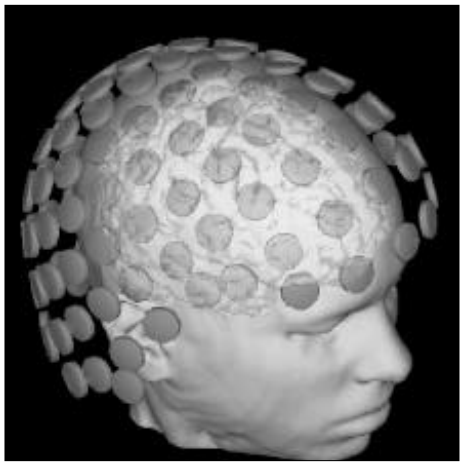
When neurons in sensory regions of the brain are activated, they produce an electric current that generates a minuscule magnetic field. The biomagnetometer lets scientists measure and analyze those fields.



The Los Alamos biomagnetometer contains more than 100 "SQUIDS," which make it possible to detect extremely weak magnetic fields generated by brain activity by converting them into easily measured voltages.

The Los Alamos researchers decided to take advantage of superconducting materials to improve upon the two-coil gradiometer. Because magnetic fields cannot penetrate superconductors, the Los Alamos biomagnetometer replaces the gradiometer's second coil with a superconducting surface shaped to surround the head like a helmet.

This surface, in a sense, "mirrors" magnetic field sources picked up by the single coil. This design not only measures the brain signals as accurately as a two-coil gradiometer, but is smaller in size and cheaper to produce and provides the function of a shielded room.

When it is completed, the Los Alamos biomagnetometer will have more than 100 coils, or sensors, each connected to a SQUID, about an inch apart. Researchers will be able to locate the source of electrical currents from the brain to within a fraction of an inch. Because the 100-channel helmet is designed to cover the entire head, it will measure in an hour what takes at least a week with earlier instruments.

By measuring electrical activity from the brain over time, researchers will eventually have a far more detailed picture of how the brain functions. Armed with this information, scientists may be able to understand how schizophrenia, Alzheimer's disease, and even drug addiction affect brain activity. That, in turn, will help them develop more effective therapies for neurological and psychological disorders.

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DATELINE: LOS ALAMOS

BIOMAGNETOMETER IS A TOOL WITH MANY APPLICATIONS

Pre-surgical mapping of a patient's brain is only one application for this new method of understanding how the brain functions. Because weak magnetic fields also are associated with other biological systems, the biomagnetometer may eventually be used to assess heart problems, examine damaged lungs and livers, and locate gastrointestinal blockages. In prenatal medicine, this technology could someday replace ultrasound as the best way to identify infants at risk for cardiac or neurological problems well before they are born.

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Dr. William Orrison, chief of neuro-radiology at the Albuquerque Veterans Affairs Medical Center, sits with a young patient who is undergoing a brain scan with an earlier version of the biomag-netometer.

In addition to its range of biomedical applications, this new technology can be used to test materials nondestructively for microscopic cracks, corrosion currents, and improper welds and rivets. Material applications measure the weak magnetic fields associated with small electrical currents that are either present or induced in materials. Imperfections in materials disturb these small currents and their associated magnetic field patterns as well.

Funded by grants from the National Institutes of Health and the Department of Energy's Office of Health and Environmental Research, the new brain-mapping helmet developed by the Biophysics Group at Los Alamos will significantly reduce the complexity and cost of neuroimaging with MEG instruments.

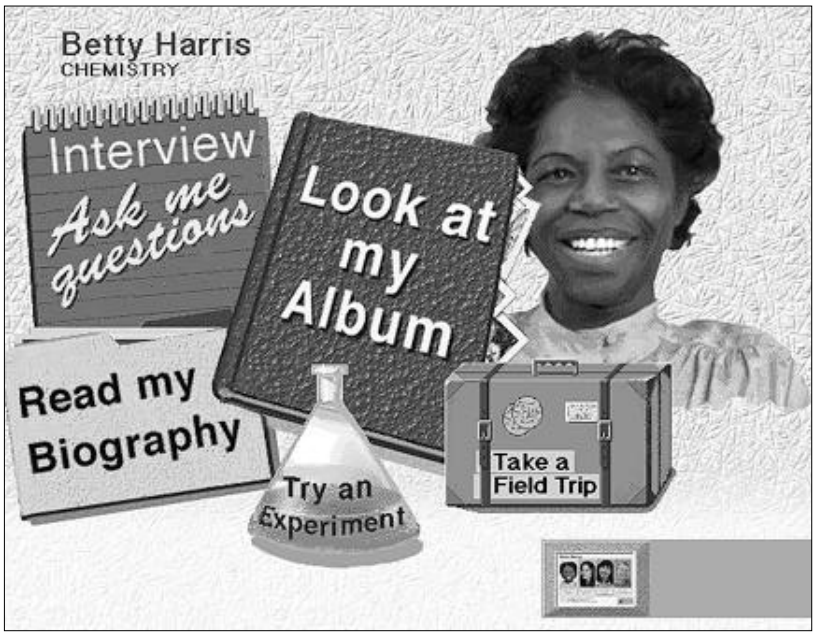
The Tenth International Conference on Biomagnetism is scheduled for Feb. 16-21 in Santa Fe, N.M. For more information about the conference, send an e-mail message to the Los Alamos Biophysics Group at biomag96@lanl.gov or call (505) 665-2545.

DATELINE: LOS ALAMOS

LOS ALAMOS CHEMIST FEATURED ON CD-ROM

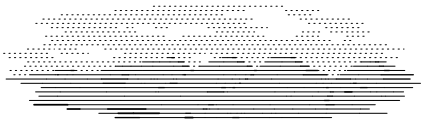
NATIONAL SCIENCE FOUNDATION TEACHING TOOL PROFILES EIGHT SCIENTISTS

Los Alamos chemist Betty Harris is one of eight women selected to be included in a "Women in Science" compact disc being produced for the National Science Foundation.



The disk, titled "Telling Our Stories: Women in Science," will be available early this year. The CD-ROM is accompanied by a teaching guide that targets fourth- through eighth-grade students and can be used as a teaching tool in classrooms. Although the project aims to provide positive role models for young girls interested in pursuing careers in science, boys also will find the CD-ROM useful.

About 15 minutes are devoted to each scientist. Users can call up subject areas of any of the women by clicking on "Look at my album," "Read my biography," "Ask me questions," or "Try an experiment." There is also a "Take a field trip" icon that will take a user to the scientist's workplace where the user can see Harris or the other scientists at work.



In addition to her job at Los Alamos, Harris is involved in science education outreach programs in northern New Mexico and acts as a mentor to college students who spend their summers working at the Laboratory. More recently, she developed the requirements for the Girl Scout Chemistry Badge. Co-worker José Archuleta assisted with the badge design. This project was part of National Chemistry Week activities sponsored annually by the American Chemical Society Central New Mexico Section, of which Harris is past chair.

"The producers of this CD-ROM understand the challenge we have in getting girls to develop and use their scientific potentials," says Harris. "Therefore, the focus and emphasis of this project were properly placed. This scientific game is fun. It will raise the students' awareness of science, and it has a learning element with positive role models."

The other scientists profiled in the two-hour-long CD-ROM are Elma Gonzalez, a plant biologist at the University of California at Los Angeles; Millie Hughes-Fulford, a molecular biologist at the University of California at San Francisco; Diana Reiss, a dolphin communications researcher from Rutgers University; Lauret Savoy, a geologist at Mount Holyoke College in Massachusetts; Susan Solomon, an atmospheric chemist at the National Oceanographic and Atmospheric Administration (NOAA) in Boulder, Colo.; Nai-Chang Yeh, a physicist with the California Institute of Technology; and Jill Tartar, an astronomer with the Search for Extraterrestrial Intelligence Project in Mountainview, Calif.

The CD-ROM also contains a database with biographical information and photographs of 130 other women in science.

The National Science Foundation contracted with McLean Media, a Sausalito, Calif., media production company for the CD. "Telling Our Stories: Women in Science" should be available this spring.

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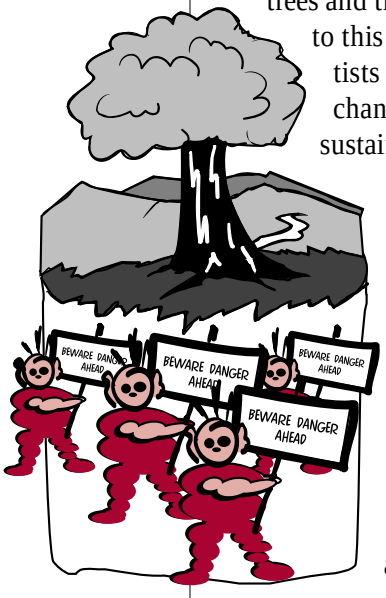
SOIL ORGANISMS ARE CRITICAL FOR ECOSYSTEM SURVIVAL IN CHANGING CLIMATES

RESEARCHERS STUDY MICROBES TO DETECT EARLY SIGNS OF GLOBAL-CLIMATE CHANGE

A Los Alamos microbiologist is collaborating with researchers from Northern Arizona University to investigate which soil bacteria and fungi are essential for plants to survive during dramatic climate change.

The researchers are comparing soil microbes in a healthy piñon-juniper woodland to microbes in a piñon-juniper woodland tenuously located on a lava field near Sunset Crater, Ariz., about 30 miles northeast of Flagstaff. The Sunset Crater volcano erupted in 1064, covering more than 1,000 square miles with hot ash and cinders and exterminating the biosystem it covered. Surrounding plants and their accompanying microbial companions slowly crept into the hotter, drier, volcanic wasteland and established new homes in the harsher environment.

The Sunset Crater area is an example of a sudden, dramatic environmental change. The researchers are studying the genetic changes in the trees and their associated microbes that have allowed them to adjust to this extreme change. Ultimately, the research may help scientists detect and monitor the subtle effects of global climate change or human-induced damage on an ecosystem before it sustains irreparable damage.



All ecosystems have a primary organism or group of primary organisms that serve as a food base to support all other organisms. In a piñon-juniper woodland, trees are the primary food source. Survival of the trees depends, in part, on soil-inhabiting microorganisms that live on or near plant roots. At Sunset Crater, the microbes associated with piñon trees are essential for the trees' survival and critical to the health of the ecosystem.

The microscopic life forms absorb minerals and nutrients from the soil and convert them to forms a plant can absorb and use. One specialized group of fungi, mycorrhizal

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Los Alamos researcher Cheryl Kuske, left, and Kaysie Banton, a Los Alamos graduate research assistant, prepare samples of genetic material isolated from Sunset Crater, Ariz., soil organisms.

fungi, lives between plant root cells and extends into the soil to help supply the plant with water and nutrients.

Bacteria-like organisms called actinomycetes living near the roots can break down and recycle nutrients into forms usable to plants. Other microorganisms, like the Pseudomonad bacteria, can help plants fend off disease-causing organisms.

The researchers are using their expertise in microbiology and cutting-edge Los Alamos technology to compare organisms found in the hotter, drier Sunset Crater woodland — a stressed environment where daytime temperatures soar well above 120 degrees Fahrenheit in the summer months — to those in an adjacent piñon-juniper woodland that has thrived for more than 1,000 years.

By culturing and counting different groups of microorganisms and identifying them using molecular DNA approaches, the researchers are identifying organisms important to the ecosystem.

All microbes have a DNA segment called the ribosomal RNA gene. The gene's chemical sequence differs slightly from one microorganism to another. These differences make the ribosomal RNA gene a useful genetic nametag or fingerprint. This tag can be used to identify and name species of microorganisms without having to grow them in the lab. Because many microorganisms cannot be grown in a lab, the tag is invaluable; it can also be used to name species about which nothing is known or to track down its nearest relative.

The researchers use an advanced laboratory technique known as polymerase chain reaction to make copies of microbial genes, which are analyzed automatically to determine their chemical sequence. Using computers, a sequence can be compared to databases that contain nearly every gene ever identified. By surveying the DNA for these key players, the researchers hope to detect changes in soil microbial communities in ecosystems where the effects of global climate change are not yet visible.

The three-year study is funded by the U.S. Department of Energy's Program for Ecosystem Research.

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YOUR EAR ISN'T JUST WHISTLING DIXIE

THEORY OF THE MECHANICS OF HEARING OPENS NEW DIRECTIONS IN AUDITORY RESEARCH

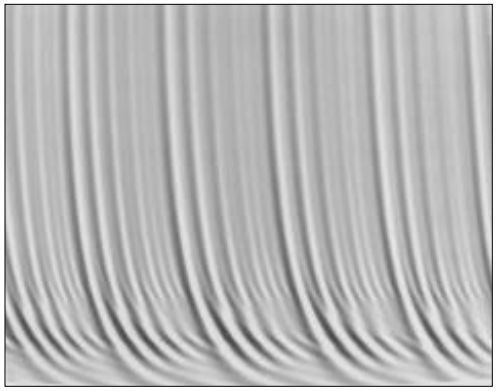
That occasional annoying ringing in your ear is an actual sound — it can even be recorded by a tiny microphone placed in the ear canal. That sound is created by the ear itself.

The ringing or whistling in the ear, common to half the adult population and associated with certain mild cases of tinnitus, is the result of amplification of a wave in the fluid of the inner ear. Los Alamos scientist George Zweig and his student Chris Shera have described these waves and explained why, under certain circumstances, the ear whistles.

Their theory of the mechanics of hearing has opened new directions in acoustic research that could lead to better hearing aids, improvements in the technology of inner-ear implants, and more accurate speech-recognition machines.

For loud sounds, the textbook understanding of hearing is essentially correct: Sound waves enter the ear canal and vibrate the eardrum, whose oscillations are transmitted by the tiny bones of the middle ear to the inner ear, creating waves in the fluid-filled tubes of the cochlea.

Sensory hair cells in the cochlea respond to the motion of the fluid, generating electrical impulses that are interpreted by the brain as sensations of tone. Low-frequency tones excite hair cells farther from the middle ear than do tones of higher frequency. Deafness is often associated with the destruction of hair cells.

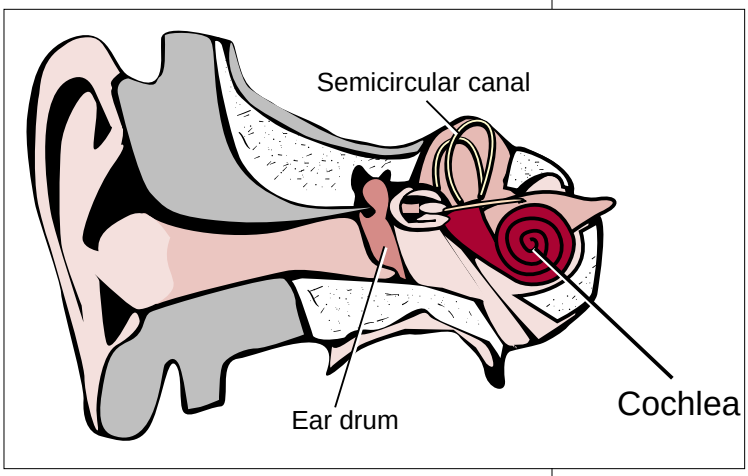


A computer-generated image of waves traveling in the cochlea in response to a vowel sound. Each wave corresponds to the opening and closing of a person's vocal folds.

However, for quiet sounds, the ear is not just a passive receiver of sense impressions. Instead, the ear responds to and amplifies faint waves generated by soft noises. Zweig recognized a symmetry that governed the behavior of these waves in the cochlea. He developed

an equation that describes what happens to these subtle traveling waves within the ear.

Zweig, in 1963, discovered the existence of subatomic particles called quarks — the smallest known building blocks of matter. His work led to the discovery in 1975 of the continuous wavelet transform, a way of displaying and extracting time and frequency information in a signal. Zweig describes wavelet transforms as a way of defining a set of acoustic units that are the quarks of sound. Continuous wavelet transforms are used to remove noise and aid the recognition of patterns in a signal.



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A cross-section of the human ear shows the inner ear and the cochlea, where sensory hair cells respond to vibrations and send impulses to the brain. Traveling waves, amplified by the hair cells, can be reflected back and forth in the cochlea, causing the ear to ring or whistle.

Understanding how the ear functions has important implications for signal processing, for how you go about extracting information from many kinds of signals, not just speech and not just signals in the frequency range of hearing. Continuous wavelet transforms are used by other researchers in mathematics and engineering, with implications for a broad range of endeavors from music production to seismic testing to submarine surveillance.

Zweig's wave equation helps explain the mechanics of the human ear. First, the equation predicted that under certain circumstances the ear creates certain kinds of sound in response to sound. Recent experiments have verified this prediction.

According to Zweig, it looks as if hair cells can generate forces themselves, so that if a wave pushes on them, they are actually able to push back. The hair cells pump energy into the wave, which moves up and down up to 100,000 times a second. The exquisitely timed sequential nudging from hair cells amplifies these faint waves to a level at which they can be detected.

Next, Zweig and Shera found that incoming waves are reflected by mechanical irregularities in the ear, producing small, backward-traveling waves. These waves, also amplified by the hair cells, travel back to the middle ear, vibrating the middle ear bones and creating

sound in the ear canal that can be recorded. These sounds, called evoked otoacoustic emissions, can be analyzed to provide clues about the physical condition of the inner ear without invasive surgery. Although not the first to record otoacoustic emission, the researchers made the most precise measurements available. That precision was necessary to verify the predictions of the wave equation.

Dateline writer Kelly Stoddard demonstrates the equipment Los Alamos researchers used to detect otoacoustic emissions.

The wave equation also explains what causes common ringing in the ear. Wave energy not transferred to the middle ear is reflected again and amplified again, combining with the original wave. This backward and forward wave amplification and reflection can set up a standing wave or resonance in the cochlea. If the process runs away with itself, the ear begins to whistle spontaneously.

Otoacoustic emissions are used to determine the mechanical state of the ear and the extent of hearing loss, even in infants who cannot respond verbally to standard hearing tests. An understanding of how the ear responds to the broad dynamic range of sound that it encounters naturally also may lead to better hearing aids. Additionally, improvements in cochlear implants — devices that electrically stimulate the ear's nerves that are ordinarily triggered chemically by hair cells — require a better understanding of the inner ear's structure and function.

Zweig hopes a clear picture of how the ear works also can help build better speech-recognition systems. The ear's mechanical response reflects the acoustic signatures or the resonant modes of the mouth, including how the vocal folds are moving in the throat. This is the kind of information needed to identify electronically what is being said and who is saying it.

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PATENTLY CREATIVE

LOS ALAMOS INVENTIONS USEFUL TO INDUSTRY

Patents are a form of "intellectual property" granted by the U.S. Patent and Trademark Office. Patents granted for scientific research and innovation are known as "utility" patents, a category that recognizes inventions useful for industry and commerce. Since its origin in 1943, Los Alamos National Laboratory has garnered more than 1,000 patents. Descriptions of some recently awarded patents follow:

NEW METHOD FOR RAPID-BASE SEQUENCING IN DNA

If all the DNA inside a single human cell, about 3 billion base pairs, was stretched out, it would be approximately a meter long. As part of the Human Genome Project, Los Alamos scientists are developing a new method for rapidly decoding the instructions contained in this enormous amount of DNA. In this new approach, a long, single strand of fluorescently tagged DNA is hung in a flowing sample stream. An enzyme is added that attaches to one end of the DNA strand, where it sequentially cleaves the end nucleotide as it works its way up the strand. The cleaved nucleotides drop one at a time through a focused laser beam, where the labeled bases are detected and identified. (Each labeled base forms one side of one rung of the DNA ladder.) Because this approach allows faster sequencing than was previously possible and working with very long strands of DNA, it significantly reduces the amount of chemistry and handling involved in the sequencing process. The apparatus and detection technology are based upon flow cytometry, an analytical method invented at Los Alamos in the 1960s. Today, Los Alamos manages the National Flow Cytometry Resource, which is funded by the National Institutes of Health. The task of rapid DNA sequencing will aid biomedical scientists in understanding causes of genetically inherited diseases, an important step in developing possible therapies. Los Alamos scientists James Jett, Richard Keller, Babetta Marrone, and John Martin recently received the Laboratory's 1995 Distinguished Patent Award for their new approach to rapid DNA sequencing.

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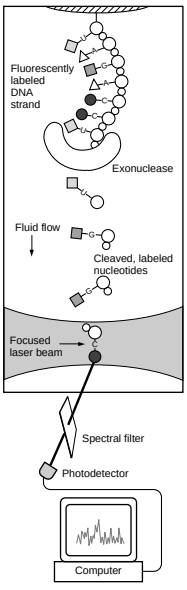
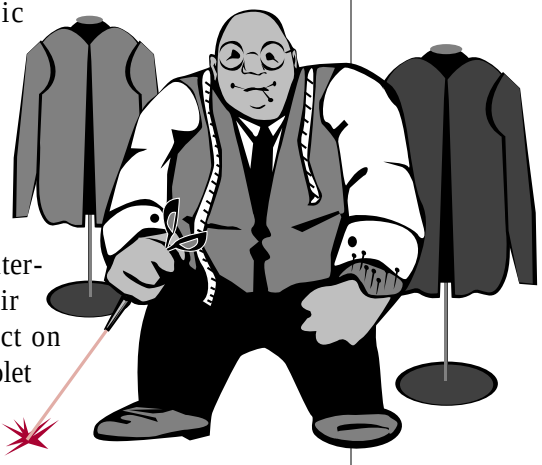
The new Los Alamos approach to rapid-base sequencing of DNA will aid scientists in understanding the causes of genetically inherited diseases.



DATELINE: LOS ALAMOS

LOS ALAMOS DEVELOPS "LASER SCISSORS"

A laser for cutting patterns out of one or more layers of fabric could cut costs for the textile industry. Currently, many layers of cloth are cut by large reciprocating knives controlled either digitally or manually. The new Los Alamos-developed process focuses an ultraviolet excimer laser through a series of lenses and a holographic filter to cut through multiple layers of materials with the entire pattern cut simultaneously. In much the same way as a photographic enlarger exposes an image by allowing light to pass through the negative onto light-sensitive paper, the laser passes through a holographic-patterned filter to cut the material in the desired shape by exposing the fabric to intense ultraviolet light. The ultraviolet light from the laser interacts with the textile fibers, changing their chemical and physical properties. Its effect on the cloth is similar to the effect of ultraviolet light from the sun deteriorating automobile upholstery. When focused to very fine spots along the pattern line, the "laser scissors" burn through the fabric without otherwise damaging it. The invention will greatly reduce the amount of time the textile industry spends on pattern cutting, currently one of the most costly production steps.



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NEW TECHNIQUE USES RESONANT ULTRASOUND INSPECTION TO FIND CRACKS IN MANUFACTURED COMPONENTS

This new Los Alamos technique for detecting crack-like flaws in components will help with quality control in the manufacturing process. Resonant inspection is a fast, inexpensive, and nondestructive testing technique for finding flaws in any type of rigid object. This technique uses a continuous ultrasonic stimulus, which is delivered to a transducer attached to the test object. The frequency of the stimulus is swept over a range, determined by the size of the object, and causes the object to ring or resonate. A flaw, crack, or error arising during the manufac-

turing process — or caused by wear and aging — shifts and dampens the test object's resonances. Most other nondestructive techniques are too slow or too expensive to test 100 percent of the parts produced in a volume manufacturing environment. This rapid, simple, and inexpensive Los Alamos technique can be used to test every part in a high-volume production line. This technology is currently being marketed by Quatrosonics Inc. in Albuquerque, N.M.

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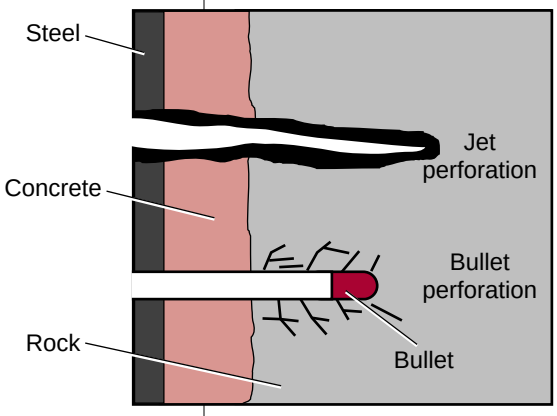
HYPERVELOCITY PROJECTILE LAUNCHER IS BETTER THAN BULLETS

A new projectile launcher that shoots holes in oil well casing provides improved access into surrounding rock. The Los Alamos invention will enable oil companies to extract more of the petroleum contained in reservoir rock. In oil production, wells are typically holes lined with steel casing. Because the steel liner is normally cemented into place, holes must be made through the casing to allow oil to flow into the well. Traditionally, holes the size of a dime are made either by explosive devices called shape charges or by bullets fired through the casing into the formations producing oil. Shape charges produce comparatively deep holes of about a foot that are lined with crushed rock of poor permeability, while bullets produce shorter holes surrounded by a desirable zone of cracked, uncrushed rock. In laboratory tests, the Los Alamos projectile launcher, which combines the best attributes of both the explosive and bullet devices, has produced deeper bullet penetrations that are surrounded by cracked rock. These two advantages should result in increased production of oil from the surrounding strata. The hypervelocity projectile launcher integrates defense program ideas for projectile launchers into perforating oil, gas, and geothermal wells.



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DATELINE: LOS ALAMOS

BRIEFLY ...

Los Alamos scientist Gerald Myers attended the first-ever White House Conference on AIDS Dec. 6. As director of the HIV Sequence Database and Analysis Project, Myers contributed his knowledge of the worldwide spread and evolution of the human immunodeficiency virus that causes AIDS, the acquired immune deficiency syndrome. Los Alamos catalogs and analyzes HIV genetic sequence information from around the world. The database serves nearly 1,500 researchers and institutions in more than 50 countries. The conference, sponsored by the White House Office of National AIDS Policy, was scheduled to raise public awareness about the impact the epidemic is having on individuals and their communities. (See related article titled "Molecular Medicine for the 21st Century" in the November 1995 issue of *Dateline: Los Alamos*.)

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