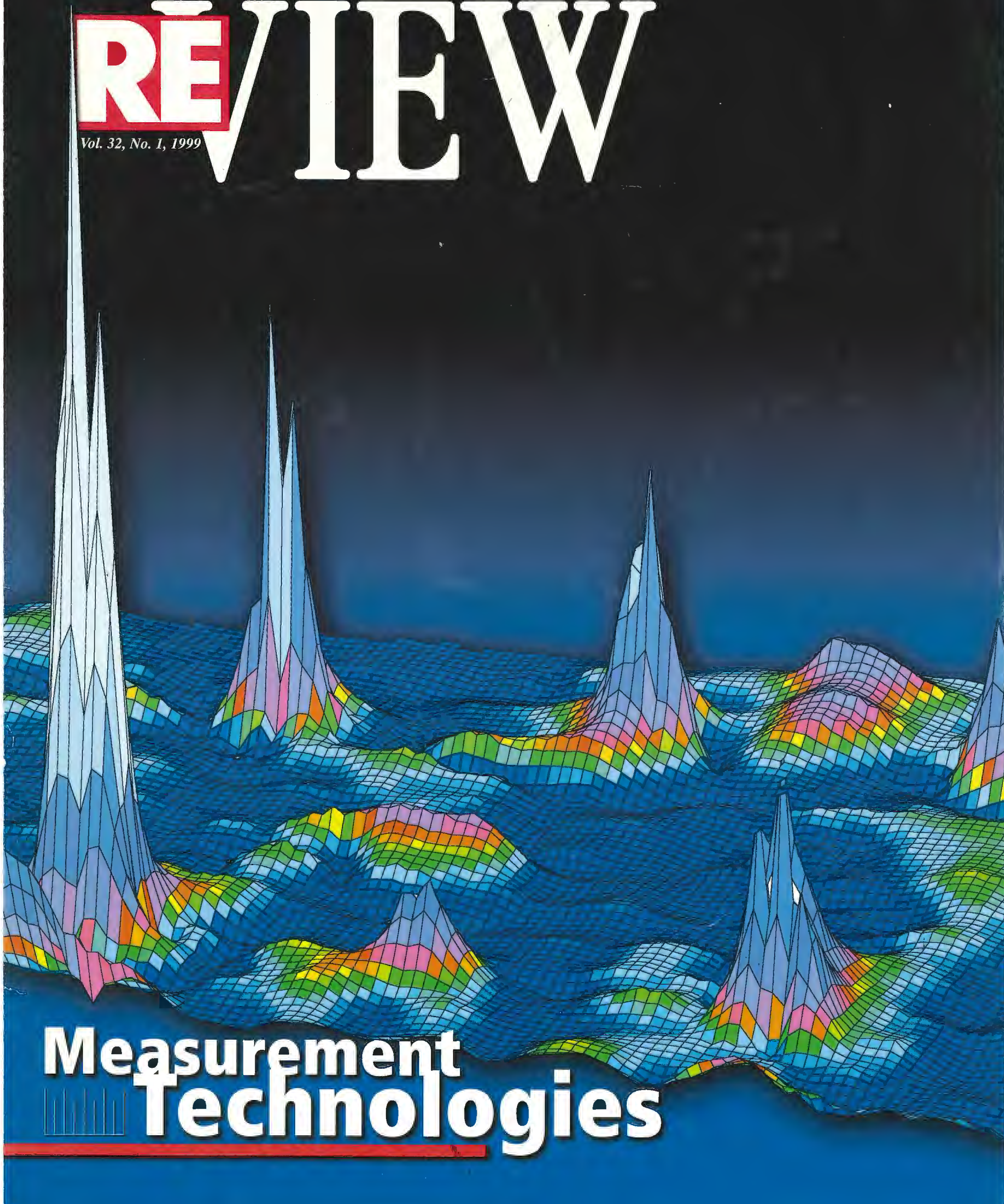
Managed by Lockheed Martin Energy Research Corp. for the Department of Energy

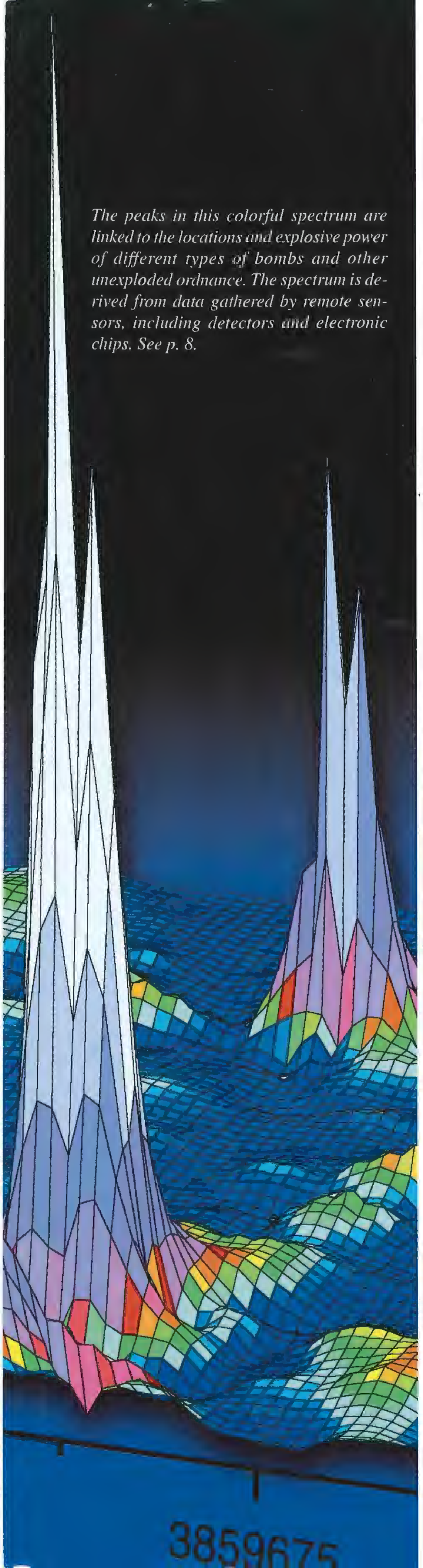
Oak Ridge National Laboratory

REVIEW

Vol. 32, No. 1, 1999

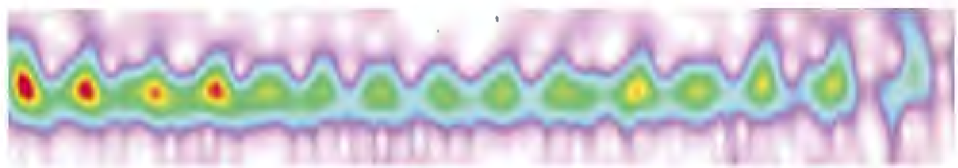


Measurement Technologies

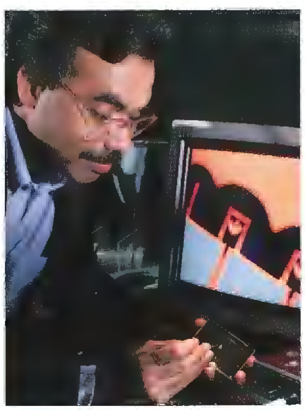


The peaks in this colorful spectrum are linked to the locations and explosive power of different types of bombs and other unexploded ordnance. The spectrum is derived from data gathered by remote sensors, including detectors and electronic chips. See p. 8.

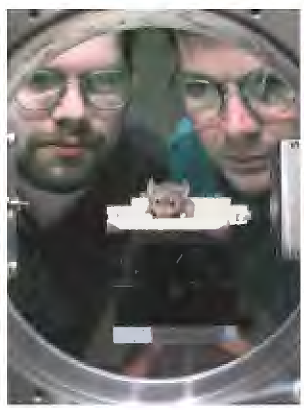
Features



Wavelet transform of a heartbeat signature in the noise signatures coming from a truck as detected by a geophone. See pp. 27–28.



Thomas Thundat picks up a platinum-coated cantilever chip that was designed at ORNL and fabricated at the Massachusetts Institute of Technology. See p. 11.



Kevin Behel (left), a graduate student from the University of Tennessee, and ORNL's Mike Paulus recently scanned this live mouse with a MicroCAT prototype. See p. 20.

This "critters on a chip" sensor (described on p. 15) processes signals from bacteria attached to the chip that are genetically engineered to light up in the presence of certain pollutants.

Measures of a Successful National Laboratory

Without the ability to make measurements, humankind could not track time, make maps, and build and deploy weapons. We could not develop mathematical, musical, navigational, commercial, or administrative skills. We could not describe things precisely in terms of weight, length, and volume. We would still be relying on the medieval barter system because we would have no money.

Ever since Galileo's experiments in the 16th century, scientists and engineers have greatly appreciated the importance of measurements. Many physical laws have been deduced from measurements (e.g., the velocity of light). Better materials and labor-saving, time-saving, and energy-saving devices could not be developed without measurements (e.g., the Wright brothers gathered wind tunnel data on airfoils to help them design an airplane they could fly). Computer models for making predictions about the physical and biological world are only as accurate as the measurements on which they are based.

Over the past four centuries, many measurement instruments were invented and improved upon for use by researchers, enabling scientific advances and the development of modern products. Since the 1940s when we built radiation detectors to monitor workers and equipment at the Graphite Reactor, Oak Ridge National Laboratory has been involved in the development of new measurement technologies. Almost half of the 96 R&D 100 awards given by *R&D* magazine to Oak Ridge scientists (in recognition of the 100 best technical innovations of the year) have been for developments of new measurement devices and techniques.

In this special issue, we showcase the variety of "smart sensors" being developed at ORNL for many applications in the public interest. These intelligent measurement instruments that merge sensitive detection abilities with computing and signal transmission capabilities range from miniature detectors to electronic chips to remote-sensing technologies. The versatility of our array of smart sensors is a tribute to a hallmark of Department of Energy national laboratories—their multidisciplinary and multiprogram teams.

For future health applications, we are developing sensors to measure and transmit the body's vital signs, determine whether esophageal tumors are cancerous, monitor brain injuries, diagnose lung disorders based on breathing sounds, and map dead tissue from burn victims. We are forging very small chips to help medical personnel diagnose diseases and develop drugs to combat them as well as to sniff the air for toxic gases and, with the help of microorganisms, detect pollutants in the ground. In the effort to reduce the threat of war and terrorism, we are devising remote-sensing techniques to detect land mines, biological and chemical warfare agents, and explosives at airports. Our work will enable authorities to gather or improve the quality of information needed to identify crime suspects. For the U.S. steel, textile, and semiconductor industries, we have developed measurement and inspection techniques that are increasing their competitiveness.

We are also developing advanced measurement techniques to help our researchers monitor the health and behavior of genetically altered mice and predict how global climate change might affect forest productivity. We are designing new instruments for the Spallation Neutron Source, a research facility proposed for ORNL by DOE. Results from this unique measurement tool for scientists and engineers are expected to improve our quality of life early in the next century.

Al Trivelpiece

Al Trivelpiece
Director of Oak Ridge National Laboratory

REVIEW

Editor and writer—Carolyn Krause
Assistant editor—Deborah Barnes
Technical editor— Deborah Counce
Consulting editor—Bill Appleton
Designer—Linda Dickert
Illustrator/cover designer—Greg Lamb
Photographers—Curtis Boles, Tom Cerniglio, Jay Nave, and Jim Richmond

The Oak Ridge National Laboratory *Review* is published two or three times a year and distributed to employees and others associated with or interested in ORNL.

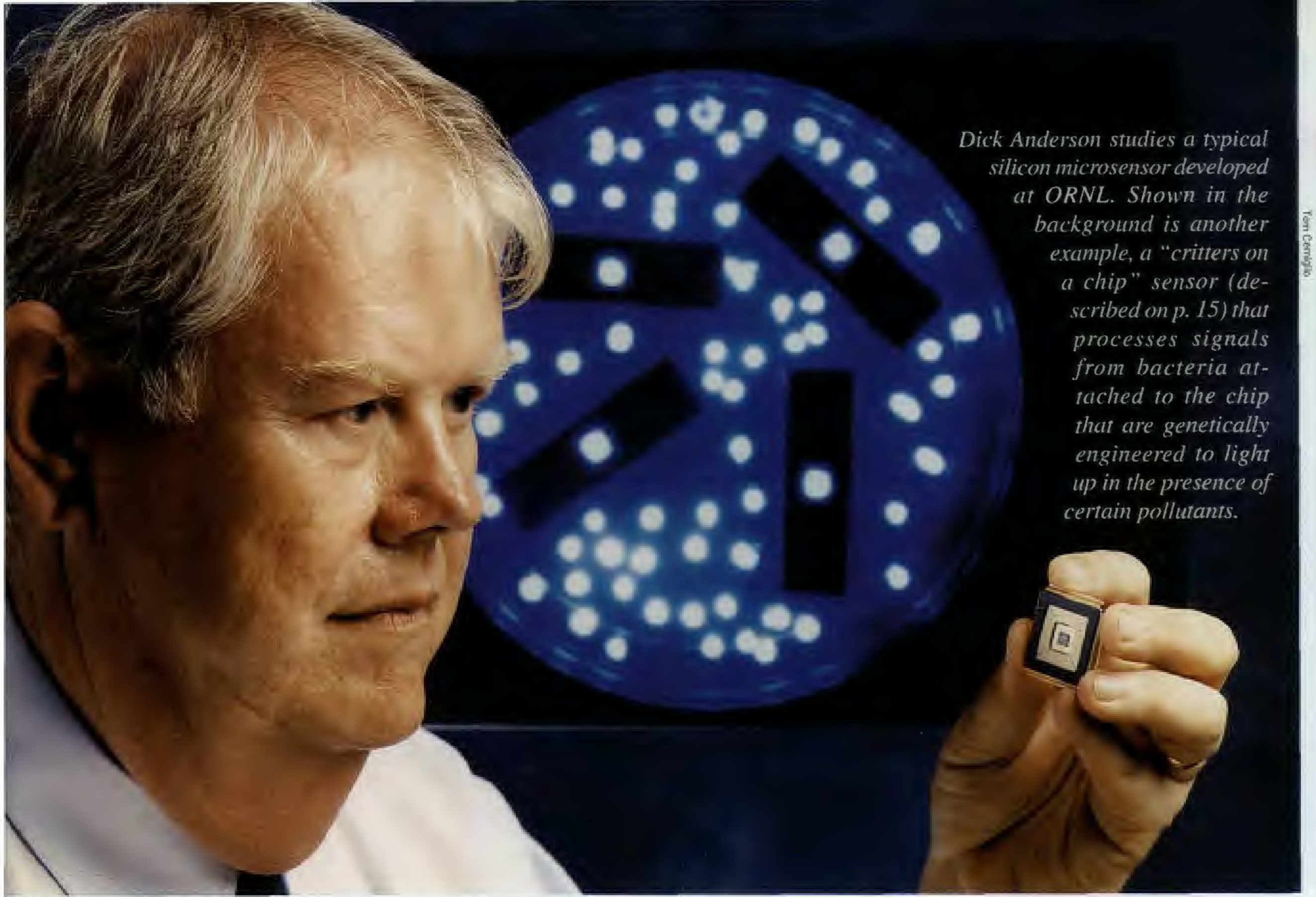
Editorial office address:
Building 4500-South, M.S. 6149,
Oak Ridge, TN 37831-2008
Telephone: (423) 574-7183;
FAX: (423) 574-8518;
Electronic mail: krausech@ornl.gov
ORNL *Review* Web address:
www.ornl.gov/ORNLReview/

The *Review* is printed in the United States of America and is also available from the National Technical Information Service, U.S. Department of Commerce, 5285 Port Royal Road, Springfield, VA 22161

ORNL is managed by Lockheed Martin Energy Research Corp. for the Department of Energy under contract DE-AC05-96OR22464

ISSN 0048-1262

Oak Ridge National Laboratory is a multiprogram, multipurpose laboratory that conducts research in energy production and end-use technologies; biological and environmental science and technology; advanced materials synthesis, processing, and characterization; and the physical sciences including neutron-based science and technology.



Dick Anderson studies a typical silicon microsensor developed at ORNL. Shown in the background is another example, a "critters on a chip" sensor (described on p. 15) that processes signals from bacteria attached to the chip that are genetically engineered to light up in the presence of certain pollutants.

Tom Cerniglio

ORNL and the Smart Sensor Revolution

Through its developments of sophisticated instruments, electronic chips, and computer algorithms, ORNL is advancing the smart sensor revolution.

By Dan McDonald

Jewels of light from a city at night and smoke from factory stacks are enduring images of the industrial revolution. This prevailing phenomenon started in the late 18th century and spawned the industrial plants that provide us today with power, products, and unprecedented, widely distributed wealth. The industrial revolution replaced our muscle power with mechanized tools of production driven by steam and electrical power. At ORNL, in spite of our late start in the 1940s, we helped this revolution roll along by developing designs for nuclear power plants and other energy sources. We developed the first control systems to operate these facilities efficiently and safely. And we invented new instruments needed to monitor and control these facilities.

In his 1980 book *The Third Wave*, Alvin Toffler argued that the basis for wealth has entered a new era, or "wave," dominated by information technology. (In the first wave, wealth was based on the ownership of land and agriculture. In the second wave, the industrial revolution, wealth was created through machines.) The information revolution described by Toffler took off in the mid-1970s with the advent of desktop microcomputers to enhance our brain power by doing clerical and intellectual tasks much more quickly, reliably, and accurately.

Within two decades a large majority of the nation's professionals had a personal computer (PC) in the office and many owned one at home. ORNL researchers developed ways to use digital computers to control and analyze reactors and other processes. The availability and increasing power of PCs revolutionized the development and use of instruments at ORNL and elsewhere. The reason: PCs can control the measuring instruments and sort through and compare streams of data and make calculations much more quickly and more accurately than a human can. As a result, computerized instruments are becoming faster, more sensitive, and more accurate than previous instruments and are extending measurement capabilities into altogether new areas.

As suggested by Paul Saffo, director of the Institute of the Future in Menlo Park, California, this marriage of sensing and computing in the 1990s will be the basis for a new revolution in which computers, provided with direct sensing capabilities, can interact directly with their environment. These smart sensor technologies, some of which have been developed at ORNL and are described in this special issue of the *ORNL Review* on measurement technologies, extend our senses, allowing us to "see" the stars and manipulate atoms and even single electrons. These sensors receive and respond intelligently to a signal or stimulus, like ultrasonic sensors that enable grocery store doors to "see" you coming and open automatically to let you in.

Some ORNL-developed sensors "hear" sounds that tell us that a submarine is operating too loudly, that a machine is malfunctioning or is about to malfunction, or that a person is ill with a specific respiratory disease. Other sensors "sniff out" chemicals to warn of the presence of toxic gases at hazardous levels. Still others use lasers and optical fibers to "see" cancerous tumors in parts of the body. Special cameras combined with software provide "machine vision" (pattern recognition) that can be used to detect flaws in fabrics while they are being woven or to detect and classify defects in semiconductor wafers during manufacture.

Many advances in sensor technology are driven by the automobile industry's need for inexpensive, reliable measurement and control technologies. In modern automobiles, sensors feed data to microprocessors controlling actuators that activate mechanical devices, ensuring smooth operation of anti-lock brakes, cruise and traction controls, and fuel injection systems. Even more advanced sensors, actuators, and computer controllers will be incorporated into future cars for satellite-based navigation systems to help drivers reach their destinations faster and for radar collision avoidance systems to reduce the number of automobile accidents. In future airbags, chips that detect an abrupt change in acceleration will also sense a person's weight and size and adjust the airbag inflation force accordingly.

The goals of ORNL research in sensors and measurement include miniaturization and intelligence—designing smaller, smarter sensors on silicon chips. Such chips will combine sensing with computing, or signal processing, as well as signal transmission to an external receiver. These smart sensors are making possible smart cars, smart buildings, and smart machines.

Measures of Our Success

ORNL has traditionally been deeply involved in the measurement sciences. Our multidisciplinary organization is a particular strength in developing advanced sensors. Almost half of the R&D 100 awards given by *R&D* magazine to Oak Ridge researchers (who lead the other Department of Energy laboratories in the number of such awards received) have been for developments of measurement techniques and devices.

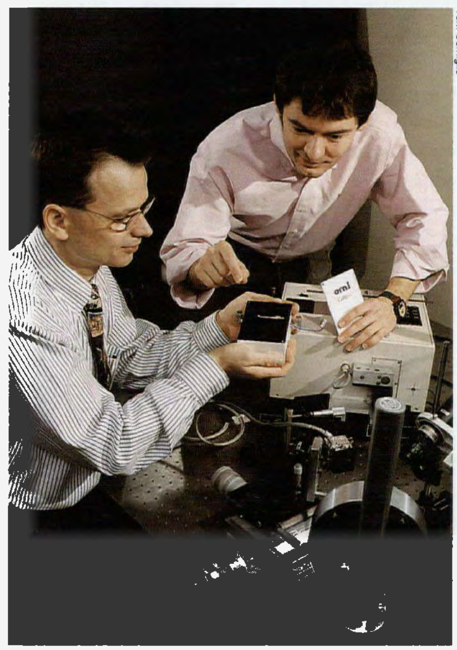
We have years of experience developing instruments, beginning with radiation detectors needed to monitor ORNL's reactors and our employees. Many of the fundamental principles of reactor control and protection systems developed at ORNL for the Laboratory's early reactors are used widely in commercial nuclear power plants. In 1975 our noise analysis measurements, with which we learned to detect nuclear plant anomalies using the reactor's "noise" signature, explained why the General Electric (GE) Company's boiling water reactors were experiencing some internal damage. Our results led to a governmental decision to keep them operating, but at lower power, until GE solved the problem. Later ORNL noise analyses in the mid-1980s showed it was feasible to measure the stability of boiling water reactors, and this measurement concept was later marketed by GE.

In another energy area, we developed measurement technologies to determine the temperature, energy transfer, and other parameters in fusion energy plasmas. ORNL measurements of the electron density profile at the edge of the plasma have advanced the science and technology of heating fusion plasmas with radiofrequency power.

We measured the radioactivity emitted after the 1979 accident at the Three Mile Island nuclear power plant. We measured uranium, mercury, and many other pollutants in soil, water, and air. We found that the health risks of the public's average exposure to environmental tobacco smoke may not be as high as other studies suggest.

We invented the routinely used commercial device for identifying and measuring concentrations of body fluid constituents that indicate disease states. We developed instruments to detect carcinogens in the environment and DNA indicators of the presence of diseases.

We used radioactive isotopes and various instruments to follow the movements of nutrients and pollutants and the carbon dioxide and water vapor exchange rates in forest ecosystems. Our monitoring technologies are helping us predict the effects on forest productivity of air pollution, increased concentrations of atmospheric carbon dioxide, and the expected effects of global warming—changes in daily temperature and rainfall patterns.



Tom Cerniglio

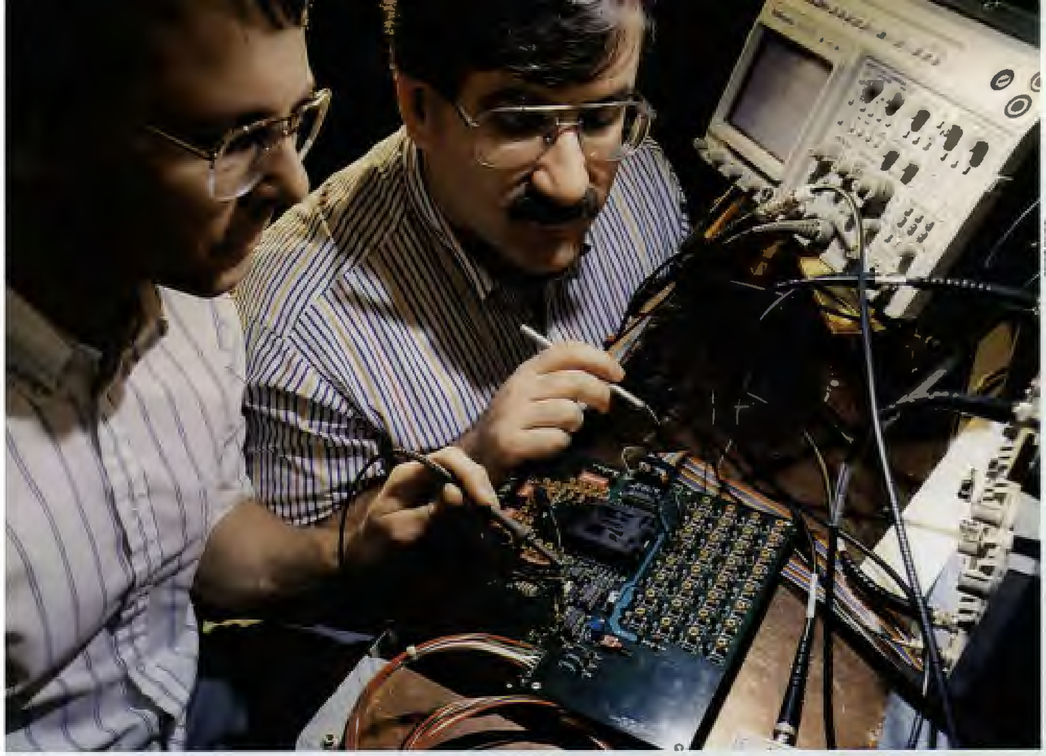
Panos Datskos (left) and Slo Rajic show the prototype of the calorimetric microspectrometer they developed. Called CalSpec, this device can detect chemicals indicating the presence of natural gas as well as vapors from explosives, toxic materials, and chemical warfare agents. For this development, the two researchers and their colleague Chuck Egert received an R&D 100 award in 1998.

ORNL's Capabilities

We have smart people from many different fields who work together to devise smart sensors to solve tough problems. For example, we have applied our multidisciplinary strengths to develop a variety of approaches to solve one of the world's worst pollution problems—buried land mines that kill and maim people and prevent the use of large tracts of land. Three of our sensor technologies highlighted in this issue of the *Review* are being developed to detect the chemical signature of plastic explosives that have leaked out of mines into the soil, from which they may vaporize into the air. (1) Our direct-sampling ion trap mass spectrometer, which is being reduced from the size of a desk to that of a briefcase, can sniff out explosive molecules in the soil or air. (2) Microcantilevers (tiny springboards attached to electronic chips) coated with platinum bend or vibrate in the presence of the explosive TNT. When TNT is attracted to the platinum coating, it reacts, causing a detectable mini-explosion and resulting deflection of the microcantilever. (3) ORNL researchers have genetically engineered bacteria to light up in the presence of trace amounts of TNT from land mines.

Helping Our Customers

Originally, ORNL developed measurement and control systems to meet the Laboratory's needs. Today we have many outside customers because of our expertise in mixed analog and digital chip design. Mixed-analog-digital chips are the keys to the integration of analog transducers and electronics with digital computers and signal processors on the same chip. Several ORNL divisions are designing and building entire "instruments on a chip," and much progress has been made toward the next level of integration and complexity—the "lab on a chip." In these microscopic systems, analog and digital electronics are being combined with the ability to handle micro quantities of liquids or vapors. DNA and proteins can be analyzed on a single chip, providing information that could identify crime sus-



Alan Wintenberg (left) and Glenn Young check a fixture for testing ORNL-designed integrated-circuit electronics for a silicon detector being developed for the quark-gluon plasma experiment at Brookhaven National Laboratory's Relativistic Heavy Ion Collider. The experiment could help scientists better understand the actions of subatomic particles in the universe at the start of the Big Bang.

pects and lead to the development of new drugs.

We have a growing expertise in advanced signal processing—directed at extracting very weak but meaningful signals from a noisy environment—and in developing algorithms (step-by-step procedures to enable a computer to recognize patterns). As a result, we are inventing devices capable of machine vision. For the U.S. government, we have developed an automated inspection of stamps and currency, to weed out defective items, and a heartbeat detector that can spot intruders or escaping prisoners concealed in closed vehicles. For the medical community, we developed a lung diagnostic system for detecting and classifying respiratory disorders. We are developing an algorithm-guided laser system to locate and destroy burned tissue to reduce pain and hasten healing for burn patients.

Our machine vision expertise has enabled us to support industry through the development of software and hardware systems for detecting and classifying defects in semiconductor chips and textiles. In this way, we are helping the semiconductor and textile industries reduce production of defective items, increase quality, and cut costs.

We are working with industry in other ways, too. For example, Perkin-Elmer is collaborating with us in commercializing our "critters-on-a-chip" technology for environmental applications. This chip hosts an electronic sensor that responds to bacteria on the chip that are designed to emit light in the presence of specific chemicals, such as soil pollutants.

For the police community, through videotape enhancement techniques, we have extracted valuable information from videotapes of people present during store robberies. This information has been used as evidence in court to convict one suspect.

We are developing new measurement techniques in support of the Department of Energy's Industries of the Future program in which DOE helps the energy-intensive industries that produce aluminum, chemicals, forest products, glass, metal-casting, mining, steel, and agricultural products rethink how they manage technology. For the steel industry, for example, our engineers have devised a technique for determining surface temperature during critical stages of the process of producing galvanneal steel for making rust-free automobiles.

Also for DOE, we have developed instruments for ensuring that nuclear material is being safely stored and accounted for and for showing that weapons-grade material is converted into reactor fuel. ORNL research on glow discharge ionization, electrospray and quadrupole ion trap mass spectrometry has led to tools that could help detect hidden explosives and tiny airborne particles that could cause lung disease, monitor hydrocarbon levels in low-emission vehicles, and determine structures of biomolecules such as DNA and proteins. We are developing snapshot laser radar as a remote sensing technique for possible use in detecting chemical compounds in smokestack plumes and in characterizing air vortices to guide the safe spacing of aircraft during landings and takeoffs.

For the nuclear physics community at DOE's Brookhaven National Laboratory, we are developing detectors to help physicists better understand the universe a few seconds after its birth. A Spallation Neutron Source is expected to be built by DOE at ORNL by 2006 to measure changes in atomic-level structure and interactions among molecules in materials. Such measurements could lead to stronger materials, faster electronic devices, safer and faster transportation, longer-lasting body implants, and more effective drugs.

For the functional genomics community, we are developing instruments to help relate the structure of a gene to its function. We are designing a wireless sensor that can be implanted under the skin of a mouse to measure its temperature, pulse rate, and activity in a cage to help determine the physiological and behavioral effects of its defective genes. We have developed a miniaturized CAT-scan device to image mouse mutations such as skeletal defects, fat deposits, enlarged kidneys, and other abnormally shaped organs, as well as growing tumors and other manifestations of disease.

For the U.S. military, we are developing a more rugged and sensitive mass spectrometer system for detecting biological and chemical warfare agents. We are designing telesensors to help medics locate wounded soldiers and determine their condition (e.g., detect rises in body temperature and drops in blood pressure). We are developing an ultrasound sensor to monitor brain injuries.

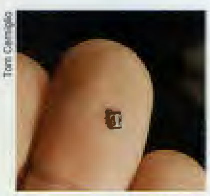
Instruments, detectors, and sensors are getting smarter and smaller. ORNL is playing a big role in these improvements as we help the newest technical revolution to roll along.

Dan McDonald is director of ORNL's Instrumentation and Controls Division. The work he describes reflects the contributions of a number of ORNL divisions.

ORNL is developing electronic chips and other high-tech diagnostic tools for quicker, more accurate assessments of hospitalized civilians and injured soldiers.

Hi-Tech for Health

On Christmas Eve in 1994, Tom Ferrell's 18-month-old son, Brian, was hospitalized with pneumonia. He was on a respirator in intensive care for two weeks. "I was dismayed to see all the wires connected to my son," says Ferrell, a researcher in ORNL's Life Sciences Division (LSD). "My wife and I couldn't pick him up and hug him easily. I wanted to find a way to develop a wireless sensor that monitors vital signs—body temperature, pulse rate, blood pressure, and blood oxygen—and alerts medical personnel to a sudden health problem."



Fortunately, Ferrell found out that the U.S. Defense Advanced Research Projects Agency (DARPA) was supporting development of a "personal status monitor" for soldiers. So he wrote a proposal, and by early 1996, the funds started rolling in. A year later a team from ORNL, the University of Tennessee at Knoxville (UTK), and the University of Virginia had developed a temperature-measuring telesensor chip.

The chip, which is about one-eighth the size of a postage stamp, uses bipolar transistors whose electronic properties are sensitive to temperature. It can be attached to a finger or placed in an ear. There it can measure body temperature and transmit a reading when queried by a receiver in a remote intelligence monitor.

Although developed for military uses, the temperature chip could be useful at home or in the hospital. For example, a chip could warn of a spike in body temperature that might lead to a seizure in a child or brain damage in a cancer patient undergoing chemotherapy. By heeding the instant information and making the appropriate response, such as taking a pill, patients can avert a health crisis.

Wireless monitors could vastly improve decision making by medics in the military. On the battlefield, some soldiers are mortally wounded, some are badly injured but conscious, and others are hurt yet are able (usually with treatment) to resume fighting. While under fire, medics must decide quickly which wounded soldiers must be treated first to get them back on their feet and ready to fight. Medics also must determine which wounded soldiers can be saved from death by rapid treatment and transport to a hospital.

"These choices are difficult to make in the heat of battle without instant information," says Ferrell. "Our proposed technology would improve the speed and quality of the information flow."

ORNL researchers are also developing wireless chips for soldiers that can measure pulse rate (to help a medic determine whether a soldier is still alive) and blood pressure (which drops dramatically if a wounded soldier is bleeding). The idea is that each soldier would wear several wireless microchips embedded in clothing, a finger ring, a boot, or even an earring. Each chip would send measurements by radio signals to units on the soldier's belt and helmet. The units would then analyze the physiological data to determine if the soldier is injured or ill. If either is the case, radio signals would be sent to the helmet of a medic to alert him that this soldier, among the ten soldiers in his care, needs his immediate attention.

"The wireless, digital chip has several advantages over conventional equipment," Ferrell says. "Wearing a tiny chip is much more comfortable than being attached by wires to a machine. The chip allows automated monitoring. It enables medical personnel to diagnose a condition remotely. It is low in cost. Because the chip system is so portable, it is easier to transport a patient whose vital signs must be constantly monitored."

A young patient who suffers from grand mal seizures is tethered by wires and cords to a medical monitoring machine. A telesensor chip could detect temperature spikes and relay timely information on the need for treatment to prevent this boy from having a seizure.

What are the ultimate goals of researchers working with Ferrell in LSD and at UTK, in collaboration with Stephen Smith, Alan Wintenberg, Nance Ericson, and others in ORNL's Instrumentation and Controls (I&C) Division? "One aim," says Ferrell, "is to develop an array of chips to monitor a person's body functions all at once. Another goal is to give each chip a radio signal with a unique identifier pattern so that alerted medical staff will know who needs to be cared for immediately."

Shedding Light on Cancer

A woman woke up feeling chest pain and intense nausea. She rushed to the bathroom and vomited blood. She called her doctor, described her symptoms, and told him that she had suffered severe indigestion for years. He suspected cancer of the esophagus, the muscular tube through which food passes from the pharynx to the stomach. He sent her to the nearby Thompson Cancer Survival Center (TCSC) in Knoxville, Tennessee.

Cancer of the esophagus is one of the most fatal types of cancer in the world. That's the bad news. The good news is that it can be controlled if diagnosed and treated early.

In the past, the only way to find out accurately whether a patient had the early stages of esophageal cancer was to surgically remove tumor cells from the esophagus. These cells were then sent to a special laboratory and studied under a microscope to determine if the tumor was cancerous or benign. A technology partly developed at ORNL will eventually allow some patients to avoid surgery if their esophageal cells prove to be noncancerous.

The woman described above had to have a surgical biopsy, but she was glad to participate in a test of the optical biopsy sensor developed by Tuan Vo-Dinh of ORNL's LSD and Bergein Overholt and Masoud Panjehpour, medical researchers at TCSC. She learned that preliminary research studies of optical biopsy at TCSC have a high accuracy rate.

"If results of future tests are successful, use of the optical biopsy sensor may eliminate the need for surgical biopsy in many future patients being tested for cancer," Vo-Dinh says. "It will also provide a much faster diagnosis than surgical biopsy. As a result, earlier treatment can be administered and patients without cancer won't have to worry so long about the possibility of having it."

For the optical biopsy test, while the patient is sedated, the doctor inserts an endoscope—an instrument that allows visual examination of the interior of an organ such as the stomach—through her mouth and into her esophagus. Traveling through the optical fiber in the endoscope, blue light from a pulsed nitrogen dye laser illuminates tissue in the patient's esophagus. An optical fiber cable is inserted in another channel of the endoscope to collect and transmit light produced by her esophageal tissue after it is excited by laser light. Upon absorbing the light, the tissue emits light with a characteristic pattern of wavelengths, called a laser-induced fluorescence spectrum. Normal tissue has a spectral pattern different from that of cancerous tissue.

Vo-Dinh and his colleagues developed an algorithm that enables a computer to compare the measured fluorescence patterns with the known spectral characteristics of light from both cancerous and normal esophageal cells. The light pattern from the woman's cells matched that of cancerous cells. She also learned from the surgical biopsy that she has a cancerous tumor but, because it's in an early stage, treatment should make her well.

"Because the results of these tests have been successful for esophageal cancer," Vo-Dinh says, "we are planning to develop optical biopsy techniques for use in detecting cancer in the colon, cervix, lung, and bladder." (See p. 13 for information on Vo-Dinh's development of a multifunctional biochip that may be used to diagnose diseases.)

Non-invasive Diagnoses of Brain Injury

When you're hit over the head, blood from an artery may begin spilling between your skull and brain. You may not have any symptoms of epidural hematoma until pressure in the cranium grows, blocking blood flow through the brain. To keep patients from undergoing this "second injury," doctors may take CAT scans and monitor the brain using surgically implanted sensors to help determine the appropriate treatment.

A group led by Vo-Dinh is developing a non-invasive, portable, easy-to-use, and relatively inexpensive device for monitoring brain injury patients. It uses a focused beam of ultrasound waves of an appropriate frequency and a special instrument design that provides an efficient signal for detecting a brain injury. If a lesion, blood clot, or tumor is present, the left-right symmetry of ultrasound echo patterns in the brain may be distorted, indicating the presence of a pathological condition or abnormality. The device has been tested on livestock such as pigs. It will be tested on other animals and may be ready for clinical trials later in 1999. It may also be used to monitor spinal cord injuries.

"This technique should be a significant advance in the care of people with head trauma to limit or prevent brain damage," says Vo-Dinh. Vo-Dinh's collaborators on the project are Stephen Norton (former ORNL staff member) and two members of Vo-Dinh's group—Joel Mobley, a postdoctoral research associate, and Paul Kasili, a graduate student. The development of the ultrasound monitor is supported by the U.S. Army Medical Research and Mate-

Tuan Vo-Dinh of ORNL (left) and Bergein Overholt and Masoud Panjehpour, both of Thompson Cancer Survival Center of Knoxville, developed a new laser technique for nonsurgically diagnosing cancerous tumors in the esophagus. The technique is now being tested in clinical trials.

riel Command. The device will likely be used to save the lives of both soldiers and civilians.

Lung Diagnosis Monitor

A soldier with a chest wound lies bleeding on the battlefield. How critical is the wound? Has the lungs' ability to function been impaired? Is the victim about to suffer pulmonary distress? If the medic could get an accurate and rapid diagnosis of the problem, the correct therapeutic intervention could be started to save the soldier's life. Medical personnel could then give the proper care to boost the soldier's chances of survival.

In response to the need for rapid diagnoses of lung disorders and distress, Glenn Allgood and Dale Treece, both in the I&C Division, and the Walter Reed Army Institute of Research (WRAIR) are developing a high-tech device that monitors and diagnoses the sounds of breathing. This advanced pulmonary monitoring system for identifying lung disorders is designed for both field and clinical use.

"We envision that this diagnostic system may someday provide Army medical personnel with a rapid, accurate diagnostic tool that will help them manage life-threatening respiratory problems," says Allgood, the principal investigator. "The technology is being developed for use in mobile hospital units, helicopters, and hospital emergency rooms. But one day it may be used at home.

"It could become a diagnostic tool embedded in crib mattresses to monitor babies' breathing for signs of respiratory failure or distress linked to problems such as sudden infant death syndrome. It could be used to monitor people having asthma and pneumonia or to determine whether a person experiencing breathing problems has a lung disorder or instead is suffering from stress or some other problem accompanied by respiratory changes."

The lung diagnostic system will combine novel sensors to be placed on the chest or thorax region and an advanced algorithm suite to distinguish between acoustic signatures from normal lungs and those expressing pathological disorders. Fortunately, disorders such as emphysema, pulmonary fibrosis, and pneumonia have their own characteristic acoustic signatures—unique patterns of abnormal sounds superimposed on normal breathing sounds shown as a series of peaks of different heights and distances from one another. So detection of these signatures can help doctors identify lung disorders.

The ORNL-developed algorithm has been tested on a small data set from patients with healthy lungs and known lung diseases to obtain the acoustic signature for each condition. Signatures linked to known disorders are stored in a data base. The ORNL algorithm compares the acoustic signature of a patient with an unknown disease with the signatures in the data base. If a match is detected, the disease can be diagnosed.

Tests show that the algorithm can accurately analyze data obtained from digital stethoscopes and thorax sensors. The data may be displayed on a laptop computer or small computer worn on the body. ORNL is developing another device that may be more useful for the battlefield and better able to obtain data in lower frequency ranges.

In this simulation, Jeff Ball plays the role of an injured soldier who may have a serious chest injury. After placing a thorax monitor on Ball, a medic, played by Bob Vines, checks his wearable computer for breathing "signals" that indicate a particular lung disorder.

Here's one scenario of how it could work. In the battlefield, as part of his combat equipment, the soldier could either wear the sensor or have designated places on the body where the medic could put one (such as the optical acoustic sensor with a fiber-optic coupler invented by David Gerdt of Empirical Technologies Corporation). The sensor would then be linked, either wirelessly or by a tether, to a wearable computer carried by the medic. Acoustic measurements from the soldier would then be analyzed, providing a qualified measurement of lung function. The medic would then down link the data and administer appropriate care.

This device is being evaluated at ORNL to determine its ability to distinguish among different pathological disorders. Clinical tests of the ORNL algorithm using new sensor configurations will be conducted in 1999 at WRAIR.

New Hope for Burn Victims

When Karla was trapped in a house fire, she received third-degree burns over 90% of her body. In the burn therapy unit, doctors surgically scraped and cut out the dead tissue to promote growth of new tissue. They had to quickly extract the tissue to prevent infection. This technique of débridement is very painful but was necessary to save her life.

A group led by Glenn Allgood is developing an alternative method that is expected to ease the pain of burn therapy. It will use a two-laser system to detect and remove the dead tissue almost simultaneously down to the cellular level. The idea is to avoid the needless removal of healthy tissue, a problem with today's methods.

"We are aware of a prototype laser system that scans a burn area, determines the laser power requirements, and then removes a layer of the dead tissue, repeating the process until the area is clean," Allgood says. "The problem is that the patient may move between the imaging and the débriding. Our laser system will work almost instantly, so the patient will be in the same position between tissue mapping and removal."

Laser light is reflected differently from burned tissue than from normal tissue. The reason: Unlike dead tissue, normal tissue contains blood—in particular, hemoglobin, the iron-containing pigment in red blood cells. Laser light of a certain frequency is reflected back from hemoglobin in a characteristic pattern that differs from that of light scattered from dead tissue. Recent ORNL experiments on interlipid fluid (which mimics hemoglobin) suggest that laser radar can determine the extent and depth of burned skin.

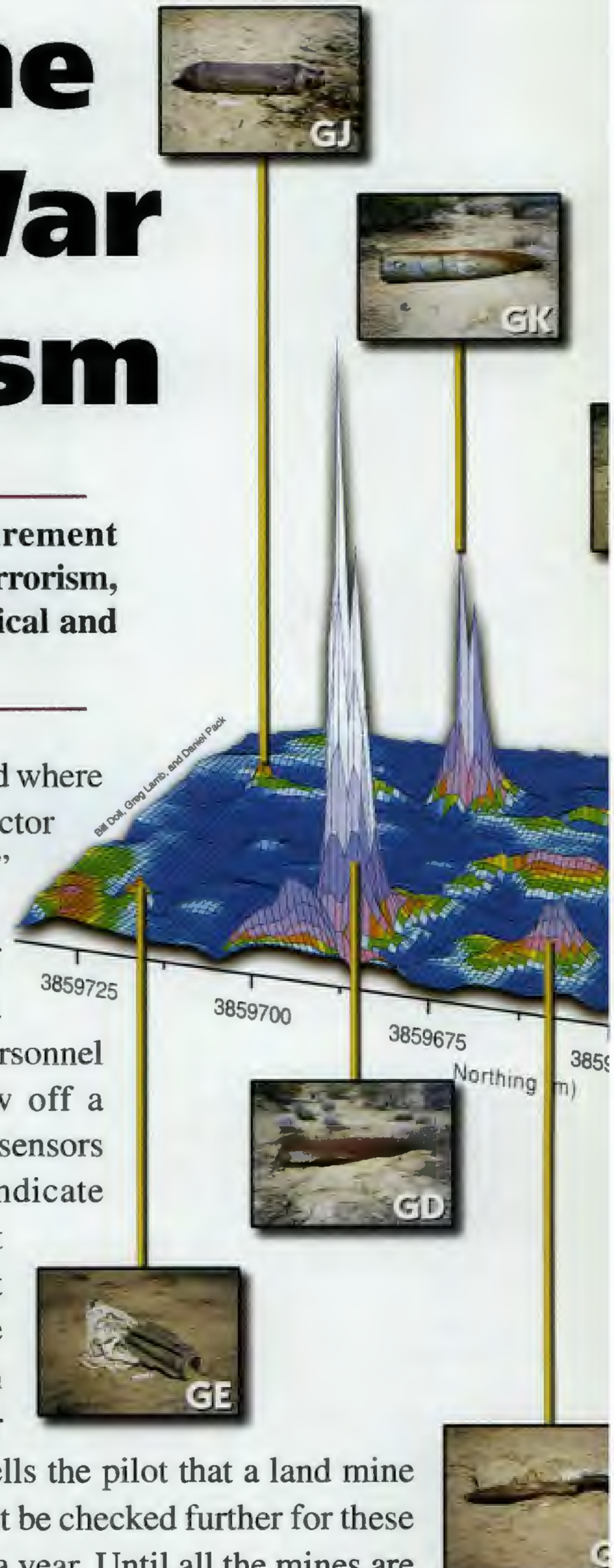
Funded by the U.S. Army Medical Research and Materiel Command, Allgood, Don Hutchinson, Roger Richards, and Bill Dress, all of the I&C Division, have developed a light detection and ranging (lidar) system that combines a coherent frequency-modulated continuous wave laser with a unique configuration of optical components. They have determined the differences in reflection patterns for simulated dead and healthy skin and recorded them in a data base for the proposed laser treatment system.

They have prepared an algorithm that would compare the real-time laser light reflection patterns gathered by the optical components with the stored data. The instant information will enable a computer to construct a three-dimensional image map that shows where dead tissue meets the healthy blood layer below the burn. Using the lidar map, the computer will precisely guide a pulsed laser in a less traumatic "burning" of the dead tissue, leaving the healthy tissue intact.

"We believe," says Allgood, "that this technique will hasten the healing of burn patients."

Reducing the Threat of War and Terrorism

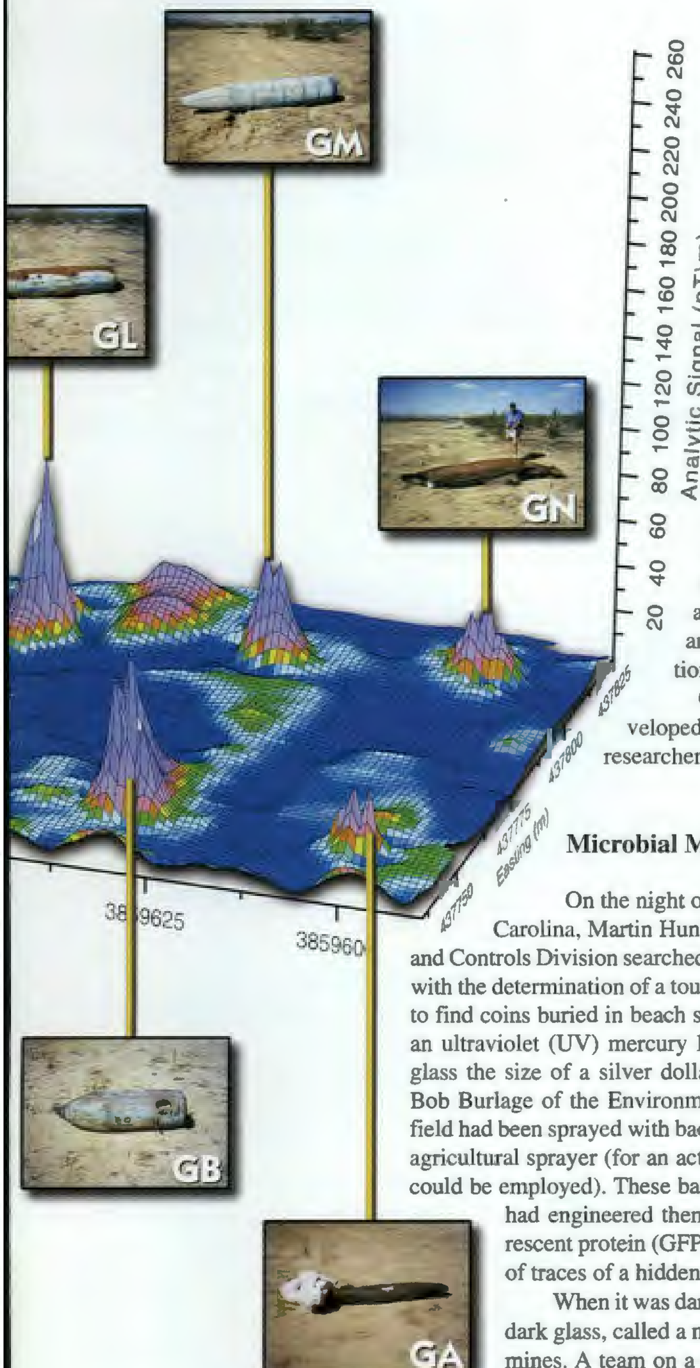
ORNL is developing visualization and measurement technologies that could reduce threats of war and terrorism, such as land mines, unexploded ordnance, biological and chemical warfare agents, and airport explosives.



A future scenario: A helicopter zooms over a grassy field where land mines may lurk. An electromagnetic induction detector on the helicopter "sees" signs of ground disturbance and evidence of a buried object. Is it a rock, tin can, or anti-personnel mine that could blow off a walker's leg? Infrared sensors and video cameras indicate that the mystery object gives off more heat than the surrounding ground. A magnetometer senses the presence of metal. An on-board computer sorting through the signals from these remote sensors on a helicopter boom produces a compelling image on the screen. It tells the pilot that a land mine may be present and indicates the location. The field must be checked further for these remnants of war, which kill and maim 26,000 civilians a year. Until all the mines are detected and removed, it is not safe for the field to be farmed or developed into an industrial site.

A helicopter, with a boom carrying remote-sensing equipment, flies low over a field at Edwards Air Force Base in California.

The peaks in this colorful spectrum are linked to the locations and explosive power of different types of bombs and other unexploded ordnance. The spectrum is derived from data gathered by remote sensors.



Remote sensing using helicopters or fixed-wing aircraft or small, unmanned, radio-controlled aircraft is being investigated at ORNL as a near-term technology for reducing the threat of war and terrorism. It is also useful for identifying locations of unexploded ordnance (UXO).

"At ORNL a UXO team has been working to develop images and signatures of concealed ordnance at military bases and training sites using remotely collected data," says David Bell of ORNL's Computational Physics and Engineering Division, which is working with the Environmental Sciences Division on this project. "Eventually, we will develop a computer program to integrate the data from an array of airborne remote sensors to form an image of a land area. This visualization of the data will enable us to locate buried objects and identify the ones that contain dangerous explosives. In this way, we can achieve 'footprint reduction,' determining which land is dangerous and deserves remediation and which area is safe to develop, thus reducing cleanup costs."

Detection of UXO is one of the goals of a Department of Energy and Department of Defense (DOD) program that is funding some of the ORNL work. Other goals are to characterize and develop strategies to defeat or remove UXO safely. DOD wants better technology to supports its demining and cleanup missions. In 1997, Oak Ridge and Sandia national laboratories initiated a multilab DOE effort to develop and test better UXO detection technology; some 14 DOE facilities and numerous university and industrial partners are involved.

"Remote sensing from aerial vehicles is one way to safely detect land mines, unexploded bombs, or other hazardous materials at Department of Defense sites," says Dick Davis, director of the Defense Programs Office for ORNL. "We are also developing sensors and methods that may be used in future years to detect airport explosives and biological and chemical warfare agents, as well as UXO and land mines, including those made of plastic instead of metal. Besides traditional detection methods, chemical and biological sensors are gaining acceptance."

One potential remote-sensing method for land mine detection that has been developed at ORNL uses bacteria that emit light while eating explosives. In a recent test, researchers obtained glowing results.

Microbial Minesweepers

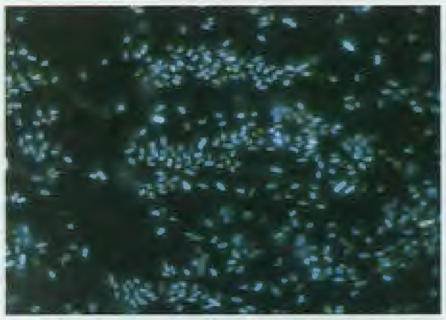
On the night of October 20, 1998, in South Carolina, Martin Hunt of ORNL's Instrumentation and Controls Division searched for experimental land mines with the determination of a tourist wielding a metal detector to find coins buried in beach sand. His tools were unusual: an ultraviolet (UV) mercury lamp and a piece of colored glass the size of a silver dollar. Under the supervision of Bob Burlage of the Environmental Sciences Division, the field had been sprayed with bacteria during the day using an agricultural sprayer (for an actual mine field, a crop duster could be employed). These bacteria were special: Burlage had engineered them to produce the green fluorescent protein (GFP) while they made a meal out of traces of a hidden explosive.

A remnant from the era of the war in Vietnam is this still "active" U.S.-made 500-pound bomb located near a family settlement in eastern Cambodia. It is estimated that more than 300,000 tons of such unexploded ordnance are still present in Cambodia.

When it was dark, Hunt shone the UV lamp on various parts of the site while looking through the dark glass, called a notch filter. He saw greenish fluorescent spots at known locations of the test land mines. A team on a cherry picker suspended 15 feet above the mine field also detected the telltale green glow in soil bathed in UV light from a laser-induced fluorescence imaging (LIFI) system. This portable LIFI system, being perfected by Bechtel Nevada for DOE, includes a video camera to collect the emitted light as images that reveal the little green spots, as well as a computer to display and store the image data. These tests of ORNL's microbial mine detection system were declared a success. The teams showed that one strain of genetically engineered bacteria can signal the presence of hidden explosives, thus offering a potentially cost-effective and safe way of locating antipersonnel mines over a wide area.

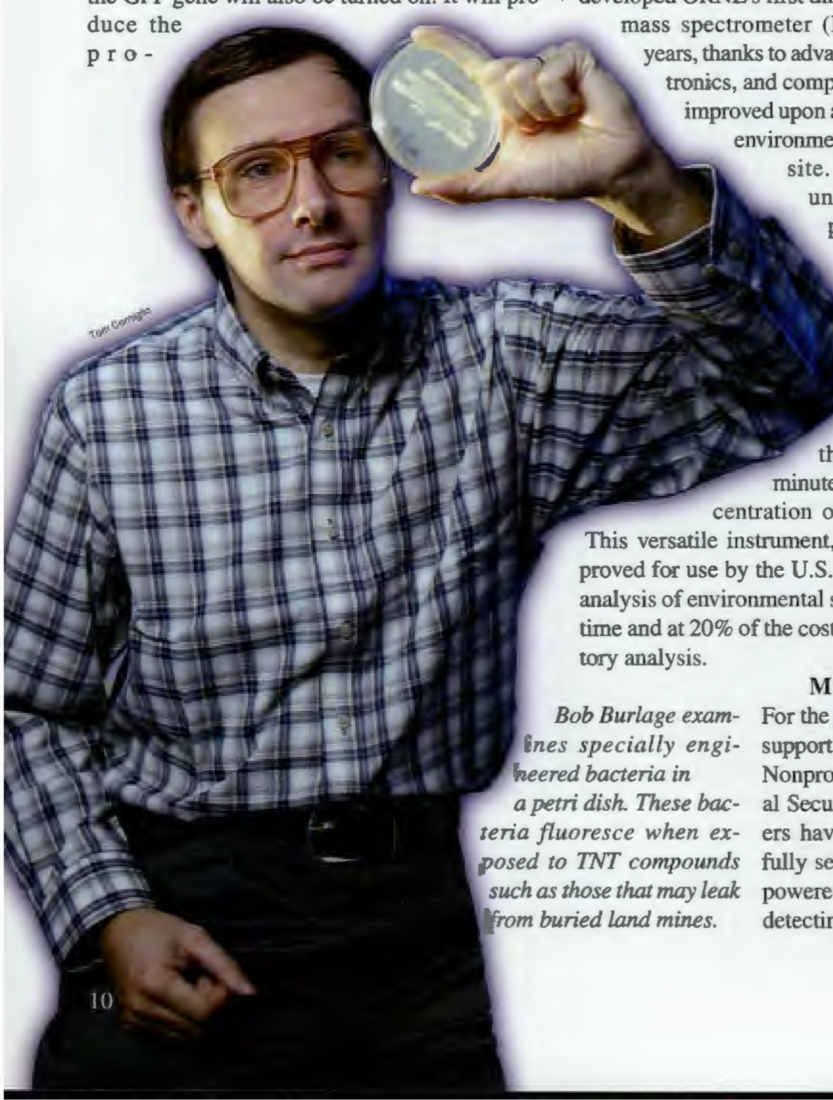
Burlage and Hunt were participating in a test around the prepared land mines constructed at the National Explosives Waste Technology and Evaluation Center in Edgefield, South Carolina. In their field test, they did not know the locations of the actual land mines containing trinitrotoluene (TNT). The mines were not fused, so they could not explode.

"Land mines leak small amounts of TNT over time, leaving a chemical trace for bacteria on the soil surface," Burlage says. "When the bacteria of one of our strains of *Pseudomonas putida* encounter the TNT, they will scavenge the compound as a food source, activating the genes that produce proteins needed to digest the TNT. Because we attached the GFP gene obtained from jellyfish to these activated genes and included a regulatory gene that recognizes TNT, the GFP gene will also be turned on. It will produce the protein that emits extremely bright fluorescence when exposed to ultraviolet light."



Bacteria tagged with the green fluorescent protein give off light. Although each bacterium is approximately one-millionth of a meter long, the fluorescence of the bacteria makes them easily visible under the microscope.

Burlage is encouraged by the results of these tests conducted for the Defense Threat Reduction Agency. He thinks it would be possible to detect land mines remotely from rolling towers or helicopters by looking for glowing microbes on soil illuminated with UV light. Says he: "No one yet has told me it can't be done." Perhaps ORNL will get the green light to develop a bacteria-based remote-sensing method for land mine detection.

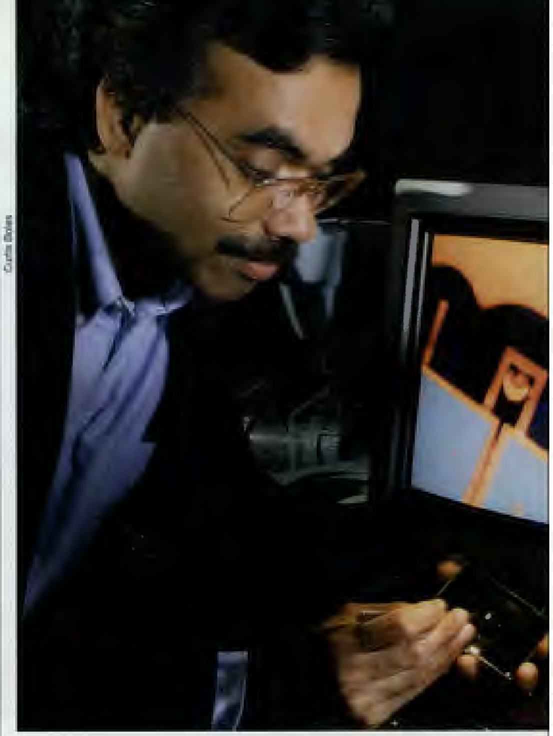


Bob Burlage examines specially engineered bacteria in a petri dish. These bacteria fluoresce when exposed to TNT compounds such as those that may leak from buried land mines.

Chemical Sensors

One of the early devices used to sniff for chemicals in the environment was built at ORNL. In the late 1980s, Marc Wise, leader of the Instrumentation Group in ORNL's Chemical and Analytical Sciences Division, and his associates developed ORNL's first direct-sampling ion trap mass spectrometer (DSITMS). Over the years, thanks to advances in ion traps, electronics, and computers, this device was improved upon and reduced in size for environmental measurements on site. Wise also added a unique modular sampling system. The result was an instrument that can rapidly sample and analyze pollutants from air, water, and soil. It tells researchers at the site within a few minutes the identity and concentration of pollutants present. This versatile instrument, which has been approved for use by the U.S. government, enables analysis of environmental samples in 10% of the time and at 20% of the cost of traditional laboratory analysis.

Multithreat analyzer. For the past three years, with support from DOE's Office of Nonproliferation and National Security, ORNL researchers have been developing a fully self-contained, battery-powered DSITMS for use in detecting threat chemicals. It will be the size of a briefcase instead of a desk.



Thomas Thundat picks up a platinum-coated cantilever chip (like the one magnified on the screen) that was designed at ORNL and fabricated at the Massachusetts Institute of Technology.

"Our multithreat analyzer is intended to be carried by a worker to any site that is difficult to reach with a vehicle or wherever portable monitoring is required," Wise says. "It might be needed to search for drugs in cargo containers or hidden explosives in an airplane cabin or mine field."

How will it work? If vapor molecules of TNT are present, for example, they are sucked through a long tube into the ion trap analyzer cell. There they are converted to ions that are trapped in the cell's electric field when a radiofrequency (rf) signal of 100 volts is applied. As the rf voltage is ramped up to as high as 7500 volts, ions of increasingly higher mass escape the trap. These ions are counted. By applying the rf voltage known to eject TNT and checking for a signal, it is possible to determine whether the explosive is present.

Warfare agent detector. An advanced DSITMS is the heart of a new chemical biological mass spectrometer (CBMS) being developed for the U.S. Army at ORNL. The CBMS will more accurately detect chemical and biological warfare agents and warn soldiers to wear protective gear or to avoid contaminated areas. An improved technology is needed: During the Persian Gulf War, Army detectors could not easily distinguish among vapors from diesel fuel, pesticides, rocket and gun propellants, industrial chemicals, and chemical warfare agents. Many false alarms were sounded.

Concerned that soldiers could be exposed to biological warfare agents (e.g., anthrax spores), as well as chemical agents (e.g., nerve agent VX) during hostilities and terrorist incidents, the U.S.

Army Soldier and Biological Chemical Command began funding development of the first-generation CBMS in Germany. In 1996 it asked ORNL to lead the development of the second-generation one because of our mass spectrometer expertise.

"The Army wants the next-series instrument to aller, lighter, faster, less expensive, more ve, more easily maintainable, and able to and distinguish among a wider variety of ıe chemicals and microorganisms, as well micals on the ground," says Wayne Griest, ;er of the CBMS Program at ORNL. "The BMS should be more accurate than the de; used today in determining if warfare are present."

ınovative technologies have been devel-ıy five ORNL divisions and three contrac-collect and heat airborne particles, handle nd control the mass spectrometer. In 1999 nitial units of the six-module CBMS will lt at ORNL. They will be tested on site on ; concentrations of warfare agents in fed-approved facilities. Orbital Sciences Cor-ɔn will develop an economically produc-strument for military use by 2000.

he final product will improve protection ;. troops. It should not sound any false ;, but it is hoped there will be no need for ıes.

ɔcantilever Sensors

ı 1991 Thomas Thundat of LSD was using mic-force microscope to examine the ef-humidity on DNA. The humidity degrad-performance of the microscope's cantile-ıich is used to map the atomic mountains lleys of surfaces, just as a phonograph sty-ces grooves in a vinyl record. It occurred ndat that this microscopic springboard had tential to be a sensor. Thanks to new mi-chining techniques, his group was able to silicon chips as small as rice grains from barely visible cantilevers project. Each chip is rugged and extremely sensitive yet ittle and uses little power. The cantilever technology has been licensed for several fields of application to Graviton, Inc., in San Diego.

Thundat and his colleagues showed that a cantilever bends or changes its natural vibration in a measurable way if it is coated with a material that attracts another material from the air. For example, a cantilever coated with a gelatin absorbs water, causing it to bend and measure humidity. Cantilevers can also be used to measure changes in temperature, sound wave velocities, and fluid pressures and flow rates.

"Cantilevers can store electrical charge or resist the flow of electricity," Thundat says. "When a cantilever bends or changes in its vibration, this ability is altered in a way that can be measured electrically. Also, by steadily bouncing a laser diode light off the cantilever, we can tell when it bends or wiggles by measuring changes in the angle of light deflection in an optical position-sensitive detector."

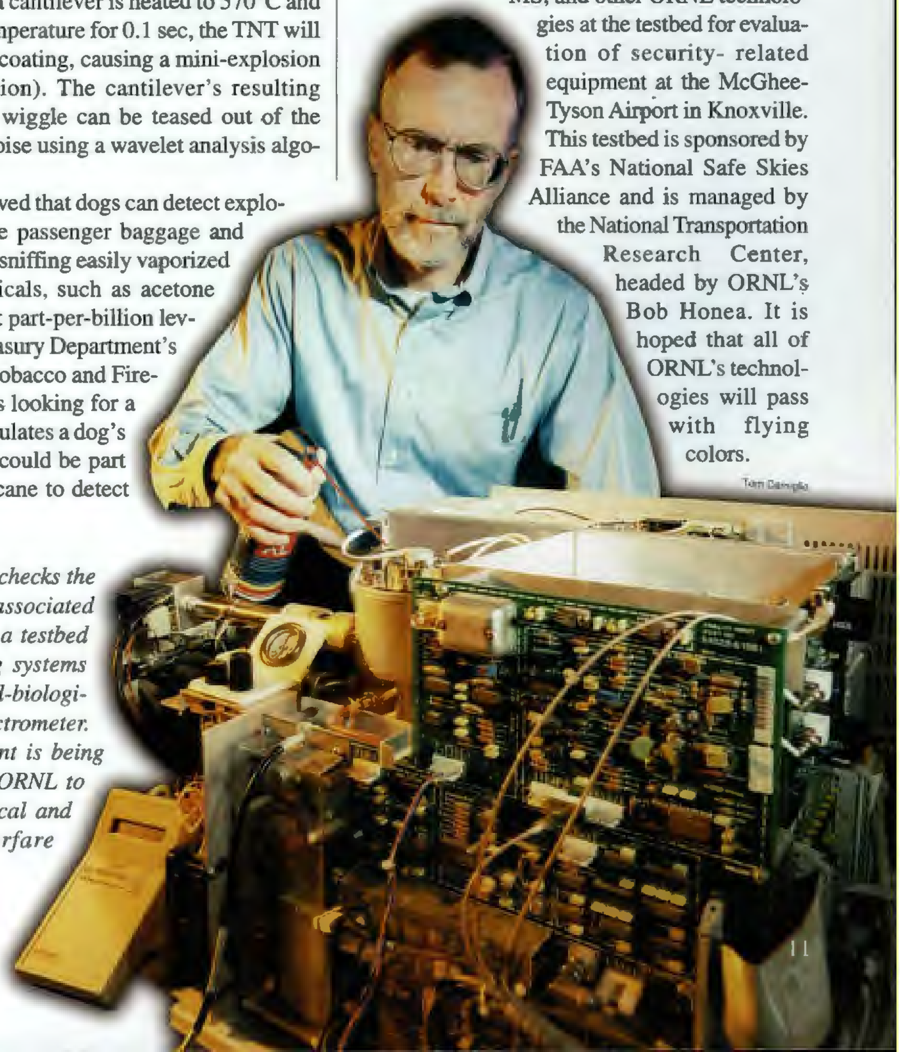
Thanks to funding from the Federal Aviation Administration (FAA), Thundat and his colleagues are developing a matchbox-size device to detect explosives in airport luggage and land mines. The device will contain cantilevers coated with platinum or a transition metal. If TNT is present when a cantilever is heated to 570°C and held at that temperature for 0.1 sec, the TNT will react with the coating, causing a mini-explosion (autocombustion). The cantilever's resulting characteristic wiggle can be teased out of the background noise using a wavelet analysis algorithm.

It is believed that dogs can detect explosives in airline passenger baggage and land mines by sniffing easily vaporized organic chemicals, such as acetone and toluene, at part-per-billion levels. So the Treasury Department's Alcoholism, Tobacco and Firearms agency is looking for a device that emulates a dog's nose and that could be part of a walking cane to detect the presence of an explosive. One contender is ORNL's calorimetric microspectrometer (CalSpec), which received an R&D 100 Award in 1998 (see p. 2). Another candidate technology is ORNL's "nose on a chip" device, which contains a series of cantilevers individually coated to pick up a different specific organic compound (see p. 14 for details). A computer will determine if the detected compounds spell out the signature of an explosive.

Efforts are under way to obtain industrial partners to help test, miniaturize, and manufacture these ORNL technologies. Meanwhile, there are plans to evaluate the cantilever sensors, DSIT-MS, and other ORNL technologies at the testbed for evaluation of security- related equipment at the McGhee-Tyson Airport in Knoxville. This testbed is sponsored by FAA's National Safe Skies Alliance and is managed by the National Transportation Research Center, headed by ORNL's Bob Honea. It is hoped that all of ORNL's technologies will pass with flying colors.

Tom Cerniglio

Bruce Warmack (left) and Chuck Britton examine an ORNL chip they designed with Thomas Thundat and others; this "nose on a chip" contains 640 microcantilevers.



Tom Cerniglio

Wayne Griest checks the analyzer and associated electronics in a testbed for evaluating systems of the chemical-biological mass spectrometer. This instrument is being developed at ORNL to detect biological and chemical warfare agents.

John Smith

Mike Ramsey shows an early version of the lab on a chip.

In 1987 ORNL's Mike Ramsey proposed carving a winding tube in a glass chip, injecting a few drops of liquid into the tiny tube, and "pumping" the liquid through it using an applied electric field. His colleagues laughed at him. They didn't realize that, thanks to microfabrication techniques used to make silicon chips for electronic devices, it was possible to construct a "lab on a chip"—a miniature device for separating molecules and measuring chemical reaction rates using very small liquid samples.

Incredible Shrinking **Labs:**

Chipping Away at Analytical Costs

ORNL is developing chips ranging in size from a match ti a match box for health and environmental applications.

Such a postage-stamp-size chip based on OI designs is now being tested and c mercialized for DNA and protein analysis Caliper Technologies, Inc., a Califc company on whose scientific board directors Ramsey sits. The chip can ana DNA and small molecules for such uses as DNA sequenc DNA fingerprinting of blood at crime scenes (see p. environmental monitoring, detecting chemical warfare ag and developing new drugs.

Thanks to internal lab funding for his idea, in 1991 Ramsey and his colleagues in the Ch and Analytical Sciences Division (CASD) began developing "microfluidic structures" and d strating that they can separate chemicals in very small volumes. He also gave scientific talks pro the concept.

"Just as the electronic industry shifted from vacuum tubes to transistors to microele chips," Ramsey says, "I felt that the chemical analysis community would have a similar moti to reduce analytical instrument size from a few cubic feet to several cubic centimeters. Such turization offers low cost, low weight, high speed, high reliability, and operational simplici chemical analysis it saves materials and labor and reduces discharges to the environment."

In the lab chips, molecules rather than electrons flow through labyrinths of tiny chann chambers outfitted with valves, filters, and pumps. In 1994 Ramsey and his colleagues publi paper in the journal *Analytical Chemistry* on how to use electric fields to make liquids glide q around the hairpin turns of a channel on a dime-size "serpentine chip." The liquids carry a because, in a capillary, the liquid pulls protons off the glass wall. By applying the electric fiel chip ports simultaneously, the ORNL lab on a chip avoided the leakage problems of a simil designed by the Swiss group that first published a paper on the concept.

A lab on a chip can analyze a volume of liquid 10,000 times or more smaller than that used in a conventional analytical instrument. Smaller volumes permit faster mixing because molecules don't have so far to travel. Chemicals in a liquid droplet can be mixed and separated very rapidly. In fact, in an "Oh wow" experiment, Ramsey and his ORNL colleague Steve Jacobson separated two species in less than a millisecond—100,000 times faster than conventional methods.

The pharmaceutical industry prizes analytical techniques that use small samples and quickly produce results. Generating large quantities of enzymes for drug design experiments is very difficult and expensive. Now, scientists no longer must synthesize and test compounds one at a time to see which will block an enzyme related to a disease state. Instead, they can make small quantities of many related substances and, using many lab-on-a-chip systems, screen them simultaneously for biochemical activity.

The ORNL group recently tested the ability of a lab on a chip to determine the effectiveness of various inhibitors in blocking enzyme reactions with a substrate. The test enzyme was reacted with a sugar, producing a chemical that emits light. A laser light was shone on the product, causing it to fluoresce. By determining the strength of the fluorescence, a computer linked to a light detector measured how fast the product formed. When an inhibitor was introduced into the mix, it blocked the reaction between the enzyme and sugar, reducing the rate at which the fluorescent product was generated. The inhibitor that slowed the reaction rate down the most might be the best candidate for an ingredient in a disease-fighting drug.

Parallel lab-on-a-chip systems also may offer the most economical way to rapidly analyze large DNA samples to determine the sequence of their chemical bases. Chips promise to carry out repetitive sequencing tasks for tens of thousands of genes more quickly and cheaply using smaller samples than other technologies.

Chips based on ORNL designs are already being used in desktop instruments linked to personal computers to provide a compact analytical instrument. The lab on a chip is small, but its potential is large.

Biochips for the Doctor's Office

You feel terribly ill, so you call your doctor. You are asked to come to the waiting room where the nurse takes a drop of blood from your finger. After about 40 minutes, you are escorted to the doctor's office. The doctor says, "I have good news for you. According to this biochip, you don't have tuberculosis, the AIDS virus, or any signs of genetic predisposition to cancer. You just have a bad case of the flu."

Someday your doctor may be relying on a matchbox-size diagnostic device invented at ORNL. This "multifunctional biochip" has been developed by Tuan Vo-Dinh of ORNL's Life Sciences Division (LSD), in collaboration with Alan Wintenberg and Nance Ericson, both of ORNL's Instrumentation and Controls (I&C) Division. It will provide quick results using only a drop of blood. It will be highly selective and sensitive, able to distinguish between a bacterium and virus or between a chemical and biological organism.

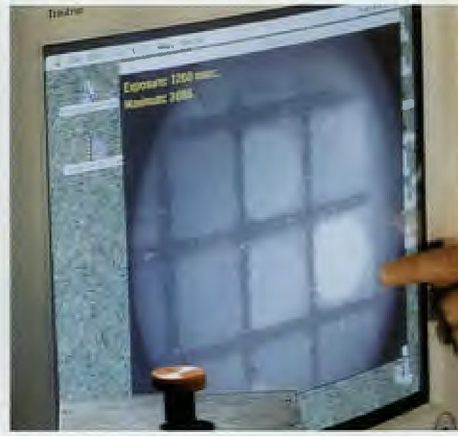
"By integrating microelectronics, optics, and biological material in a single system," Vo-Dinh says, "we have developed a second-generation device—a multifunctional biochip that will be able to simultaneously detect a variety of biomedical targets. One chip may hold specific DNA sequences, antibody probes, and protein receptors. It will process up to 100 samples in 30 minutes. It will be useful for DNA sequencing; gene identification and mapping; screening blood, vaccines, food, and water supplies for infectious agents; and diagnosis of diseases, including AIDS, hepatitis, genetic cancers, and Alzheimer's disease."

The multifunctional biochip has multiple components in a miniature format, including a sampling platform, excitation sources, and electro-optic sensor arrays. Here's how it would work with DNA. On the sampling platform are attached short DNA fragments, each of which has a different sequence of chemical bases. The chip site and sequence of each fragment is known. The patient's blood is processed for viral or bacterial material yielding DNA fragments of unknown sequences that are then tagged with a fluorescent dye. These blood fragments are introduced to the platform. Because a DNA sequence will link up with its mirror image, some of the tagged DNA fragments will pair, or "hybridize," with the affixed fragments having the complementary sequence. The unattached fragments are then washed away.

A diode laser or light-emitting diode illuminates the array of DNA sites with light of one color, causing fluorescence at the sites of paired DNA fragments. Below each site is an array of tiny light detectors (photodiodes) with electronic circuitry that detects the fluorescence and sends an electrical signal. The "smart" analog and digital circuitry in the integrated electro-optic chip collects each signal, determines the total sequence of the captured DNA fragments, compares it with the known sequences of various bacteria and viruses, and issues a diagnosis.

Vo-Dinh's group has demonstrated that the biochip works on synthetic DNA templates from a region of the AIDS virus, the tuberculosis bacillus, and a cancer gene. In 1998, the biochip was licensed to a private company. Because of its speed of diagnosis and because it does not rely on radioactive substances (whose disposal is expensive), the biochip is expected to reduce health care costs.

Tuan Vo-Dinh inspects an early version of the DNA biochip, now called the multifunctional biochip. It holds antibodies and proteins, as well as DNA, for disease detection in the doctor's office someday.



Mitch Doktycz checks the alignment of a robot's dispensing probes as he prepares to construct a set of flowthrough genosensors. The dispensing probes transfer DNA sequences from laboratory plates to individual wells of the genosensors. Inset: White spot on microscope's computer screen shows where fluorescent DNA has paired with DNA affixed in one of the 100 wells in the genosensor (half an inch on a side).

Tom Cerniglio

Flowthrough Genosensor

Knowing the structures and functions of genes in the human genome is a holy grail of biology. Researchers in LSD have devised a three-dimensional approach to the problem of sequencing DNA bases. Instead of a checkerboard array of affixed DNA sequences with which tagged mirror-image sequences can pair (as in Vo-Dinh's biochip), Ken Beattie and Mitch Doktycz have developed a "flowthrough genosensor" made of glass or silicon for DNA sequence analysis. This miniaturized chip is expected to increase the speed, economy, and throughput of genome mapping and sequencing for certain uses.

For example, by comparing particular DNA sequences, the genosensor can help biologists find genetic differences between individuals and determine the genetic basis for diseases. It can identify more quickly and accurately those microbes that "eat" a specific pollutant by detecting the signature gene producing the enzyme that metabolizes the target chemical. It can help determine which genes are active in various body organs and what their functions are.

"We built a porous glass chip with an array of tiny tubes, or channels, arranged parallel to each other and perpendicular to the array," Beattie says. "Because these 10-micron channels penetrate the chip, a solution of target DNA will 'flow through' rather than 'over' the chip and will contact DNA probes attached to the channels' inner surfaces.

"The porous structure leads to a greatly increased surface area, allowing a higher degree of miniaturization. Also, because the channels are so small, the molecules are brought together into close contact, speeding the hybridization."

Each of these genosensor "chips" measures less than half an inch on a side and contains about 100,000 channels. The researchers' recent development of silicon genosensors opens the possibility of using electronic components to manipulate fluids and detect hybridization.

"We have been developing a robotic spotting system to position DNA probes on the flowthrough genosensor," Doktycz says. "The robot can dispense these probes just a few hundred microns apart to create an array of a few thousand different probes on a dime-size surface."

The sequence and location of each immobilized DNA strand in the array are recorded on a computer. This information is critical to identifying and sequencing the target DNA.

The researchers also developed a fluorescence imaging system to locate target DNA sequences, which they tag with a fluorescent dye before flowing them through the chip. A solution with a low concentration of the target DNA is injected through a slender tube and into the genosensor, which is mounted onto the fluorescence microscope. The target DNA molecules pair with the immobilized probe molecules whose sequence is complementary. When light of the right wavelength from the microscope is shone on the target DNA fragments, their tags fluoresce, revealing the locations of hybridization events. The image of the bright and dark spots on the genosensor is magnified in the microscope and displayed on a computer monitor. The resulting image is then analyzed to determine sequences contained in the target DNA molecule or quantify the amount of specific target sequences.

The flowthrough genosensor appears to be a significant step in pursuit of biology's holy grail.

Nose on a Chip

When he arrives home from vacation, Clarence's smart alarm system deluges him with messages. Natural gas is leaking from the furnace. Smoke is present in a guest bedroom. Food is spoiling in the refrigerator. In the garage, a paint can lid apparently has come loose, and a container of insecticide is leaking.

Such a warning capability may be possible someday, thanks to ORNL's invention of a "nose on a chip." This wireless electronic nose can simultaneously detect and measure a variety of vapors in the air and signal a receiver to sound an alarm or display a message.

Already tests of this first battery-operated cantilever array sensor chip set have shown it can simultaneously sense various combinations of hydrogen, nitric oxide, mercury vapor, and alkane thiols in the air. Because the device is inexpensive and can provide instant results, it could soon be incorporated into household gas appliances to warn of hazardous leaks.

The electronic nose consists of an array of tiny fingerlike sensors sculpted along a small silicon chip, plus electronic signal processing and transmission capabilities on other integrated circuits. Hundreds of these springboard-like sensors, called cantilevers, can be carved in a 1-cm^2 silicon chip using standard circuit manufacturing techniques. Selectively coating each cantilever sensor in an array with the right chemical can customize the chip to detect thousands of chemicals. This concept is an extension of an invention patented by ORNL's Thomas Thundat and Eric Wachter.

A properly coated cantilever bends or changes its vibration ever so slightly when it interacts with a target chemical in the environment. For example, because mercury vapor is attracted to gold, a gold-coated cantilever will absorb airborne mercury and bend according to its mass, resulting in an electrical signal indicating the detection of mercury.

Kim Young examines the "nose on a chip," which uses cantilevers coated with different chemicals to detect multiple gases.

"Most existing chemical sensors can detect only one species and require large amounts of space and electrical power," says Chuck Britton, one of the developers and a member of the I&C Division. "Our innovation is to use miniature arrays of low-power-consumption sensors and electronics on a single chip to detect many different species simultaneously."

The chip electronics convert the continuous (analog) signals into digital data. An I&C team led by Steve Smith has equipped the wireless electronic nose with a transmitter that first turns the digital data into radiofrequency signals with unique identifier patterns and then sends them to a receiver. The receiver, which includes a computer to analyze the data, could be programmed to sound an alarm if a gas level gets dangerously high.

Copies of the wireless electronic nose can be produced inexpensively, using standard processes for semiconductor manufacturing. "Ultimately," says Bruce Warmack, leader of the LSD group that developed the microcantilevers as sensors, "these chips could be made so inexpensively they could be thrown away after they are used."

The project was supported by the internally funded Laboratory Directed Research and Development program. The key to the success of the electronic nose was the collaboration among three ORNL divisions. Expertise in integrated circuit design came from the I&C Division; in cantilever design, from LSD; and in selection and synthesis of coatings, from CASD. The multidisciplinary approach should improve the accuracy and versatility of the nose on a chip, giving new meaning to the phrase "the nose knows."

Critters on a Chip

A future scenario: Numerous silicon chips, each the size of a match tip, are sprinkled over contaminated soil. Bioluminescent bacteria intentionally placed on each chip feast on the pollutants and begin to glow. Their blue-green visible light is absorbed by the silicon, creating electrical charges that are fed into the chip's circuitry. Signal-processing microelectronics measure the tiny electrical current. From some chips, signals are sent to a pollution engineer's electronic receiver, which sounds an alarm.

The "critters on a chip," which were genetically engineered to emit light as they eat and digest certain environmental pollutants, have detected naphthalene and toluene in the soil. The chip electronics reveal the concentration of each pollutant, which is related to the amount of electric current produced.

The critters-on-a-chip technology developed by Mike Simpson of the I&C Division in 1996 could be used to map soil contamination. Other possible applications are to detect specific chemicals in soil or groundwater, including spilled fuel, toxic metals such as mercury, and explosives that may have leaked from land mines. Oil exploration companies might want to use the technology to detect hydrocarbons that indicate the presence of nearby oil and gas deposits.

ORNL researchers are now working with Perkin-Elmer Corporation, a large environmental instrument company, to commercialize the critters-on-a-chip technology. A growing demand for such wireless chips is anticipated because they can be deployed where other devices can't—groundwater, industrial process vessels, and the battlefield.

Simpson and his colleagues developed a prototype device by coupling *Pseudomonas fluorescens HK44*, a novel naphthalene bioreporter microorganism developed by the University of Tennessee Center for Environmental Biotechnology (UT-CEB), to an optical application-specific integrated circuit (OASIC) developed at ORNL. A measured electrical signal was obtained when the OASIC chip was exposed to moth balls, which are made of naphthalene. A second prototype used the toluene-sensitive *Pseudomonas Putida TVA8*, also developed at UT-CEB.

Simpson is improving the chips to increase their longevity. "The key is to place the bacteria on a transparent silicon nitride film that protects the etched silicon chip from damage in the presence of hazardous chemicals," Simpson says. "To increase the shelf life of the chip, the bacteria could be freeze dried, and a micromachine on the chip could activate its living sensors when needed by dumping water and nutrients on the dormant bacteria."

The idea is to avoid having quitters on the chip.

Mike Simpson shows the bioluminescent bioreporter chip, dubbed the critters on a chip. Genetically engineered bacteria on the chip emit blue-green light when they encounter a pollutant they like to eat. The light is detected by the chip electronics, and the resulting electrical signal reveals the identity and concentration of the pollutant.

Cars, Clothes, and Computers: Help for Industry

The white stripes of phosphor on this metal specimen glow red when illuminated by a black light. Some phosphors have no trouble surviving and functioning in high temperatures such as those produced by this propane torch.

ORNL has developed measurement and inspection techniques that may increase the competitiveness of the U.S. steel, textile, and semiconductor industries.

Cars get us to work, clothes make us feel good at work, and computers help save us work. And it takes work on the part of American industry to manufacture the materials that provide us with these luxurious necessities. In making these materials into products, manufacturing operations are often plagued with inefficiencies. Too much defective material is being produced. Too much energy is being wasted. Too many workers are spending too much time looking for occasional flaws.

Automated measurement and inspection methods are needed to increase the production of high-quality material, reduce the production of defective material, save energy, and free up personnel to work on tasks that increase a company's earnings. In other words, the goal is to raise production efficiency to reduce the costs of products, improve their quality, and increase their market share.

ORNL has the capabilities to develop measurement techniques that will help industry become more competitive. Two of our techniques are considered promising for increasing efficiency in the steel and textile industries and one is already helping the semiconductor industry. Our technologies may help increase the quality of cars, clothes, and computers.

Thermometry for the Steel Industry

Cars today don't rust the way older vehicles did. The reason: The steel industry uses a "galvannealing process" to produce the corrosion-resistant sheet metal now used in virtually all the world's automobiles. The process combines zinc atoms with iron atoms in a steel surface at high temperatures. The protective layer of zinc-iron alloy that is formed prevents the steel from rusting through. In fact, because of this galvanneal coating, lifetime guarantees against rust through can be offered by the automotive industry.

Getting the galvanneal coating right for automobiles and other products is not easy. First, a sheet of steel is dipped in a liquid bath of zinc at about 450°C. Then the steel sheet passes through a cascade of furnaces, raising its temperature to as much as 700°C. During heating, iron atoms from the molten steel sheet drift into the zinc coating to form the zinc-iron alloy. But, is the molten steel surface always at the right temperature to ensure formation of the best galvanneal coating? Making sure the temperature of galvanneal steel is on the mark has long been a problem for the steel industry, a problem that ORNL is helping to solve.

The galvannealing process of alloying zinc with iron at the surface must be controlled at production rates of 30 meters per second or higher to ensure the surface quality necessary for the automotive market. When the galvanneal coating is incorrectly formed, the material is rejected as second-rate steel, costing the U.S. steel industry $4 billion per year and reducing its competitiveness with steelmakers worldwide. Hence, getting these coatings consistently right was identified by the U.S. steel industry as the key to the future competitiveness of their galvanneal product line.

The problem is that the surface alloying process varies as the temperature of the metal surface changes, yielding a product of nonuniform quality. One challenge has been to devise a method that accurately measures the temperature of the molten material as it forms an alloy and cools. A second challenge has been to relay information instantly to steel producers so they can adjust furnace operation to get the right temperature—and best product.

To address these challenges, the American Iron and Steel Institute (AISI) accepted a proposal by ORNL and the University of Tennessee at Knoxville (UTK) to develop a totally new, first-principle-based technique for determining the surface temperature of galvannealed steel. The ORNL and UTK engineers designed and built a novel instrument system in collaboration with National Steel, the partner steel company. The project is part of the Advanced Process Control Program supported by 15 AISI-member steel companies and the Department of Energy's Office of Industrial Technologies. Bailey Engineering of Mechanicsburg, Pennsylvania, is now developing the concept of the prototype instrument built at ORNL into a commercial product that will be available soon to the steel industry.

"Real-time steel temperatures cannot be measured precisely using the conventional method because it assumes that the surface properties are constant," says Steve Allison of ORNL's Engineering Technology Division, a principal developer of the technique. "The problem is that properties of the zinc-covered surface rapidly change as the coated steel cools from a molten to solid state, causing errors in the temperature measurement by as much as 40°C. Because our device uses a thermal phosphor method, it has demonstrated accuracy within better than 3°C. Clearly, it is more reliable than the conventional method."

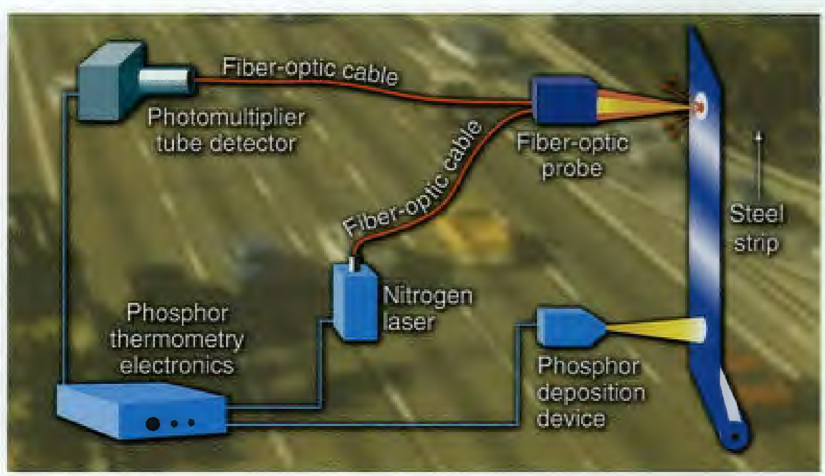
How does the thermal phosphor technique work? A steel sheet is partly dusted with white phosphor powder using a computerized phosphor-deposition system. Two optical fibers are positioned between the moving steel sheet and the temperature measurement equipment. As the sheet travels between the furnaces at up to 30 meters per second, short pulses of ultraviolet light are fired from a low-power nitrogen laser through an optical fiber leading to the molten steel. The laser pulses excite the phosphors, which emit light for a short time based on how hot they and the steel substrate are. The emitted light travels through the other optical fiber to a light detector (photomultiplier tube). It measures the time for the phosphorescence to decay, and a computer uses the real-time data to calculate the surface temperature of the galvannealed steel.

"To apply the phosphor to the moving sheet," Allison says, "we had to solve some interesting problems in mechanical design, fluid mechanics, and optics. We had to figure out how to illuminate the phosphor and gather the light for temperature measurements. So we assembled a team of diverse skills and expertise from ORNL's Engineering Technology and Instrumentation and Controls divisions, UTK, and National Steel."

The team was asked to determine whether phosphor powder might damage the quality of the steel. Results of tests done by ORNL and National Steel indicated no adverse effects on either the coated steel's surface appearance or its ability to be painted.

Other ORNL co-developers of the technique were Wayne Manges, Ruth A. Abston, William Andrews, David L. Beshears, Michael Cates, Eric

ORNL engineer Ruth Ann Abston adjusts the phosphor deposition device in front of the galvanneal sheet.



Schematic of galvanneal phosphor thermometry components. A thin phosphor layer deposited on the steel strip is illuminated using laser light. The duration of measured fluorescence from the excited phosphor layer indicates the steel's temperature.

B. Grann, Timothy J. McIntyre, Matthew B. Scudiere, Marc L. Simpson, David N. Sitter, and Todd V. Smith.

Early prototypes were tested at National Steel's Midwest Steel Division in Portage, Indiana. On May 31, 1998, the final version developed at ORNL was successfully demonstrated on a galvanneal line at the Bethlehem Steel plant in Portage. The demonstration was part of DOE's Technology Showcase held at this facility, where the system is permanently installed.

The new process should result in less second-rate material and eliminate the need for costly off-line tests to determine if the galvanneal coating is correct. Accurate, reliable temperature measurements will ensure a quality product, reducing waste and saving energy. These improvements, if implemented throughout the U.S. steel industry, could save steelmakers as much as $70 million a year, increasing their competitiveness worldwide. And such a savings might lead to more affordable cars or, at least, larger earnings for the steel industry.

Inspection System for the Textile Industry

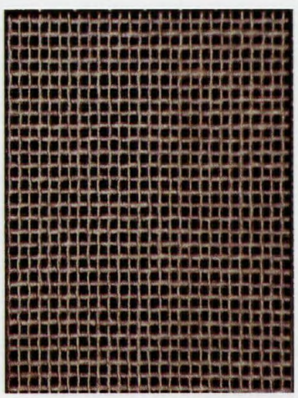
Defective material, a grudgingly accepted by-product of textile production, continues to be a problem in the American textile industry, long a source of our clothing, carpeting, medical dressings, protective outerwear, and automotive airbags. Erratic loom operation and errors in human inspection in U.S. textile mills result in excessive, reduced-price, second-grade merchandise. But technology may soon be a boon to textiles.

Reducing costs through technology is considered a key to making the industry more competitive. Currently, offshore competitors are a major economic threat. Since 1980, the U.S. textile industry has lost approximately 400,000 jobs to foreign manufacturers. If this trend continues, another 600,000 jobs may be lost by 2002.

To stem these losses, ORNL, the Oak Ridge Y-12 Plant, and other DOE laboratories have been working with the U.S. textile industry to weave new technology into textile operations. Under a collaborative research and development agreement (CRADA), a team of Oak Ridge researchers—including Glenn Allgood, Dale Treece, and John Turner, all of ORNL's Instrumentation and Controls (I&C) Division, have already helped the American Textile Partnership. They have developed automated inspection for the weaving industry under the CRADA's Computer-Aided Fabric Evaluation (CAFE) Project. Automated inspection is expected to improve quality and lower costs, increasing worldwide demand and market shares for U.S. textiles.

Today's textile mills use high-speed looms to weave yarn into cloth. Inspectors in the mill manually feel and visually examine the cloth, looking for defects. Sometimes they become fatigued and miss the less obvious ones. Sometimes defective material passes through the entire textile system into the marketplace. If the fabric's flaws are noticed by retailers or consumers, the material is marked down or returned as a loss.

Because of current off-line inspection methods, potentially thousands of yards of defective, off-quality material could be made before the problem is recognized. Therefore, to provide 100% reliable inspection, the CAFE industry partners asked the participating laboratories to invent new technologies to automate and improve the current process for inspecting fabric while it is being woven. This was an immense task, considering that the U.S. textile industry produces 5805 square miles of cloth a year.



One-inch image plane of 28 pick goods is captured electronically for display. The cloth has a horizontal and vertical structure typical of all woven material. The horizontal threads (fill yarns) are the ones imaged and analyzed by the pick measurement device.

Oak Ridge researchers led by Allgood first had to familiarize themselves with the complexities of cloth and textile manufacturing. "We had to know about cotton and polymers, different weave types, and yarn thicknesses," Allgood says. "We observed the weaving process in which horizontal filling, or 'pick' yarn, is laid down at a right angle to the 'warp' yarns that run lengthwise through the fabric. We learned that the regularity and density of pick yarn—that is, the number of strands per inch—strongly affect fabric quality and the amount of yarn used."

So they set out to develop an optical device to measure pick density and to locate in real time fabric flaws—unexpected variations in the measured pick density, such as missed picks or picks that are too close together or too far apart. The result was the pick measurement device, which is cheaper than conventional camera systems used for textile inspection and easier to install on existing looms. The device uses a laser to bounce light off the yarn with a set of cylindrical lenses arranged to gather the reflected light and build an image of only picks, not warp yarns. The image on the array appears on a desktop computer screen as a one-dimensional image of the fabric with each pick represented.

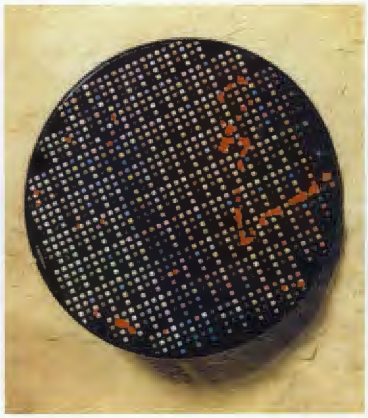
An ORNL-developed algorithm enables a computer to evaluate all the images, count the picks, calculate their density, and spot density variations. By matching these variations with known flawed patterns, it locates and names defects according to their classification. The computer will sound an alarm and can display an electronic defect map in the textile mill control room when flaws are first detected. Thanks to this nearly instant feedback, mill operators will be able to correct loom operation quickly to minimize the production of second-rate material. The map also provides data on the amount and quality of material headed for the mill's "downstream processes" such as printing, dying, cutting, and sewing operations. As a result, material yields are optimized and second-rate material is not processed for sale as a high-quality product. The pick measurement device team received a Technical Achievement Award at the 1998 Lockheed Martin Energy Research Corporation Awards Night ceremony.

"We also developed an economic model so that our industry partners would know what the inspection system had to be able to do for the price to make it a worthwhile investment for the textile industry," Allgood says.

The pick measurement device prototype tested in Oak Ridge was installed in 1997 at the Glen Raven plant in Burnsville, North Carolina. It was then moved to the Institute of Textile Technology (ITT) in Charlottesville, Virginia, for final testing. The device has been patented and licensed to ITT, which—with the help of Appalachian Electronic Instruments, Inc. in Ronceverte, West Virginia—will manufacture, market, and sell the device to the textile industry. The cost of the commercial device is estimated to be $1200 and the cost of using it is estimated to be 1% of that for a human inspector. It is believed the device will find widespread use in the textile industry and will help make U.S. textile manufacturers more competitive in both U.S. and world markets.

Defect Recognition for the Semiconductor Industry

The U.S. semiconductor industry is reducing waste, raising its productivity, and lowering its costs in producing electronic components for computers, thanks to a software tool developed at ORNL. Working with SEMATECH, which was created in 1987 as a partnership between the U.S. government and the semiconductor industry to make the U.S. semiconductor industry more competitive, ORNL developed an algorithm that recognizes defect patterns on silicon wafers and identifies the manufacturing problems causing the defects. This "spatial signature analysis" (SSA) tool has been licensed to 14 semiconductor manufacturers and equipment suppliers.



A scratch-and-spray deposition pattern is shown on this wafer map.

Because the manufacturing process involves hundreds of steps, the opportunities for defects to form are many. Defects in the dies on the wafers—tiny luminescent squares dotting 8-inch black disks—mean that these dies for carrying traces of electrical current are unfit for use in microprocessor chips, the "brains" of desktop computers. A certain pattern of defects, or signature, usually indicates a particular manufacturing problem. For example, a scratch across many dies on a wafer could be a sign of mechanical mishandling of the wafer by an industrial robot.

"SSA rapidly extracts only meaningful information from huge amounts of data on the wafers obtained from lasers and microscopes," says Ken Tobin, a senior research scientist at ORNL and one of the developers of the algorithm. "It quickly identifies defect patterns and traces them to manufacturing malfunctions, enabling industry engineers to find and fix the problem fast."

"An excellent use of this tool is the detection of scratches caused from wafer handling in real time," says Marylyn Bennett of Texas Instruments in Dallas, Texas. "If we could automatically detect and prevent scratches alone, the potential savings would be about $100,000 for every lot of wafers saved." SSA was fully integrated into the Texas Instruments data management system in November 1997.

Lockheed Martin Energy Research Corporation (LMER), which manages ORNL, recently licensed the ORNL-SEMATECH SSA technology to 14 companies, many of which are SEMATECH member companies. The licensees are eight semiconductor manufacturers—Advanced Micro Devices, IBM, Intel, Lucent Technologies, Motorola, National Semiconductor, Rockwell, and Texas Instruments—and six semiconductor equipment suppliers—Applied Materials, Defect and Yield Management, Inspex, KLA-Tencor, Knights Technology, Inc., and ADE, Inc.

SSA technology was developed by Kenneth Tobin, Shaun S. Gleason, and Thomas P. Karnowski, all of the Image Science and Machine Vision Group in ORNL's I&C Division, under a CRADA between the Defect Reduction Technology Group at SEMATECH in Austin, Texas, and DOE, which provided half the funding.

In 1998, the developers won three awards for the SSA technology: a Technical Achievement Award from LMER, a Marketed Technology Award from the American Museum of Science and Energy in Oak Ridge, and a Department of Energy Federal Laboratory Consortium Award for Excellence in Technology Transfer.

Other industries that may benefit from this knowledge-based tool include manufacturers of textiles, flat panel displays, and optical and magnetic disks.

ORNL has developed measurement technologies that may help reduce or eliminate waste in the steel, textile, and semiconductor industries. For consumers, these advances may mean higher-quality and lower-cost cars, clothing, and computers.

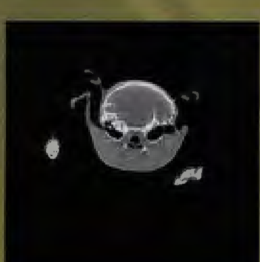
Tom Cerniglio

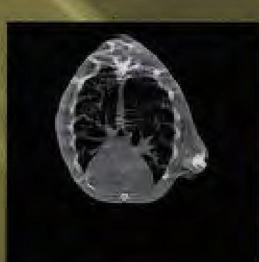
Ken Tobin (left), Shaun Gleason, and Tom Karnowski show the display of results from the spatial signature analysis algorithm they developed.

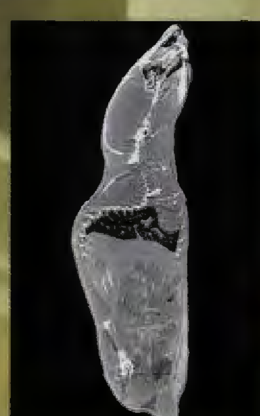
Of Mice, Monitors

Curtis Boles

ORNL researchers are developing techniques to monitor the health and behavior of mice to determine the genetic changes affecting the experimental animals.







The MicroCAT provides three-dimensional images with 10 times the resolution of systems used today.

Three-dimensional images show the fat deposits and skeleton of a mouse born with an obesity gene.

and Medicine

Thanks to new technologies and applications of familiar technologies, mice that look normal but carry subtle mutations are being monitored at ORNL in the same ways as hospital patients. These monitoring technologies are helping biologists rapidly identify which mice have a particular mutation, saving time and money and producing interesting scientific results.

ORNL is home to one of the world's largest experimental mouse colonies. This DOE user facility currently houses more than 70,000 mice representing about 400 mutant strains. A mutant strain is produced by altering or eliminating at least one gene in parent mice through radiation, chemical mutagens, or genetic reengineering. A mutant strain could be a model for a human disease if each mouse's disorder is due to a change in or deletion of a gene that has a counterpart gene in humans with a similar disorder.

One new technology that is impressing research biologists is the MicroCAT system developed in ORNL's Instrumentation and Controls (I&C) Division by a team led by Mike Paulus and Hamed Sari-Sarraf. This ultra-high-resolution imaging tool generates three-dimensional images with over 10 times the resolution of conventional X-ray-computed tomography systems.

"Thanks to new high-resolution X-ray detectors on the market and the fact that only low-energy X-rays are needed for small animals, we get very sharp, high-contrast images of the internal organs and tissues of mice," Paulus says. As a result, the MicroCAT shows promise for detecting concealed mutations or signs of disease in mice, such as skeletal defects, abnormally shaped organs, and tumors.

The MicroCAT system has been used to study mice with various conditions, including polycystic kidney disease (PKD), which can cause high blood pressure, kidney failure, and premature death in children. Both people and mice born with PKD have an abnormal kidney gene (first identified in mice at ORNL). ORNL's research biologists had been using manual, time-consuming techniques to confirm that mice believed to be born with PKD as a result of genetic reengineering are developing the disease.

Kevin Behel (left), a graduate student from the University of Tennessee, and ORNL's Mike Paulus recently scanned this live mouse using the MicroCAT prototype.

"Now, we bring our mice to Mike Paulus and he scans one every five minutes with the MicroCAT," says Dabney Johnson, head of the Mammalian Genetics Section of ORNL's Life Sciences Division. "For some mice, he gets images that show fluid-filled cysts inside their kidneys. If these mice die early, his results suggest that PKD was the cause."

MicroCAT is also used to study mice that are fat. "Like people, fat mice can have fat deposits in different places," Johnson says. "But we have identified an obesity gene that causes mice with the gene to have fat deposits in known regions of the body. In the past, we would sacrifice fat mice and dissect each one to determine which fat pads are oversized."

Now, using MicroCAT, Paulus can image a mouse's soft tissue, and with the help of an algorithm, compute the tissue's volume-to-density ratio to locate the fat pads. If the final image shows abnormally large fat deposits, the mouse has the obesity gene. Studies of mice with this gene could help scientists find treatments for obesity in humans.

"By using the MicroCAT," Johnson says, "we won't have to rely only on visible genetic mutations and physical examinations to detect mutations. We won't have to dissect the mouse to study internal organs. We are looking forward to having our own MicroCAT system in our biology laboratories next year."

Johnson is also looking forward to using another ORNL-developed technology—a sensor system surgically implanted under the skin of a mouse's neck that measures several physiological indicators in the mouse. The sensor data are transmitted periodically by radiofrequency (rf) signals to a local receiver for display on a computer and analysis by a geneticist. Nance Ericson of the I&C Division, who leads the implant development team, has shown that the miniaturized instrument can measure body temperature, pulse rate, and activity in mice. He plans to add multiple rf receivers to provide triangulation, so biologists can track changes in the position of a mouse in its cage. Johnson plans to use the implanted sensor system for round-the-clock physiological monitoring of certain mice to determine their patterns of activity and sleep.

"Some of our mutant mice born with a pink coat color because of the deletion of a gene may also be missing a nearby gene that codes for a brain protein," Johnson says. "As a result, they may have a disease found in humans—Angelman syndrome." Common characteristics of people afflicted with this disorder are an abnormal gait, lower activity level, mental retardation, an inability to verbalize thoughts, and a biorhythm problem that makes it difficult for them to sleep.

Johnson hopes that use of the rf activity sensor will allow biologists to identify mice that have low activity levels and odd sleep patterns that could be linked to Angelman syndrome. Studies of mice known to have Angelman syndrome may lead to a remedy to help people with the disease.

Another way to detect hidden mutations and disease indicators in mice is to analyze their blood and urine, a common practice for assessing human health. Gary Sega of ORNL's Chemical and Analytical Sciences Division is using gas chromatography/mass spectroscopy (GC/MS) to analyze mouse blood and urine for unusual concentrations of biochemicals and toxic metabolic products. One finding has been particularly valuable.

Some mutant mice at ORNL may have a genetic disease that also afflicts humans—hereditary tyrosinemia. Normal mice and humans break down tyrosine, an amino acid available in food, thanks to the action of a gene (identified at ORNL in mouse DNA). But people and mice with the disease lack this gene's protein product, which is needed to carry out one step of the metabolic process; as a result, a biochemical product that is not broken down builds up to a toxic level, poisoning the liver. People with the disease are put on a tyrosine-free diet.

Now, ORNL has a way of identifying the mutant mice that have hereditary tyrosinemia. Through GC/MS analysis of mouse body fluids, Sega has identified high concentrations of the liver-destroying toxic product in some mice, indicating they have the disease. This toxic product was found to have the same chemical composition as the one produced in humans with tyrosinemia disease. "By studying mice with this disease," Johnson says, "we may get insights into how to combat it in humans."

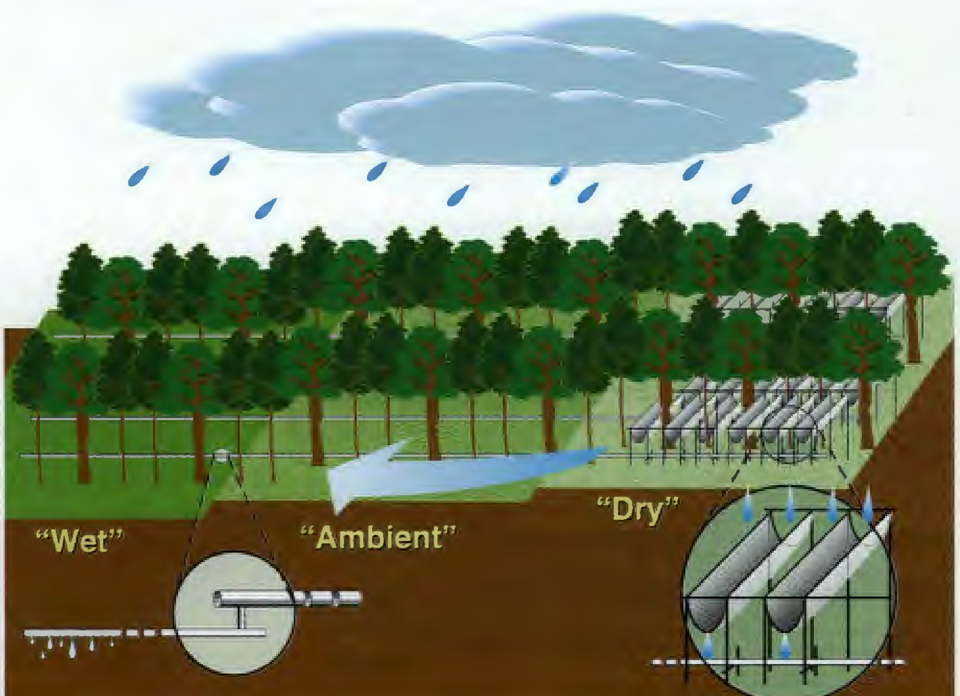
ORNL monitoring technologies for mice should help researchers more rapidly determine the functions of genes that are found in both mice and humans. By determining which proteins are produced by these genes and what they do in the body, scientists can then work to determine the structure of these proteins and develop drugs based on this information. Thanks to technologies that monitor mice, we may soon be seeing advances in medicine.

Hardware for Hardwoods:

Monitoring Effects of Global Change on Forests

ORNL researchers are using advanced measurement technologies to help them predict how global climate change might affect forest productivity.

A transparent cuvette and an infrared gas analyzer are used to measure CO_2 and water vapor exchange rates in leaves of a sweetgum tree in South Carolina. Trees like this one are grown in high-density plantations that are provided with supplemental water and nutrients.



The Throughfall Displacement Experiment (TDE) on the Oak Ridge Reservation was initiated in 1992 to evaluate the response of an upland oak forest to soil conditions "wetter" and "drier" than ambient rainfall conditions in East Tennessee. Rain is collected in sub-canopy troughs on a "dry" plot, moved across an "ambient" plot, and then distributed onto a "wet" plot. The TDE was designed to simulate scenarios of altered precipitation that might result from global climate change.

Just as people breathe and perspire, trees play give and take with the air. Carbon dioxide (CO_2) and water vapor are released from tree leaf pores to the atmosphere. CO_2 is drawn from the air through the leaf pores for photosynthesis, the process by which trees use the energy of sunlight to convert carbon to food and fiber. In ORNL's Walker Branch Watershed on the Oak Ridge Reservation, the flow of gases between forest trees and the atmosphere has been measured for 30 years. By using sophisticated instruments in this mixed hardwood forest, ORNL environmental scientists have found that a 1-hectare stand annually accumulates 8550 kilograms of carbon as dry mass and loses 6.3 million liters of water.

Why are scientists interested in measuring these carbon and water exchange rates among some of ORNL's oak, poplar, hickory, maple, and loblolly pine trees? "We've learned over the years that this information helps us judge the health of a tree," says Stan Wullschleger, a researcher in ORNL's Environmental Sciences Division (ESD). "Trees that take up CO_2 at a high rate are usually growing well. Similarly, a tree that releases considerable water vapor to the atmosphere is likely to be healthy because it has enough water to cool its leaves and transport nutrients to its leaves and branches. Exchange rate measurements also may indicate the physiological capacity of trees to withstand stresses such as air pollution, insect attacks, and acid rain."

If increasing levels of atmospheric CO_2 from fossil fuel combustion result in a warming of the earth's surface, changes in daily temperature and rainfall patterns are predicted. ESD scientists are already studying the possible effects of these projected climate changes on tree health and forest productivity. "Measurement technologies have become increasingly important to environmental scientists," says ESD scientist Sandy McLaughlin, "because we are being asked to predict the physiological resilience of plant ecosystems at regional and global scales under conditions expected to be present if global warming occurs."

Trees may grow larger or faster in some regions because the atmosphere's concentration of CO_2 has risen. Or, because of global warming, tree growth may be slowed by longer periods of drought, and the growth could be retarded even more if air pollution levels are high. Exchange rate measurements will help scientists explain why a forest's productivity is high or low.

"If a tree is exposed to drought, its water use will decline, and we'll detect this reduction with our measurements of water vapor transfer rates," Wullschleger says. "Such a tree may experience reduced growth because of an inadequate supply of nutrients. Also, because leaf pores tend to close under drought conditions to hold in what little water the tree has, the tree's uptake of photosynthetic CO_2 will be reduced, further slowing its growth."

Forests may be affected by climate change, but they may also have an impact on climate. "Carbon measurements," says Wullschleger, "will tell us the potential of the landscape to remove and store atmospheric CO_2, reducing the greenhouse effect that induces global warming."

In the 1950s and 1960s, ESD researchers made exchange rate measurements using radioisotopes and cumbersome radiation detection equipment. In the 1970s regulatory agencies frowned upon the use of radioactive isotopes in the environment, so ESD researchers switched to infrared gas analyzers (IRGAs). An IRGA consists of an infrared radiation source, a gas cell, and a detector. The uptake of CO_2 by leaves and plants enclosed within the gas cell is measured as a change in infrared radiation reaching the detector and, thus, a change in detector output.

The early IRGAs were bulky, labor intensive, and slow to make measurements. Today, ESD scientists are using commercially available IRGAs that are compact, portable, robust, and capable of providing estimates of carbon and water exchange within seconds. IRGAs are being used in DOE's Biofuels Feedstock Development Program to investigate the role that soil water, nutrients, and air temperature play in determining the productivity of plantation-grown hardwoods in South Carolina.

ESD scientists will also use IRGAs to determine the amounts of carbon and water used by cottonwood, sycamore, and sweetgum trees grown using different types and levels of irrigation and fertilization. "This work will provide insights into the growth potential of hardwoods under different conditions for the pulp and paper industry," Wullschleger says. "It will give needed information on the productivity of short-rotation forests for use as bioenergy crops."

Two major experiments using IRGAs and other sophisticated measurement devices are being conducted on the Walker Branch Watershed to address global change issues. They will help ESD scientists predict the effects of drought, excessive precipitation, and increased atmospheric concentrations of CO_2 on forest productivity.

In a DOE-funded study known as the Throughfall Displacement Experiment (TDE), a series of troughs capture and transfer rain water. One half-acre plot receives about one-third more rainfall and another plot receives about one-third less rainfall than an adjacent half-acre plot receiving ambient rainfall. The goal is to understand how forests adjust to changes in precipitation that might result from global warming.

ESD's Paul Hanson, who is leading the TDE experiment, says, "Throughout six years of sustained rainfall reductions, large oak and maple trees grew normally because sufficient water had been stored in the forest soil. But flowering dogwood and other shallow-rooted trees growing in the forest shade died in greater numbers when artificially reduced precipitation was applied during a drought year." According to Wullschleger, "remotely operated sap flow devices provide a reliable early indication that large trees fare better during a drought than small trees." The reduced rainfall was found to result in increased organic matter in soil litter layers, suggesting that more carbon may be sequestered in the soil if climate change brings longer periods of drought.

The response of a ten-year-old sweetgum plantation to a 50% increase in the ambient concentration of atmospheric CO_2 is being measured by ESD's Free Air CO_2 Enrichment (FACE) system. Originally supported by the internally funded Laboratory Directed Research and Development Program and now by the National Science Foundation and DOE, the FACE facility has been operating since April 1998. It relies on a computer-controlled flow gauge system that, by taking wind speed and direction into account, maintains desired CO_2 levels within circular plots surrounded by free-air injection ports.

"We are measuring changes in each tree's canopy size, stem and root growth, and rates of photosynthesis and water and nutrient use," says ESD's Rich Norby, who leads the FACE research. Minature video cameras inserted into buried tubes allow the researchers to monitor root activity. "We hope to answer this question: How will limited light, nutrient, and water availability in a closely spaced forest stand affect the ability of this forest to use the 'extra' CO_2? The findings should be of interest because recent research suggests that some tree species, but not others, may thrive during global warming because the extra carbon they absorb compensates for the reduced availability of water." During the first year of exposure to the increased CO_2 concentrations, photosynthesis was stimulated, stem growth increased, and the trees conserved water.

Since the late 1970s, McLaughlin and his colleagues have measured the effects of pollutants, such as ozone, on forest trees. They have moved from laboratory exposure chambers to much larger, open-top field chambers. More recently, they have developed sensitive systems for detecting responses of unchambered forest trees to variations in pollution stress. Ground-level ozone is a pollutant produced when hydrocarbons and nitrogen oxide from cars and coal-fired power plants react in the atmosphere. ESD studies show that plant growth capacity can be reduced by chronic exposure to ozone.

In a five-year study for the U.S. Forest Service in the 1990s, McLaughlin developed a technique that sensitively measured the effects on loblolly pine growth of exposure to ambient levels of ozone, high temperature, and reduced soil moisture on the Oak Ridge Reservation. Aided by statistical analysis by Darryl Downing of ORNL's Computer Science and Mathematics Division, McLaughlin found that the growth rate of trees exposed to ambient ozone levels was reduced even more during very dry periods in the summer. The finding suggests that global warming combined with ozone pollution could harm large populations of loblolly pines, which are so important to the economy of the South.

For future monitoring of forest productivity, ESD researchers envision outfitting airplanes and satellites with remote-sensing cameras that are sensitive to light reflected from leaves. Then they could rely on hardware above rather than in the hardwoods.

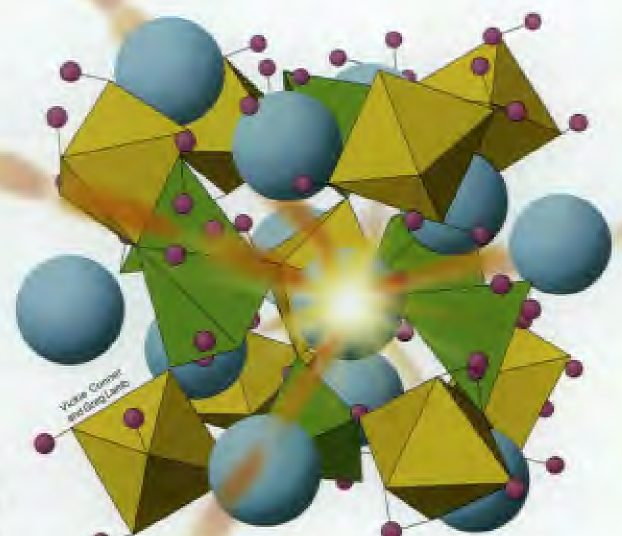
Jim Richmond

These suspended pipes release carbon dioxide to a test sweetgum plantation on the Oak Ridge Reservation. Scientists are determining how a carbon dioxide–enriched atmosphere affects the growth of one species of forest trees.

New Measurements Using Neutrons:

Benefits of the Spallation Neutron Source

The Spallation Neutron Source proposed by DOE for ORNL will be a unique measurement tool for scientists and engineers. Applications resulting from measurements at the world's most powerful neutron source should improve our quality of life.



Neutron from a pulsed beam (coming from lower left) scatter from atomic nuclei in this hydrogarnet crystal.

Spanning the length of five football fields, it will measure distances between atoms. It will help biologists determine protein shapes and activities so they can design more effective therapeutic drugs. It will help chemists "see" the tiniest details of chemical structure so they can formulate longer-lasting lubricants and tastier low-fat foods. It will help engineers develop faster electronic devices, longer-lasting body implants, and safer and more-energy-efficient automobiles and aircraft.

The Spallation Neutron Source (SNS) proposed by the Department of Energy for ORNL will be a world-class measurement tool for scientists and engineers. It is slated to begin operating in 2006. Several ORNL neutron scientists recently commented on the potential benefits of the SNS.

"Neutron scattering at neutron sources," says John Hayter, "turns out to be the best, often the only, and sometimes the lowest cost, tool that scientists have to study the structure of and interactions among atoms in 'real-life' materials. The SNS is expected to fill gaps in our knowledge because its pulsed neutron beams will be the most intense in the world, providing more neutrons per pulse than any other source."

To make measurements using neutron scattering, neutron detectors are needed to measure the angles and energies of neutrons deflected from experimental targets. Work is under way at the Laboratory to develop improved neutron detectors using fiber-optic and semiconducting technologies. Led by Thomas Mason, SNS scientific director, ORNL researchers are working with Argonne National Laboratory researchers to design state-of-the-art neutron spectrometers and diffractometers that will be used at the SNS.

Because the SNS will be the world's brightest source of neutrons, it will allow scientists to study very small samples that cannot be examined using current technologies. "Sometimes only small samples are available," says Hayter. "A material may be so new that little is available. Or it might take too long and cost too much to generate a larger sample."

"The ability of neutrons to precisely locate light atoms, particularly hydrogen, in small quantities of samples containing large biological molecules, such as proteins, should be important to the pharmaceutical industry," says Gerard Bunick. "The SNS will be useful for studying mechanisms of protein activity and understanding how to design drugs to combat diseases by blocking critical protein functions in disease-causing bacteria and viruses."

The SNS will allow scientists to follow the movements of molecules in a lubricant when it is repeatedly heated and squeezed on a bearing. It will enable studies of other complex fluids, such as blood, and soft materials, such as the permeable walls of body cells.

"Understanding these materials at the molecular level using the SNS could speed the development of time-released drug-delivery systems that target specific parts of the body," says Bill Hamilton. "Such drugs might be contained in vesicles, or membrane sacs within sacs, whose walls would be broken down by body chemicals, gradually releasing the drug in precise doses when and where it is needed. SNS studies also could speed development of artificial blood made of vesicles that mimic the action of human blood cells."

Knowing how atoms are arranged in new crystalline compounds with known properties is the key to understanding how to modify materials to make them work in desired ways. Such specially tailored materials could be used to make a faster electronic device or a longer-lasting artificial hip or knee joint.

"Neutron scattering is a powerful tool for determining crystal structure," says Bryan Chakoumakos. "It also reveals changes in structure while a material is exposed to changing temperatures, pressures, or other environmental influences. It could help a ceramic engineer design a new material for cookware that won't break when heated up. It could help geologists develop more accurate computer models for understanding large-scale earth processes, such as earthquakes, crustal tectonics, and the geomagnetic field."

Thanks to neutron studies of atoms in magnetic materials, the world is benefiting from credit cards, audiotapes, videotapes, computer disks, and compact discs. "The SNS will help researchers continue to develop smaller, lighter, and stronger magnets and create useful magnetic materials as small as thin films and single files of atoms," says Herb Mook, head of the Neutron Scattering Section in ORNL's Solid State Division. "It will also enable scientists to determine the structure of high-temperature superconducting materials and the effects and behavior of magnetic fields in respect to these materials. SNS neutron data will be useful in developing high-current superconducting materials for underground transmission lines and very high-field magnets for particle accelerators and medical imaging devices."

Because of environmental concerns and other barriers to commercializing new polymers, the plastics industry is increasingly blending existing polymers to form a material with the best possible properties. "By using small-angle neutron scattering at the SNS or ORNL's High Flux Isotope Reactor," says George Wignall, "we will be able to determine quickly how well polymers will mix, how long they should be ground and compressed, at which temperature they should be melted together to get the best mixing, and which mixtures will form the best products."

If interest picks up in recycling plastics to slow the need for new landfills and to recover resources, the SNS could be particularly useful for practical polymer research. "It could help scientists understand which polymers can be melted down and mixed—and which can't—to form useful polymer blends," Wignall says. "It can help us determine how compatible different plastic components are, design strategies for reprocessing waste plastic, and evaluate the usefulness of the resulting blend material."

Nobel Laureate Clifford Shull was among the ORNL researchers who pioneered neutron scattering by using neutrons from the Laboratory's Graphite Reactor.

Neutrons can be used to map an engine part or boiler material for residual stresses that predispose it to cracking, wear, accelerated chemical attack, and even failure during use. "Engineers want to know when a part is likely to fail and whether use of different materials and manufacturing processes, such as heat treatment, would produce a part that will last longer," says Steve Spooner. "Neutron scattering results combined with computer models can provide these answers. The SNS will allow effective measurements of residual stresses in composites, which are being used increasingly to make cutting tools, aircraft structures, and engine parts because they are stronger and lighter than other materials. Neutron measurements of microscopic stresses in samples made different ways will help identify the manufacturing processes that produce the strongest composites."

"The SNS will be a very sensitive tool for locating embrittling hydrogen atoms in weldments and turbine blades, imaging the location and density of hydrocarbons in fuels and lubricants in operating engines, and characterizing the migration of water in cements and rock," says Cam Hubbard. "It will permit measurement of temperature in difficult-to-reach locations, such as the crown of a piston in an operating engine."

To build a large engineering marvel such as a safer, more efficient turbine jet engine, researchers will rely on information from the SNS. It will help them better understand how metallic alloys in turbine blades behave under extreme stress at a microscopic level.

"Neutron scattering began at ORNL in the late 1940s with the pioneering research of Ernie Wollan and Clifford Shull, work for which Shull received the 1994 Nobel Prize in Physics," says Bill Appleton, former associate director for the SNS and now ORNL's deputy director for science and technology. "The Laboratory has continued and expanded that work ever since. Now, a worldwide community of scientists and engineers use neutron scattering. Their contributions have given us marvelous new materials, new knowledge, new drugs, and new products that have boosted the American economy. To continue these extraordinary advances, we need precise measurements of materials at the molecular level—measurements that only an extraordinary tool like the SNS can provide."

Neutrons have a neutral charge, but their impact on the world should continue to be positive.

The Joint Institute for Neutron Sciences will consist of meeting facilities, laboratories, a communication center, and housing for researchers from university, industrial, and government laboratories using the SNS.

Shampoo is one of many complex fluids studied with neutrons whose molecular structure changes as a one-directional force is applied, making the thick liquid thin enough to spread through hair.

Tom Cerniglio

Healthier, low-fat foods (like certain types of ice cream) that have better taste and texture will be made with guidance from neutron scattering.

Tom Cerniglio

Bytes Help Take the Bite out of Crime

Tom Cerniglia

Stephen Jacobson observes a magnified image of the lab on a chip (center of photo) on a video monitor linked to an optical microscope. DNA fingerprinting of blood at crime scenes is one potential use of the lab-on-a-chip technology developed at ORNL.

ORNL is developing computer-driven technologies that will enable authorities to acquire or improve the quality of information needed to identify a crime suspect.

A woman lies dead, with her blood on a patio. A detective arriving on the scene sees a knife with blood on its handle and a trail of bloody footprints along an asphalt path.

He takes out a "lab on a chip" to do a rapid blood analysis. First, he collects blood from the victim; then he uses another chip for blood on the knife and a third for the footprint blood. He carefully labels each chip. He places one chip inside a black box containing a small laser, light detector, and electronics. He checks the screen of a laptop computer.

In five minutes, he is shown the distinctive molecular characteristics, or DNA fingerprint, of one blood sample. He then processes the other blood samples and returns to the crime lab with some potentially good evidence. At the lab, he tells his colleagues, "This method certainly beats shipping off the blood samples to a conventional lab and waiting weeks for results."

That's the forensic fantasy. However, technology being developed at ORNL may soon turn this fantasy into a reality by making it possible to obtain DNA fingerprints quickly from blood at a crime scene for later comparison with the DNA fingerprints of blood from suspects. Mike Ramsey and his group in ORNL's Chemical and Analytical Sciences Division (CASD) have received funding from the National Institute of Justice to develop the lab on a chip for rapid, onsite forensic analysis.

"One person could collect blood samples at the scene of the crime and do a fast analysis then, reducing the chance of contamination by other people's blood and eliminating the chain-of-custody problem," Ramsey says. "The chips could be made disposable to prevent cross-contamination among samples.

"We have done tests that proved that a DNA segment could be mixed with a restriction enzyme to determine the sequence of the segment's chemical bases," Ramsey adds. "We showed that we could obtain this characteristic DNA fingerprint in five minutes." The lab on a chip could also be used to identify drugs of abuse, poisons, and explosives at crime scenes.

After the Murder: Narrowing Down the Time of Death

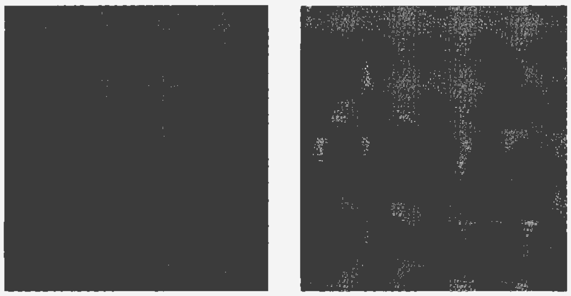
When police detectives find a murder victim, they take the body to the medical examiner,

These two different bodies have been dead the same length of time—30 days. The challenge is to find chemical markers for bodies that have decomposed differently and yet pinpoint the exact time of death.

who will seek to determine the cause and time of death. Time of death is particularly difficult to pinpoint, but it is important to know to help determine the victim's identity (if unknown) and to relate the crime to a possible suspect.

ORNL researchers are seeking a solution to this problem. Stacy Barshick, an analytical chemist in CASD, and her colleagues have been developing methods for identifying chemical signatures in a body that may be used to mark precisely the time interval since death.

"We will be investigating the chemical changes that occur in decomposing tissues from the brain, heart, lung, kidney, liver, and muscle hours to days after death," she says. This research is made possible through a collaboration with the University of Tennessee's Anthropological Research Facility, which provides cadaver samples.



VITALE improves the resolution of video images. Here it allows a police detective to read the word "Kansas" on a T shirt.

ORNL researchers will investigate the changes in the chemical composition (DNA, proteins, lipids, and their degradation products) of the different tissues as they decay. "We hope to determine which changes may be related to the time interval since death and in which tissues these changes show up the best," she says. "By measuring the changes that occur at different times in different tissue, we hope to find markers that will help forensic scientists establish the time of death."

The research is being supported by DOE's Office of Nonproliferation and National Security. The researchers will use techniques such as gel electrophoresis, liquid chromatography, gas chromatography/mass spectrometry, and electronic aroma detection for this study. The ORNL group hopes to come up with a body of knowledge in time to help solve major crimes.

Video Imaging Tool for Aiding Law Enforcement

In July 1995 in Chattanooga, Tennessee, a clerk in a convenience store was shot and killed during a robbery. The images on the videotape from the store surveillance camera were frustratingly fuzzy. So the police detectives investigating the crime sent the grainy footage to ORNL.

Using an early version of a software tool that forms a sharper image by extracting and compiling information from multiple images of the same subject, a group in ORNL's Instrumentation and Controls (I&C) Division were able to show the police a clearer picture of subtle differences in the crime scene. As a result, the detectives could see the suspect's foot and a muzzle flash from the suspect's weapon, showing that he had fired the gun in the store. Identification of the muzzle flash discredited the suspect's story to the police that the weapon had gone off accidentally in a back room scuffle with the clerk. The new evidence led to a guilty plea, a conviction, and a sentence of life in prison without parole. In this case, the ORNL technology also helped avoid a death penalty trial that would have cost Tennessee taxpayers $100,000 with no guarantee of a conviction.

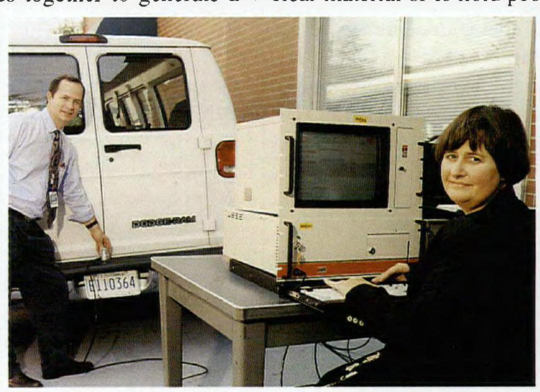
ORNL's Video Imaging Tool for Aiding Law Enforcement (VITALE) does more than detect subtle changes in surveillance data. It doubles the quality of the videotapes, which are often fuzzy because they are recycled perhaps hundreds of times. Using digitized frames of analog videotape, VITALE algorithms and other techniques sample multiple views of the same subject and "fuse" the video frames together to generate a higher-resolution image. Ken Tobin, leader of the I&C Division's Image Science and Machine Vision Group, who developed the technology with group members Tom Karnowski and Tim Gee, says the technique makes it possible "to get more pixels out of the data so that facial features are sharper and license plates are more legible." The multiframe fusion technique, whose development is being funded by the Department of Energy, has enabled the researchers to make out words and spots on T-shirts and details of facial features and other identifying marks.

The ORNL software package will be tested by the U.S. Secret Service in mid-1999 and released commercially to local and federal crime fighters by 2000. Besides law enforcement applications, it also could be used to improve the resolution of medical and satellite images.

Heartbeat Detector

It had been tried many times before. Hundreds of prisoners had used this trick to escape through the prison sally port without being seen by the guards. They had hidden in a laundry truck before it left the prison. So, when Cecil tried to sneak out of the penitentiary this way, he was surprised when the truck was stopped at the sally port. A guard entered the truck and handcuffed him. "How did you find me?" Cecil asked. "It was the heartbeat detector," the guard said.

A scenario like this may actually have taken place in a prison in Nashville, Tennessee, which uses the heartbeat detector technology developed in Oak Ridge. Originally called the enclosed space detection system, the heartbeat detector was the project of a team of engineers at the Oak Ridge Y-12 Plant, a nuclear facility that stores large quantities of highly enriched uranium. In 1994, they began developing the heartbeat detector as part of DOE's "Portal of the Future" project, whose goal is to create a system that uses sophisticated devices and methods to rapidly inspect trucks passing through vehicle portals at key facilities. The original purpose of the heartbeat detector was to prevent an intruder hidden in a truck from sneaking through the Portal of the Future, say, to steal weapons-grade nuclear material or to hold people hostage.

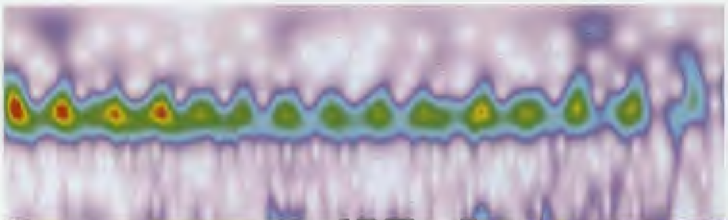


Tim Hickerson and Vivian Baylor operate the heartbeat detector in an attempt to detect the presence of a human hidden in the truck.

When the heartbeat detector was being developed at the Y-12 Plant, Steve Kercel and Bill Dress, both of the I&C Division, were asked to solve a problem mathematically to ensure that the device would accurately detect human heartbeats amid various background signals. They developed the "fast continuous wavelet transform algorithm" for a ruggedized portable computer linked to sensors.

The heartbeat signal is captured at the vehicle's exterior by a geophone, a device commonly used to detect small disturbances in the earth. The sensor signal, which includes truck vibrations from air currents and natural resonances, is fed into the wavelet algorithm. If a heartbeat is

Wavelet transform of a heartbeat signature in the noise signatures coming from a truck as detected by a geophone.



The heartbeat detector can find a person hidden in a vehicle, such as this woman concealed in a truck.

in the signal, it will be matched and detected by the heartbeat wavelet programmed into the algorithm.

The wavelet-based heartbeat detector has become recognized as a major advance in security technology. It was independently tested at the Thunder Mountain Evaluation Center at Fort Huachuca, Arizona, where it was shown to be more than 99% reliable in detecting occupants hidden in vehicles. In 1996, the Oak Ridge technology was licensed to a private company for development into a commercial product for government and corporate security operations. In 1997, the heartbeat detector received *R&D Magazine's* R&D 100 Award, as one of the 100 most significant technological product developments of the year. The detector, which was tested extensively by security personnel at the Y-12 Plant, is being implemented there.

Besides detecting prisoners and terrorists, the heartbeat detector could be used to spot illegal immigrants hidden in cars and trucks, according to Kercel. "Many people have smuggled passengers concealed in vehicles across highway borders," he says. "One common ploy is to remove the material from inside the front or back seat and stuff the passenger into the available space. Less obvious strategies are nothing short of astounding. For example, U.S. agents recently discovered two illegal aliens wrapped around the engine of a Yugo."

The heartbeat detector may well someday be at the heart of new technologies designed to keep prisoners in and terrorists and illegal immigrants out.

Elemental "Fingerprints" of Glass at the Crime Scene

A police officer stops a driver whose car resembles one involved in a hit-and-run accident nearby. Because broken glass was found at the accident scene, the officer checks the headlights of the suspect's car. He finds a broken headlamp. The driver says he has no knowledge of the accident. Nevertheless, the police officer gathers pertinent information from the driver. And he collects pieces of glass from the smashed headlight for analysis in the crime lab.

In the past, police detectives have compared the refractive indexes of glass from broken headlights and glass particles found on suspects' clothing with those of glass pieces found at a crime scene. The degree to which the glass pieces linked to the suspect seemed to match those at the scene was offered as evidence in court.

Unfortunately, this technique is less effective with newer glasses because of improvements in manufacturing. A more discriminating technique is elemental analysis, because many samples of glass differ in the concentrations of trace elements present.

With collaborators from the Federal Bureau of Investigation (FBI) and the International Forensic Research Institute at Florida International University, ORNL's Doug Duckworth (CASD), Shelby Morton (CASD), and Chuck Bayne (Computer Science and Mathematics Division) are analyzing samples of many different glasses to determine their distinctive elemental "fingerprints." Using inductively coupled plasma mass spectrometry and statistical analysis, they are measuring the concentrations of 46 different trace elements found in glass, such as barium, rubidium, strontium, and zirconium. They are also determining the elements that will be the most useful in fingerprint comparisons—those which vary considerably in concentration from glass to glass and can be measured with little error.

"We are developing a database for the National Institute of Justice that contains the elemental fingerprint of many samples so that the likelihood of a 'match' can be stated," Duckworth says. "Our goal is to produce a compact disc that would, for example, indicate the probability that glasses from different car headlights would have the same elemental fingerprint, such as identical concentrations of strontium and zirconium. Our studies should allow forensic scientists to assign a value, such as one in a million, to an association of a questioned glass to glass from a crime scene, based upon its trace element fingerprint. These studies should greatly increase the significance of glass as evidential material."

Improving Electronic Fingerprints

The FBI has 32 million electronic fingerprints in its central database in West Virginia, and thousands of prints are electronically mailed there daily for processing. When the FBI's Integrated Automated Fingerprint Identification System (IAFIS) goes online July 30, 1999, police officers should be able to take a digital print from a suspect with an electronic scanner, e-mail it to the FBI, and receive an identification and other information two hours later.

In support of the FBI, the Data Systems Research and Development (DSRD) group of Lockheed Martin Energy Systems has been developing the Electronic Fingerprint Image Print Server (EFIPS). ORNL's I&C Division has been supporting the DSRD work on EFIPS.

Currently, each person's electronic fingerprint is printed on a standard FBI ten-print paper card for final processing. Until recently, printouts of 10 to 15% of the electronic fingerprints were of low quality because of darkened or smudged backgrounds. These cards were rejected and police departments were notified to obtain new electronic prints.

To solve this problem, Jim Goddard of the I&C Division developed image processing software that lets FBI operators of quality control workstations clean up the electronic fingerprint's background. Because this software lets operators digitally improve the contrast of many fingerprints that would otherwise be rejected, most of them show up clearly when printed out. Now, only 1 to 2% of the printed electronic fingerprints are rejected by the FBI.

ORNL's contributions are expected to improve the quality of the FBI's tide of prints.

Contact Information

Hi-Tech for Health

For more information on the medical telesensor developments, contact Tom Ferrell (telephone; 423/574-6214; e-mail: ferrelltl@ornl.gov); on optical biopsy and the ultrasound monitor for brain injuries, contact Tuan Vo-Dinh (telephone: 423/574-6249; e-mail: vodinht@ornl.gov); and on the lung diagnostic monitor and on burn mapping and therapy, contact Glenn Allgood (telephone: 423/574-5673; e-mail: allgoodgo@ornl.gov).

Reducing the Threat of War and Terrorism

For more information on detection technologies for unexploded ordnance and land mines, contact Richard M. Davis (telephone: 423/574-5925; e-mail: davisrm1@ornl.gov); on the chemical-biological mass spectrometer, contact Wayne Griest (telephone: 423/574-4864; e-mail: griestwh@ornl.gov); and on microcantilever sensors, contact Bruce Warmack (telephone: 423/574-6202; e-mail: warmackrj@ornl.gov).

Incredible Shrinking Labs: Chipping Away at Analytical Costs

For more information on the lab on a chip, contact Mike Ramsey (telephone: 423/574-5662; e-mail: ramseyjm@ornl.gov); on the multifunctional biochip for disease diagnosis, contact Tuan Vo-Dinh (telephone: 423/574-6249; e-mail: vodinht@ornl.gov); on the flowthrough genosensor, contact Ken Beattie (telephone: 423/574-7912; e-mail: beattiekl@ornl.gov); on the nose on a chip, contact Chuck Britton (telephone: 423/574-1878; e-mail: brittoncl@ornl.gov); and on the critters on a chip technology, contact Mike Simpson (telephone: 423/574-8588; e-mail: simpsonml1@ornl.gov).

Cars, Clothes, and Computers: Help for Industry

For more information on the temperature measurement technique for galvannealed steel, contact Steve Allison (telephone: 423/576-2725; e-mail: allisonsw@ornl.gov); on the pick measurement device for the textile industry, contact Glenn Allgood (telephone: 423/574-5673; e-mail: allgoodgo@ornl.gov); and on the spatial signature analysis tool for the semiconductor industry, contact Ken Tobin (telephone: 423/574-8521; e-mail: tobinkwjr@ornl.gov).

Of Mice, Monitors, and Medicine

For more information on technologies and mouse genetics, contact Dabney Johnson (telephone: 423/574-0953; e-mail: johnsondk@ornl.gov) and Mike Paulus (telephone: 423/241-4802; e-mail: paulusmj@ornl.gov).

Hardware for Hardwoods: Monitoring Effects of Global Change on Forests

For more information on technologies for monitoring forest productivity, contact Robin Graham (telephone: 423/576-7756; e-mail: grahamrl@ornl.gov)

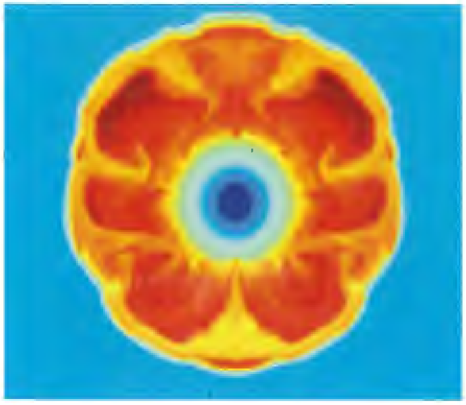
New Measurements Using Neutrons: Benefits of the SNS

For more information on the scientific aspects of the Spallation Neutron Source, contact Thomas Mason (telephone: 423/241-1499; e-mail: masont@ornl.gov)

Bytes Help Take the Bite out of Crime

For more information on ORNL technologies for detecting crime suspects, contact Vivian Baylor (telephone: 423/576-5293; e-mail: baylorvm@ornl.gov).

Next Issue ...



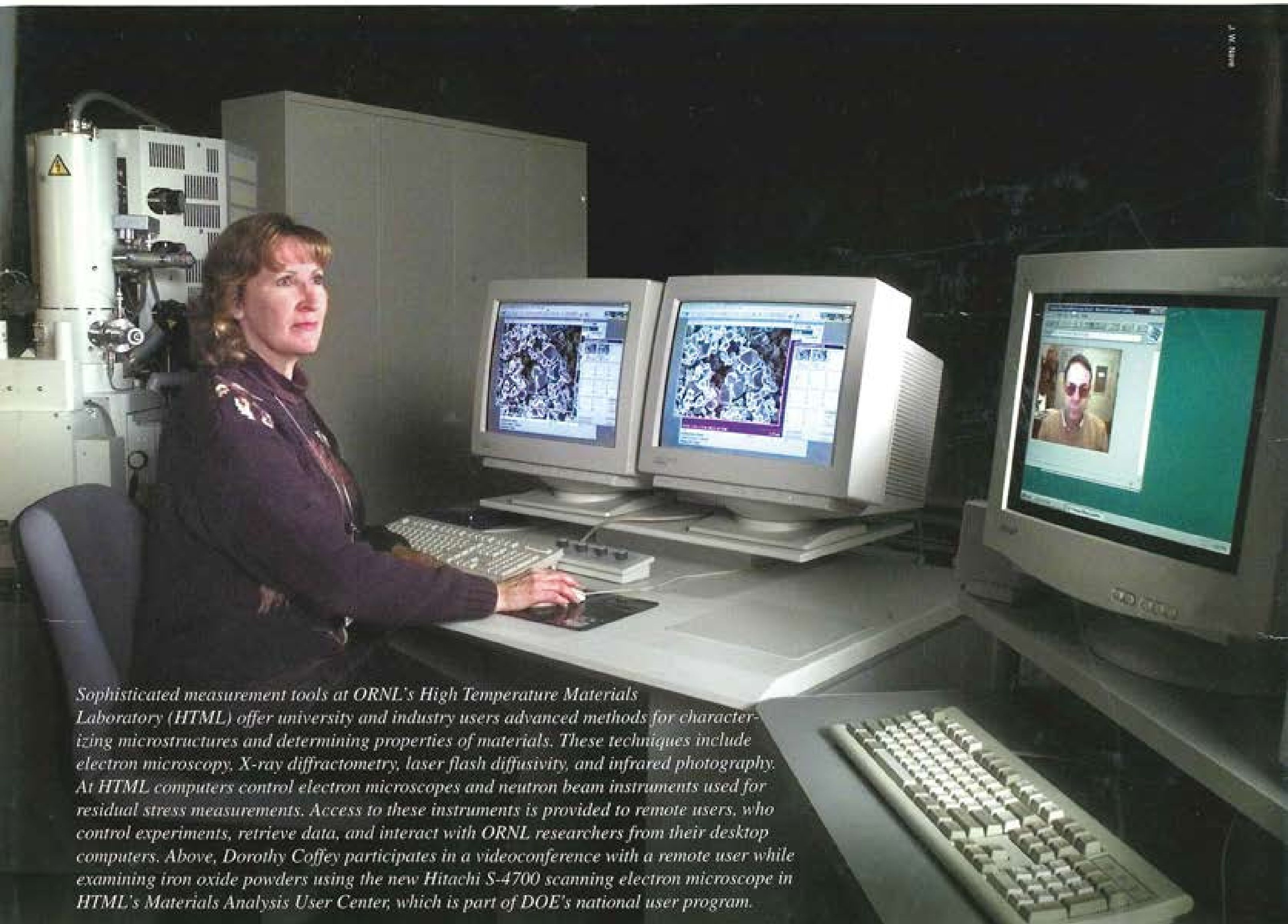
This visualization of convection in a core-collapsed supernova will be one of the images featured in the next issue of the ORNL Review.

Beams of short-lived, radioactive fluorine-17 ions were generated, accelerated, and used for astrophysics-related research at ORNL's Holifield Radioactive Ion Beam Facility (HRIBF), a DOE user facility dedicated to the production of beams of short-lived radioactive nuclei.

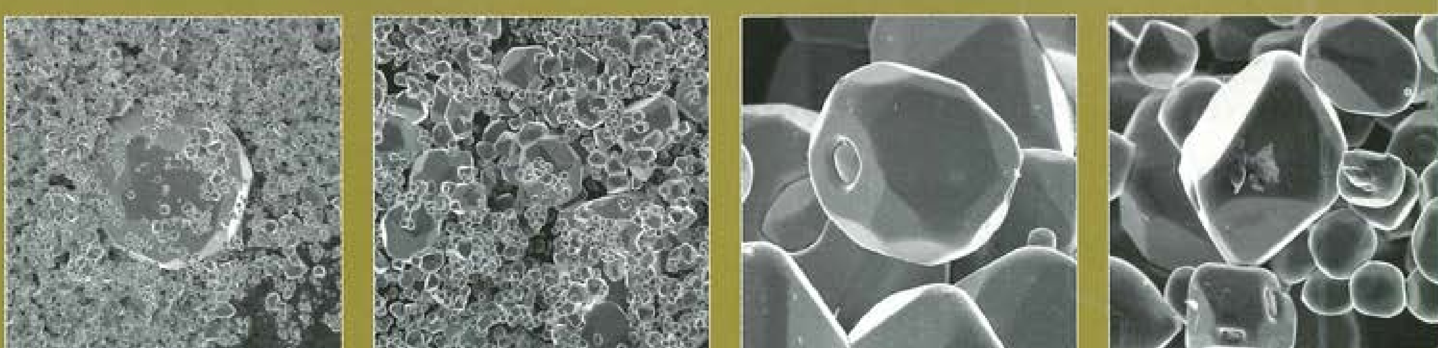
When the planned neutron scattering upgrades to ORNL's High Flux Isotope Reactor are completed, it will have the world's highest thermal neutron intensities and provide cold neutron intensities comparable to the world's best.

OAK RIDGE NATIONAL LABORATORY *REVIEW*
P.O. Box 2008, Oak Ridge, Tennessee 37831-6144

U.S. Postage
PAID
BULK RATE
Oak Ridge, TN
Permit No. 3



Sophisticated measurement tools at ORNL's High Temperature Materials Laboratory (HTML) offer university and industry users advanced methods for characterizing microstructures and determining properties of materials. These techniques include electron microscopy, X-ray diffractometry, laser flash diffusivity, and infrared photography. At HTML computers control electron microscopes and neutron beam instruments used for residual stress measurements. Access to these instruments is provided to remote users, who control experiments, retrieve data, and interact with ORNL researchers from their desktop computers. Above, Dorothy Coffey participates in a videoconference with a remote user while examining iron oxide powders using the new Hitachi S-4700 scanning electron microscope in HTML's Materials Analysis User Center, which is part of DOE's national user program.



These micrographs show the microstructural results of reacting at high temperatures (up to 700°C) and high pressures (1050 bars) various samples of fine-grained magnetite with a solution of salt (sodium chloride) and water containing different oxygen isotope (^{18}O and ^{16}O) compositions. The research was performed by David Cole using funds from the Geosciences Research Program of DOE's Office of Basic Energy Sciences.