November 2002

Science & Technology REVIEW

National Nuclear
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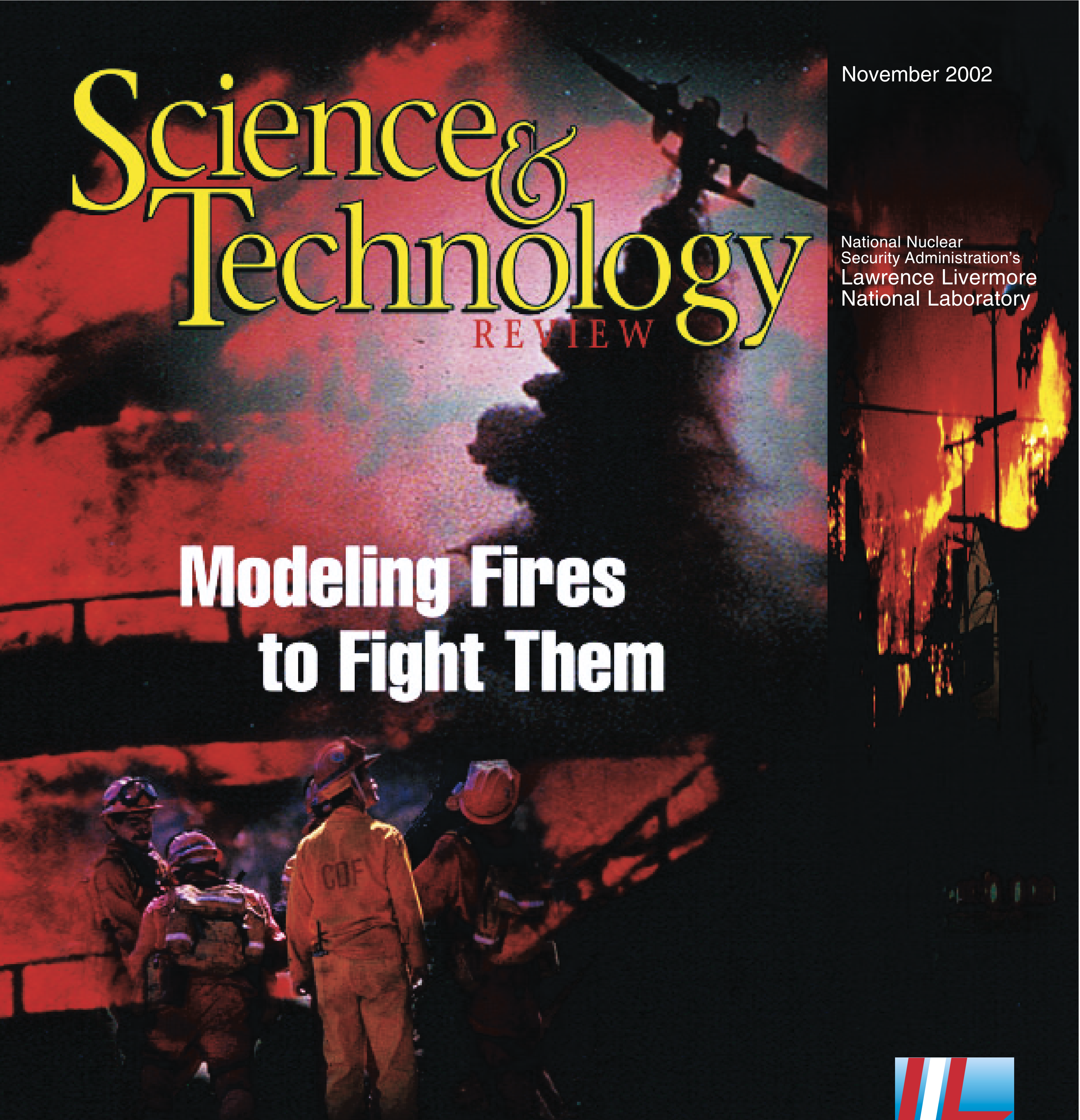
Lawrence Livermore
National Laboratory



Modeling Fires to Fight Them

Also in this issue:

- **Lawrence Fellowships Attract Brilliant Young Scientists**
- **Sensing the "Kill" of an Intercepted Missile**
- **50th Anniversary Highlight: The Evolution of Biological Research at Livermore**

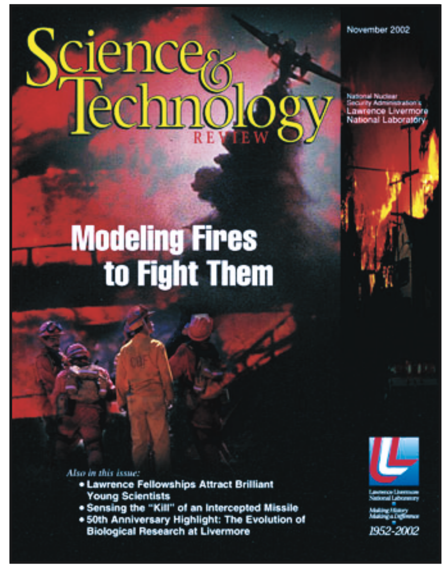
Lawrence Livermore
National Laboratory

Making History
Making a Difference

1952-2002

About the Cover

Livermore scientists, in collaboration with colleagues at Los Alamos National Laboratory, are developing and testing a powerful tool for fighting wildfires. As described in the article beginning on p. 4, this tool is a physics-based computer simulation system that can accurately predict wildfire behavior for specific weather conditions, types of vegetation, and terrain. Such a capability will help emergency response managers plan for different fire scenarios, anticipate where and how quickly an existing fire will spread, and evaluate the effectiveness of alternative firefighting strategies. On the cover is a collage of images from the 1991 Oakland–Berkeley hills fire, which began as a wildfire and ended by destroying 3,000 homes.



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About the Review

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

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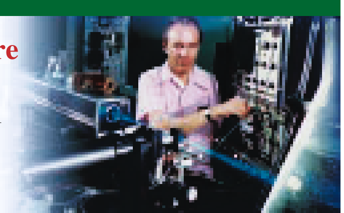

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Radiation detectors tested, developed

Livermore researchers are testing commercial instruments and developing new technologies to detect nuclear materials inside cargo containers. Funded by the National Nuclear Security Administration, this work aims to prevent the smuggling of nuclear materials into the U.S. by airplane, ship, rail, or truck.

In June, Laboratory researchers tested 19 commercially available handheld instruments that government agencies are using or might use to detect nuclear materials in cargo containers.

"One of our areas of expertise is understanding what goes into a nuclear weapon, so we know how to test equipment to find the materials for which different government agencies are searching," says William Dunlop, leader of Livermore's Proliferation Prevention and Arms Control Program.

Livermore researchers, experienced in designing and testing nuclear weapons, have assessed possible improvised nuclear devices as part of the Laboratory's nonproliferation programs, according to Dunlop. This expertise is bolstered by the program's capabilities in detecting trace elements.

Livermore and other researchers are also developing new and enhanced radiation detection systems. One new device is Cryo3, a mobile, handheld detector. Developed by researchers at Lawrence Livermore and Lawrence Berkeley national laboratories, Cryo3 is a high-resolution germanium detector cooled mechanically by a compact, low-power microcryocooler instead of by liquid nitrogen. Once the device has been tested and approved for field use, the Laboratory will help train personnel in using the new technology.

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New facility puts the pressure on materials

In July 2002, the High Pressure Collaborative Access Team (HP-CAT) began work on the newest research facility at the Advanced Photon Source (APS) at Argonne National Laboratory in Illinois. This $10-million research facility will contain beamlines for the intense, high-energy APS. Researchers will use the facility to study in high resolution the structure and behavior of materials under high pressures and varying temperatures.

HP-CAT is made up of Livermore's High-Pressure Physics Group from the Physics and Advanced Technologies Directorate; the High Pressure Science and Engineering Center at the University of Nevada at Las Vegas; the Carnegie Institution of Washington Geophysical Laboratory in Washington, D.C.; and Argonne National Laboratory.

Funded in part by the Department of Energy's Office of Defense Programs and Office of Science and scheduled for completion by May 2003, the new research facility will advance high-pressure science by allowing new types of experiments to be performed. For example, scientists will be able to measure the dynamics of electrons, atoms, and nuclei of complex materials as functions of pressure, temperature, and time. It will also allow the use of new-generation high-pressure devices such as large-volume diamond-anvil cells. Its goals are to advance high-pressure synchrotron radiation research and establish a leading center of high-pressure research accessible to the scientific community at large.

"At Livermore, we've invested in this beamline because it is an enabling capability for the Stockpile Stewardship Program," says William Goldstein, associate director for Physics and Advanced Technologies. "The highly intense, high-energy x-ray beam will allow us to characterize the structure of high explosives and of the low-symmetry phases of plutonium with unprecedented precision."

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Age of oldest objects in solar system determined

A team of geochemists, including Livermore's Ian Hutcheon, has accurately dated calcium–aluminum inclusions (CAIs), the oldest objects in our solar system, at 4.57 billion years old. The team also determined that chondrules, another of the earliest objects in the solar system, are 2 to 3 million years younger than CAIs. "By determining the age of CAIs and chondrules, we can better date asteroids and planets and learn more about the early history of the solar system," says Hutcheon.

Hutcheon, Yuri Amelin of the Royal Ontario Museum, Alexander Krot of the University of Hawaii, and Alexander Ulyanov of Moscow State University published their findings in the September 6, 2002, issue of *Science*.

Using mass spectrometers to study CAIs and chondrules, the team determined the age of the objects by measuring the decay rate of uranium-238, which is found in both objects, as it decays into lead. With an ion microprobe, Hutcheon then dated CAIs and chondrules by detecting the decay of aluminum-26, also found in both objects, into magnesium-26.

Aluminum-26 decays much faster than uranium-238. By comparing the lead and magnesium isotope content in the CAIs and chondrules, the team determined with great precision both how old the objects are and the difference in age between CAIs and chondrules.

CAIs and chondrules are millimeter-size objects found in primitive meteorites. They formed when dusty regions of the solar nebula were heated to high temperatures. The dust melted and then crystallized, forming first CAIs and then chondrules.

Larger objects, such as asteroids and planets, took longer to form and are about 10 to 50 million years younger than CAIs and chondrules.

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High-Tech Help for Fighting Wildfires

EVERY summer, we're reminded that wildfires, with their potential to cause severe destruction, are a never-ending national problem. As we witnessed this past year, the western United States is particularly vulnerable to catastrophic wildfires, a situation caused in part by allowing underbrush to accumulate. President Bush's plan to thin national forests as a way of reducing fire danger has intensified the longstanding debate about how best to manage our forests and grasslands and to fight wildfires.

At first glance, developing new tools to help fight wildfires may seem an unusual activity for a national laboratory dedicated to national security. However, Lawrence Livermore has for the past few decades successfully applied its national security expertise, especially its advanced supercomputer modeling skills, to other areas of national importance. Laboratory simulations, for example, are advancing the understanding of the mechanisms of disease, the ways in which metals fatigue and break, how buildings react to earthquakes, and how pollutants migrate underground.

The Livermore effort to develop an advanced capability to simulate past and hypothetical wildfires, train firefighters, prepare for prescribed burns, and eventually provide real-time firefighting advice is described in the article beginning on p. 4. The effort originated in a simple question posed by a visiting congressman a few years ago while he toured the National Atmospheric Release Advisory Center (NARAC), located at Livermore. The congressman asked if NARAC's unparalleled capability to predict weather and airborne emissions, as seen in the 1991 Gulf War, for example, could be used to fight wildfires.

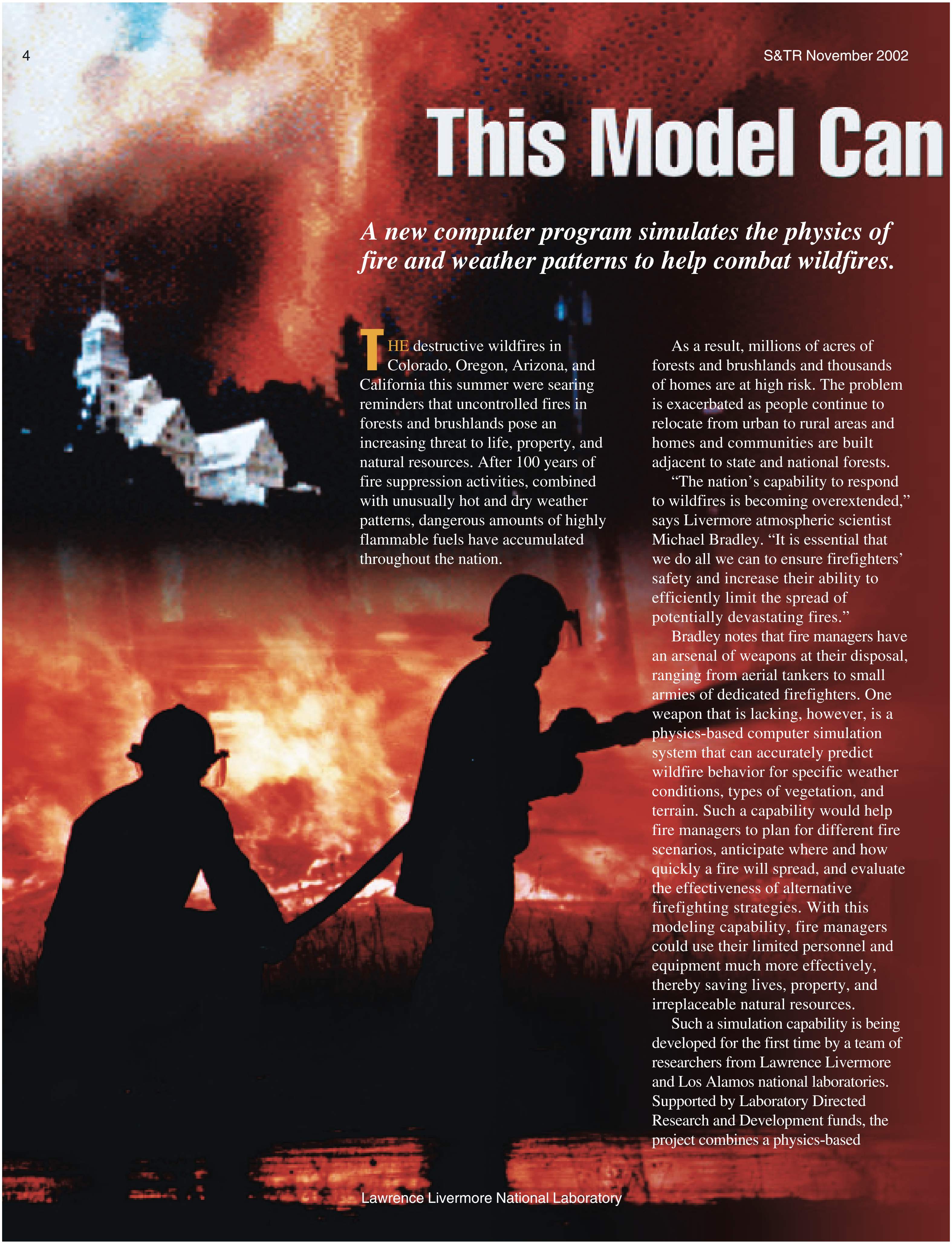
To answer that question, NARAC scientists researched the current state of wildfire simulation programs. They found that the models available to firefighters have severely limited capabilities and are based on simple laboratory experiments. They also discovered that a group of atmospheric scientists at Los Alamos National Laboratory had developed a simulation program based, for the first time, on the physics of combustion, the interactions between fire and close-in weather, and the effects of three-dimensional terrain. As described in the article, Livermore researchers collaborated with the Los Alamos scientists to combine their model, NARAC's weather and smoke prediction capabilities, and the Laboratory's supercomputing resources.

In developing the Livermore–Los Alamos wildfire simulation model, the collaborating scientists made sure that it would be more than a fascinating academic demonstration of computational capability. They sought to create a practical tool for firefighters. Livermore scientists and their Los Alamos colleagues held meetings with potential users: fire departments such as the Los Angeles County Fire Department; San Francisco Bay Area organizations such as the East Bay Regional Park District and the East Bay Hills Emergency Forum; and federal agencies such as the U.S. Forest Service, Fish and Wildlife Service, and National Park Service. On the basis of their input, the team honed the model to reflect firefighters' needs and achieve a level of fidelity never before imagined. Fire managers who have seen Livermore's simulations of the early stages of the 1991 Oakland–Berkeley hills fire have marveled at the model's accuracy and its potential as a training and planning tool.

Until now, most firefighting agencies have not considered an advanced wildfire simulation computer program as a useful planning, training, and firefighting tool. The Livermore–Los Alamos collaborators are working hard to spread the word that such a tool is available. The University of California's Division of Agriculture and Natural Resources is sponsoring workshops to communicate the capabilities of the wildfire model to the firefighting community and to encourage other scientists to help make the model even better by adding additional capabilities. In that respect, the team's goal is to have the Livermore–Los Alamos wildfire model serve as the central framework for a complete physical description of fire behavior, especially at the dangerous interface where urban areas meet forests and grasslands.

I think it's safe to say that the congressman's question has been answered with a resounding yes.

■ Leland W. Younker is associate deputy director for Science and Technology.



This Model Can

A new computer program simulates the physics of fire and weather patterns to help combat wildfires.

THE destructive wildfires in Colorado, Oregon, Arizona, and California this summer were searing reminders that uncontrolled fires in forests and brushlands pose an increasing threat to life, property, and natural resources. After 100 years of fire suppression activities, combined with unusually hot and dry weather patterns, dangerous amounts of highly flammable fuels have accumulated throughout the nation.

As a result, millions of acres of forests and brushlands and thousands of homes are at high risk. The problem is exacerbated as people continue to relocate from urban to rural areas and homes and communities are built adjacent to state and national forests.

"The nation's capability to respond to wildfires is becoming overextended," says Livermore atmospheric scientist Michael Bradley. "It is essential that we do all we can to ensure firefighters' safety and increase their ability to efficiently limit the spread of potentially devastating fires."

Bradley notes that fire managers have an arsenal of weapons at their disposal, ranging from aerial tankers to small armies of dedicated firefighters. One weapon that is lacking, however, is a physics-based computer simulation system that can accurately predict wildfire behavior for specific weather conditions, types of vegetation, and terrain. Such a capability would help fire managers to plan for different fire scenarios, anticipate where and how quickly a fire will spread, and evaluate the effectiveness of alternative firefighting strategies. With this modeling capability, fire managers could use their limited personnel and equipment much more effectively, thereby saving lives, property, and irreplaceable natural resources.

Such a simulation capability is being developed for the first time by a team of researchers from Lawrence Livermore and Los Alamos national laboratories. Supported by Laboratory Directed Research and Development funds, the project combines a physics-based

Take the Heat

wildfire model developed at Los Alamos with the extensive emergency response capabilities of the National Atmospheric Release Advisory Center (NARAC) at Livermore, including its weather prediction and smoke transport codes and Livermore's supercomputers. The effort combines the special capabilities and resources of the two laboratories, says Bradley, who leads the Livermore effort that also includes atmospheric scientists Charles Molenkamp and Martin Leach and geographical information systems (GIS) experts Charles Hall, Lee Neher, and Lynn Wilder.

Predicting wildfire behavior is not a new concept. The models most widely used by firefighters, however, are relatively unsophisticated programs based on data obtained by laboratory experiments, for example, the burn rate of pine needles in wind tunnels. Such experimental results for a variety of vegetative fuels are used in look-up tables to estimate burn rates based on the total amount of fuel, wind speed, and the slope of simplified two-dimensional terrain. The model is then used to predict wildfire behavior, guide firefighting tactics, and assist in training and planning.

"Current models do not account for the many complex physical processes that characterize real wildfires and determine their behavior," says Bradley. The models also don't reflect how the terrain and vegetation change (sometimes dramatically within a few meters), how the weather changes, and, perhaps most importantly, how the fire and weather continuously interact.

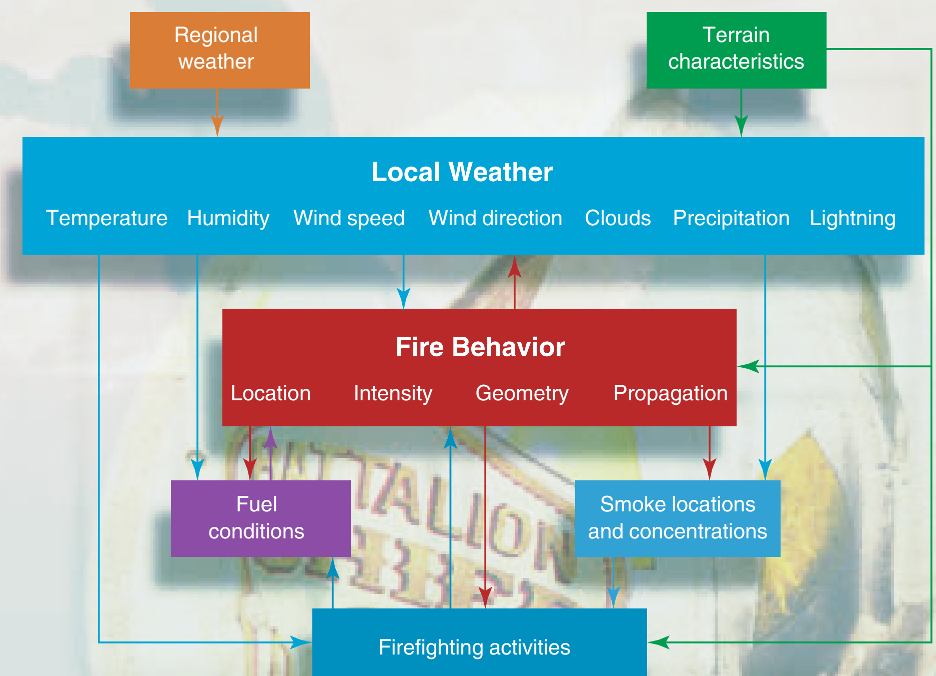
Winds, air temperature, humidity, and precipitation, for example, influence the flammability of fuel and largely determine the risk of fire ignition. In addition, wind speed and direction determine the rate of fire spread and the amount of transported embers from which new fires can be ignited. Weather conditions also determine the location and concentration of smoke plumes, which can interfere with ground and aerial firefighting operations and cause health hazards downwind.

In turn, the heat from wildfires causes rising air currents that strongly modify local weather patterns and create rapidly changing winds that may fan the fire. As a fire approaches, unburned vegetation preheats and dries and ignites more easily. All of these interacting physical processes are reflected by the Livermore–Los Alamos computer model.

Model Starts with FIRETEC

The basic fire-simulation code, called FIRETEC, has been developed over the past 7 years by a Los Alamos group headed by atmospheric scientist Rod Linn. The group experienced first-hand the destructive power of wildfires in 2000, when the Cerro Grande fire ripped through the Santa Fe national forest as well as parts of the town of Los Alamos and the Laboratory itself.

FIRETEC simulates the mechanisms of fire propagation in ways that far exceed the capabilities of wildfire models currently in use. FIRETEC predicts the spread of wildfires based on a fundamental treatment of physical processes such as combustion and turbulence and uses a terrain-following coordinate system based on digitized maps. It takes into account the two basic heating mechanisms of fire: the turbulent convective motion of heated air and the infrared radiation emitted by the fire. Using spatial resolutions of 1 to 10 meters, FIRETEC



Existing wildfire models, using data from isolated laboratory experiments, do not adequately represent the complicated, interactive processes of wildfires defined in this diagram.

also tracks the depletion of fuels and oxygen during combustion.

The code realistically represents the vegetation of an area, including the mixture of species, their densities, and their three-dimensional structure. Because the code includes a vertical fuel representation, it differentiates between grass, tree trunks, and tree crowns, thereby making simulations much more realistic. This degree of realism is needed because in some situations grass will burn without the fire spreading to tree crowns, whereas in other situations, the crowns ignite. In simple models, says Bradley, fuel is simply "flat," represented by a calculated number of tons of vegetation per acre, with no vertical structure.

To account for the interactions between fire and atmosphere, the Los Alamos group combined FIRETEC with the fine-resolution, high-gradient flow solver program known as HIGRAD, which was developed by Jon Reisner. HIGRAD delivers accurate atmospheric simulations at extremely high spatial (1 meter) and temporal (thousandths of a second) resolution.

HIGRAD, however, cannot represent the regional weather patterns within which wildfires burn. "HIGRAD simulates close-in air flow over small regions of a fire but does not take into account more remote weather processes such as cold fronts, high- and low-pressure systems, and precipitation that develop over much larger geographical areas," says Bradley.

Adding Regional Weather

To overcome this limitation, the team incorporated the Coupled Ocean–Atmosphere Mesoscale Prediction System (COAMPS), developed by the U.S. Naval Research Laboratory in Monterey, California, and later refined by NARAC scientists. COAMPS is run twice daily by NARAC to predict regional weather at scales ranging from about 1,000 kilometers down to a few kilometers. The Livermore wildfire team has run COAMPS using horizontal resolutions as fine as approximately 150 meters. COAMPS predicts winds, temperature, pressure, humidity, and precipitation for several days. The code is formulated in terrain-following coordinates, which are advantageous for atmospheric simulations over rugged terrain. "COAMPS provides the regional atmospheric environment within which HIGRAD–FIRETEC simulations run," explains Bradley.

He says that integrating HIGRAD–FIRETEC with NARAC's capabilities provides access to a wide range of resources that strengthen the wildfire simulation capability. These resources include a detailed global terrain database, global mapping system, global weather data acquisition system, and weather prediction systems. NARAC is supported by vast quantities of meteorological data that are collected daily—and sometimes hourly—from around the world.

NARAC also has the leading atmospheric smoke dispersion simulation model, called ARAC-3. Although the model was originally conceived to track radionuclide releases, the center can use it to respond to atmospheric releases of other materials, including toxic chemicals, biological agents, ash from volcanic eruptions, and, most relevantly for firefighting, smoke. Following Operation Desert Storm, NARAC provided twice-daily predictions of smoke dispersion from the burning oil wells in Kuwait. More recently, it predicted the dispersion of smoke from two massive tire-dump fires near Tracy and Wesley, California, from which smoke rose to almost 2,000 meters above ground level. (See *S&TR*, June 1999, pp. 4–11.)

Livermore also offers substantial supercomputer resources. Computer models that accurately predict the behavior of wildfires require enormous processing power that currently can only be provided by massively parallel

The Claremont Resort narrowly escaped destruction during the 1991 wildfire in the hills of Oakland and Berkeley, California.

supercomputers (machines using many processors in tandem). Wildfire simulations performed at Livermore, for example, typically use 64, 64-bit processors belonging to Livermore's TeraCluster2000 680-billion-operations-per-second (gigaops) supercomputer.

Modeling Threats and Responses

Throughout the simulation program's development, the Livermore–Los Alamos team has conferred with federal, state, and local fire managers. Many valuable suggestions have been incorporated into the program's capabilities, and several applications have emerged.

Two applications—wildfire preparedness planning and long-term planning for communities and wildland management—are available now. With adequate funding, three additional applications—analyzing specific fire threats, predicting fire behavior for prescribed burns, and training firefighters—could be ready next summer. The ultimate goal, real-time firefighting support, is several years away and awaits the development of even more powerful computers for faster turnaround.

The wildfire preparedness planning application permits realistic simulations of past or hypothetical future fires for specific locations, with high-resolution modeling of terrain, types of vegetation, and weather conditions. "This is a powerful tool for community fire preparedness planning," says Bradley.

The long-term planning application permits evaluation of vegetation management options such as thinning trees or designing fuel breaks. Such planning is especially important at the urban–wildland interface in determining the fire threat to new homes, commercial development, and open areas.

Fire behavior predictions for prescribed burns would be available to fire managers a few hours before they ignite the fuel. This advance knowledge would enable managers to decrease the risk of prescribed burns going out of control (such as happened with New Mexico's Cerro Grande wildfire) and of violating air quality standards.

Fire threat analyses would produce physics-based predictions of potential fire behavior for specific locations with a few days' notice. This feature would be particularly useful to fire managers in assessing the relative risks of fire breaking out at various locations during periods of increased threat.

As a training tool, the program would be unsurpassed at showing how different factors affect the behavior of wildfires. After specifying the exact ignition point of a fire, students could vary the weather, vegetation, fuel conditions, and firefighting methods to understand their effects. "We envision this application serving a role similar to that of a flight simulation program," says Bradley. "Students could make mistakes without risking their lives."

The program's ultimate goal is real-time support for firefighters. In this application, the program would help fire managers to make critical operating decisions regarding the deployment of firefighters and equipment. The program could also predict the relative effectiveness of various firefighting procedures, such as fuel breaks, backfires, air tanker fire-retardant drops, and helicopter water drops.

Model Validation Essential

The team has been validating the program by simulating well-

(a) East Bay Regional Parks ranger Bill Nichols (left) and Livermore researchers Charles Molenkamp (center) and Michael Bradley used global positioning system tools to determine for the first time the ignition points of the 1991 fire in the Oakland–Berkeley hills. (b) The ignition point for the second fire (which began Sunday, October 20, 1991) in Tunnel Canyon is circled.

documented wildfires. An early simulation using HIGRAD–FIRETEC successfully re-created the Corral Canyon wildfire that occurred in Calabasas, near Malibu, California, on October 22, 1996. The fire had been smoldering in the riparian (vegetation along a gully) area at the bottom of a canyon. It suddenly rushed up one side of the canyon, catching firefighters off guard and injuring several. The simulation re-creates the rapid spread of the fire, from the bottom of the drainage area to the crest of the hill, within 28 minutes, about the time the actual fire took. By comparison, a simulation of the same fire with a traditional model predicts that it would take about 6 hours to burn the same area. The difference between the two simulations is the interplay among the terrain, fire, and winds that is represented by HIGRAD–FIRETEC.

"Firefighters sometimes think they have a lot of time when they really don't," says Bradley. The Corral Canyon simulation showed that strong sea breezes channeled by the terrain pushed the fire up the hill much faster than the firefighters thought possible. The model also shows that if the riparian vegetation were replaced with dry grass, the fire spreads up both sides of the canyon. "The simulation results are encouraging because they compare so well with field observations," Bradley says.

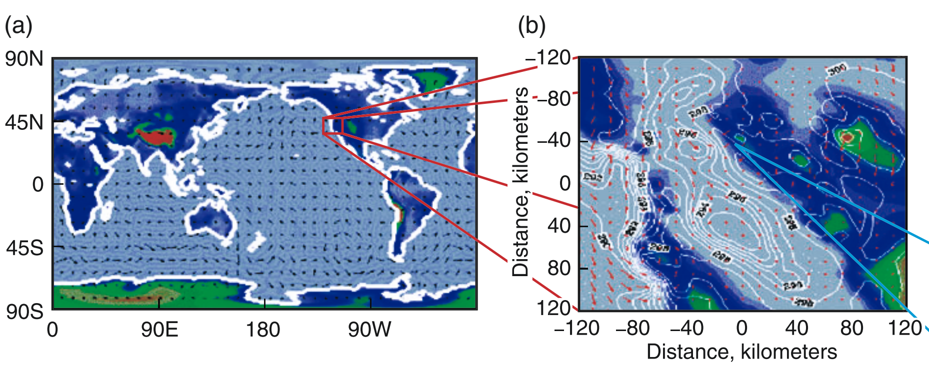
To provide a more exhaustive validation of the program's capabilities, Bradley and his group, together with Livermore GIS experts, have been reconstructing the early stages of the catastrophic 1991 fire in the hills of Oakland and Berkeley, California, and are looking at current fire dangers to neighborhoods that escaped the conflagration. Bradley is sharing the results with East Bay fire agencies, the city governments of Oakland, Berkeley, and El Cerrito, the East Bay Regional Park District, the East Bay Municipal Utilities District, the University of California at Berkeley, Lawrence Berkeley National Laboratory, and the California Department of Forestry and Fire Protection.

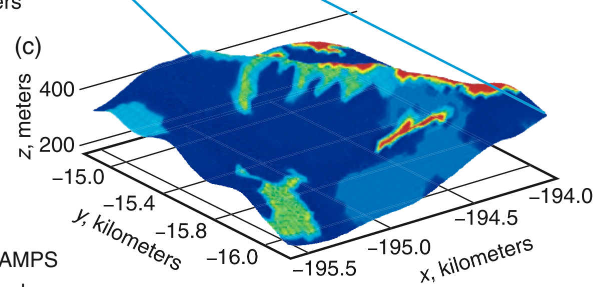
The Oakland–Berkeley hills fire claimed 25 lives and destroyed more than 3,000 dwellings. The simulations re-create its start at about 11 a.m. on Sunday, October 20, 1991, in Tunnel Canyon. (One day earlier, a small grass fire occurred about 100 meters from the ignition point of Sunday's fire. Embers from Saturday's fire, at first thought to have been extinguished, almost certainly started the Sunday conflagration.)

Working with the East Bay Regional Park District, the Livermore group produced the first global positioning satellite coordinates for the ignition points of the Saturday and Sunday fires. Next, the team built a virtual atmosphere for October 20, 1991, by using historical weather data provided by the European Center for Medium Range Weather Forecasting. The data, which had a resolution of about 120 kilometers, were fed into COAMPS to simulate the humidity, temperature, wind direction, and wind speed over the area of the incipient wildfire.

Re-creating Front Yard Weather

The COAMPS data were used by HIGRAD to simulate fine-scale weather at 10-meter resolution. "At this resolution, we're actually simulating the weather that occurred in the front and back yards of individual homes in the Oakland–Berkeley hills," notes Bradley. Volumes of detail on the terrain and





The wildfire modeling capability zooms down to extremely fine resolution. For the Oakland–Berkeley hills fire that began October 20, 1991, the team constructed (a) a virtual atmosphere by using historical weather data provided by the European Center for Medium Range Weather Forecasting. The data, which had a resolution of about 120 kilometers, were fed into the Coupled Ocean–Atmosphere Mesoscale Prediction System (COAMPS) to simulate (b) the humidity, temperature, wind direction, and wind speed over the San Francisco Bay Area. The COAMPS data were used by the high-gradient flow solver (HIGRD) program to simulate (c) fine-scale weather at 10-meter resolution over the Oakland–Berkeley hills.

vegetation were fed into FIRETEC along with the dimensions of a football-shaped scar on the hillside, which resulted from the Saturday fire.

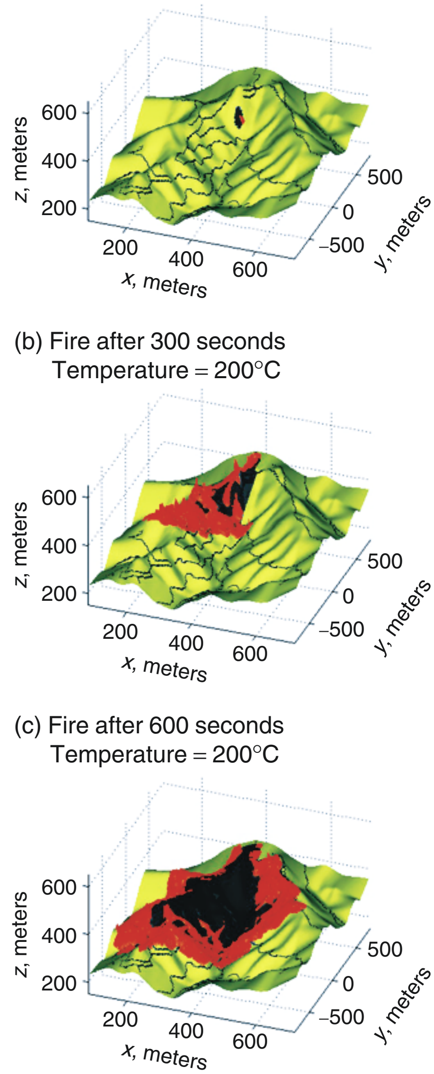
The fire was "lit" in the FIRETEC program by raising the temperature by 100°C at the exact ignition location determined earlier by the Livermore team. The simulation shows wind-whipped flames quickly spreading outward from the ignition point throughout Tunnel Canyon, which contained bone-dry trees, bushes, and grasses. Other aspects of the simulation show the direction and speed of winds (as affected by the fire) and the percentage of vegetation burned.

Bradley says that a common reaction to watching the simulations is that the fire spreads unrealistically fast, but fire officials who have seen the simulation say it is an accurate representation of what happened. "Conditions were nearly perfect for a devastating fire," Bradley says.

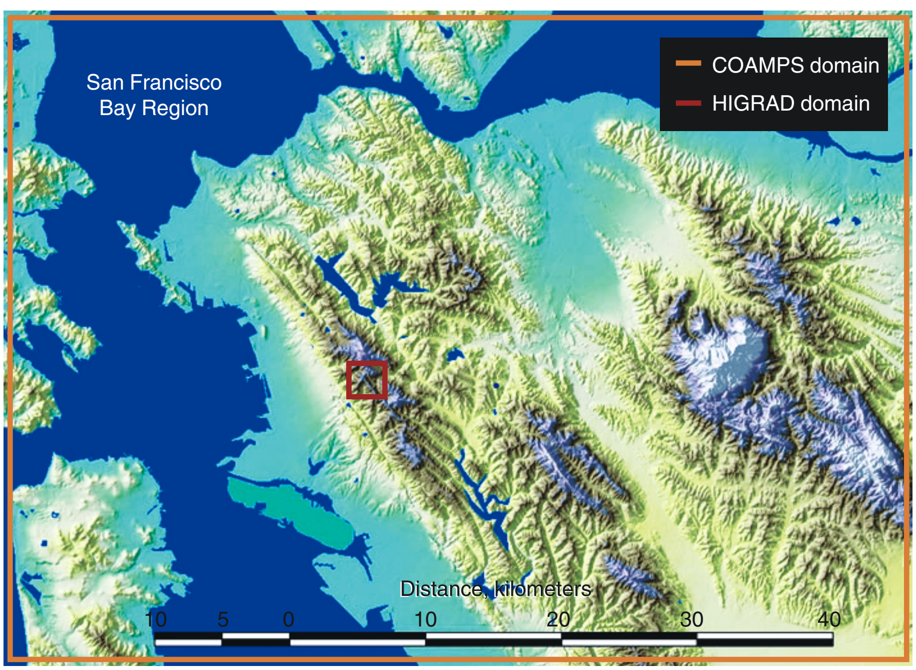
As with the Calabasas fire simulation, the Oakland hills model shows that the exact ignition location is important. If Sunday's ignition point is moved only 100 meters away, to the other side of the canyon, the fire follows a different course.

The team has also developed a fire consequence analysis capability by meshing model results with data maps created with computerized GIS tools. (See *S&TR*, September 2002, pp. 10–16.) GIS analyses make the program more useful to fire chiefs and other emergency planners by superimposing layers of digitized visual information over the simulation. The GIS map layers include roads, schools, fire stations, electrical transmission lines, and even the location of fire hydrants. A GIS layer of land parcel maps, for example, allows users to select specific homes and determine their vulnerability to wildfires.

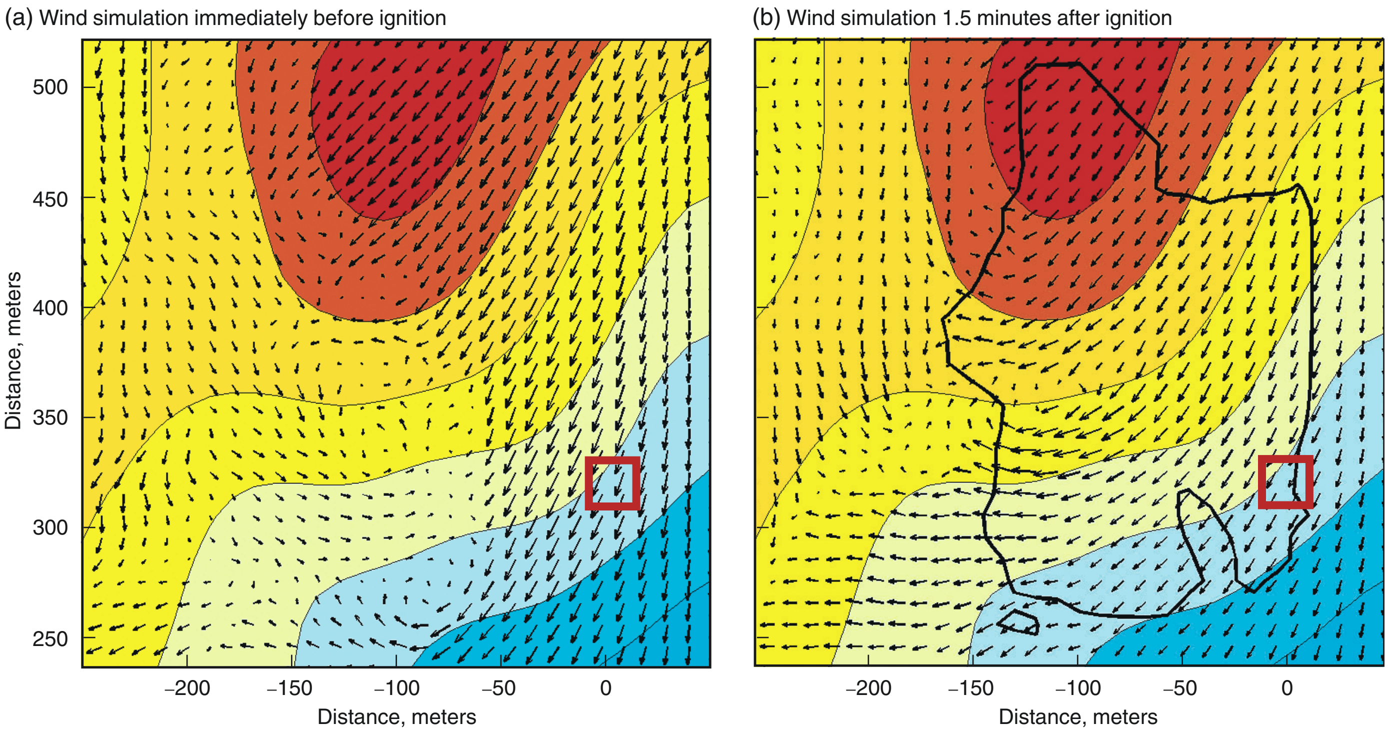
By combining the wildfire models with GIS tools, says Bradley, fire chiefs



A sequence of three frames taken from the computer simulation of the Oakland–Berkeley hills fire, which started in Tunnel Canyon. (a) A football-shaped dark area corresponding to Saturday's extinguished fire can be seen. Sunday's fire broke out just 30 meters away. (b) Three-hundred seconds (5 minutes) later, the fire is spreading quickly up the canyon. (c) Six-hundred seconds (10 minutes) after ignition, the fire has spread to neighboring canyons.



A topographical map of part of the greater San Francisco Bay Area. The Coupled Ocean–Atmosphere Mesoscale Prediction System (COAMPS) weather prediction code modeled the larger area, while the high-gradient flow solver code (HIGRAD) is restricted to a 1.6-square-kilometer area directly over the Oakland–Berkeley hills fire.



(a) A simulation of the wind with 10-meter resolution immediately before ignition of the Oakland–Berkeley hills fire. The arrows' directions indicate wind direction, while the arrows' lengths indicate wind speed. The red box is the fire's ignition site. (b) One and one-half minutes after ignition, winds are significantly altered by the fast-moving fire (perimeter is outlined).

and analysts can plan the best routes for firefighters to take as well as the safest evacuation routes for residents at risk. Planners can also readily determine the effects of thinning stands of trees or building fire breaks.

The Livermore group is particularly interested in areas in the Oakland and Berkeley hills that didn't burn in 1991 and that contain a substantial amount of vegetation, homes, and research facilities. The group hopes to evaluate the effectiveness of fuel breaks and other vegetation management techniques for areas that escaped the 1991 fire. It also hopes to simulate wildfires in Claremont Canyon and in Strawberry Canyon, the site of Lawrence Berkeley National Laboratory, the Lawrence Hall of Science, and a portion of the University of California at Berkeley campus. These simulations will not only help the group to further understand and improve the model, but they will also provide valuable information for local agencies.

Bradley notes that the Oakland and Berkeley hills areas are telling examples of the dangers posed by the urban–wildland interface, where homes are nestled within thick vegetation.

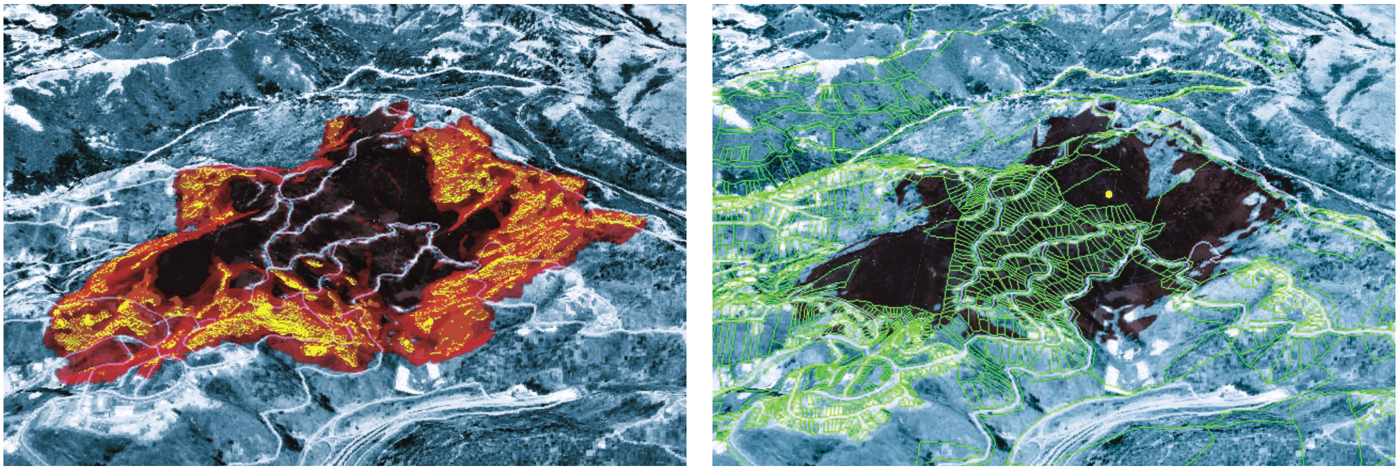
Chance to Make History

Because prescribed burns are planned far in advance, they provide the best opportunity for validating the program's accuracy. The burn location and ignition time are known before the burn occurs; the amount, type, and moisture content of vegetation are calculated before ignition; the weather conditions are known; and the behavior of the fire can be documented.

Bradley has successfully simulated smoke dispersion from several prescribed burns that were conducted at Site 300, Livermore's remote research facility. The simulations used the ARAC-3 dispersion model and compared well with observations of the smoke plume. He is hoping to use the full predictive power of the Livermore–Los Alamos model to provide reliable estimates of the fire behavior and smoke dispersion at least 24 hours before the prescribed burns are ignited at Site 300 in 2003.

"By next summer, it is possible we will be able to run the system fast enough to predict the first 30 minutes or so of the fire's behavior during a

(a) (b)



These images combine the result of (a) a computer simulation of an early stage of the Oakland–Berkeley hills fire with (b) a geographical information systems map of land parcels in the Oakland–Berkeley hills. Any home on the land parcel map can be selected to determine its address and its risk from a fire.

prescribed burn. If we are successful, it will be a truly historic event for fire science.” The team also has received several offers from fire management agencies to participate in their prescribed burn programs.

Enthusiastic Reception

The concept of an advanced wildfire simulation capability has been received positively by potential users. As the program’s development has progressed, an increasing number of agencies have expressed interest in the project, including the Los Angeles County Fire Department, the nation’s largest. In October, the University of California sponsored a wildfire physics workshop that explored how other scientists and fire managers can use the Livermore–Los Alamos program as the basis for advanced wildfire behavior studies. “We want to build a community of scientists and firefighters,” says Bradley. A second workshop is planned for early next year.

The team is looking at the current program as a central core to which additional modules can be added to strengthen its overall capabilities. For example, the increasing threat of wildfire at the wildland–urban interface makes it appropriate to include structures such as homes and businesses in the simulation system. The team is in contact with researchers at the National Institute of Standards and Technology who are developing a code that simulates burning structures. Developing such a code is a substantial task because of variations in structural materials and their contents.

A module to represent the process of fire spreading by showers of embers, called spotting, will be added to HIGRAD–FIRETEC next year. The team is collaborating on the module with researchers at the University of California at Berkeley. “This is not as simple as it might sound,” Bradley comments. “We have to decide on the embers’ sizes, how far the winds take them, and the percentage of times they start new fires.”

Eventually, the team foresees a 24-hour national wildfire prediction program being established, with fire managers and even firefighters in the field linked to NARAC with laptop computers.

Putting wildfire simulation on a solid physics-based footing can only be good for firefighters, the public, and the environment.

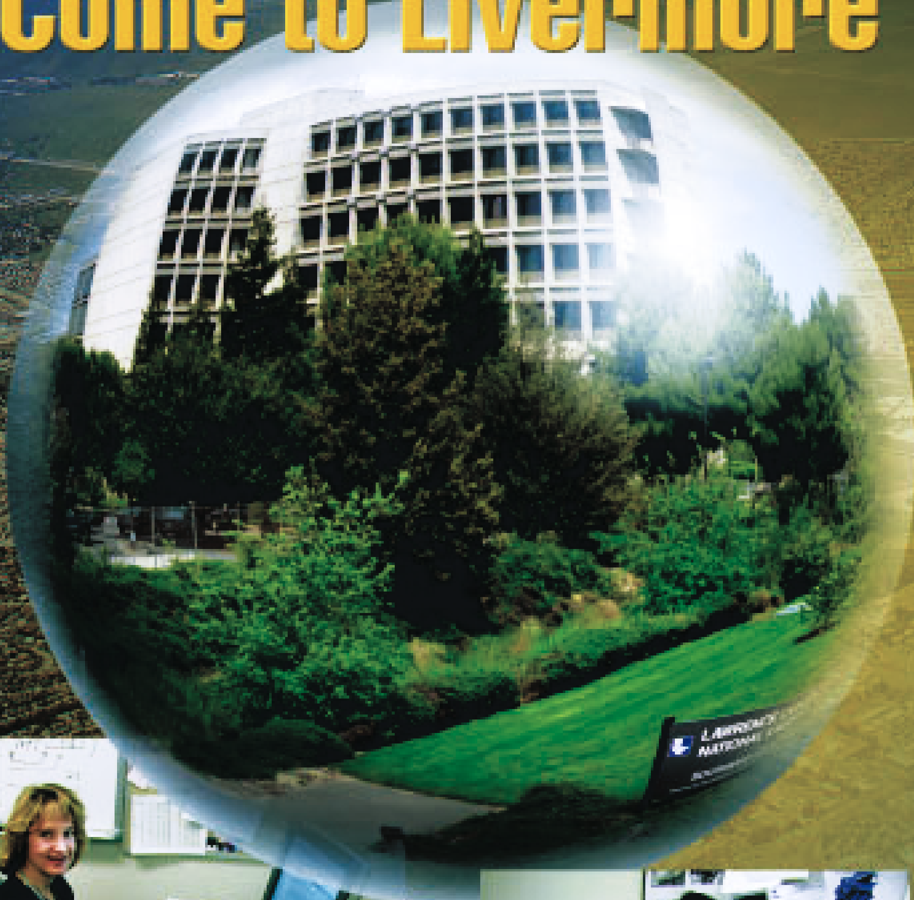
—Arnie Heller

Key Words: Coupled Ocean–Atmosphere Mesoscale Prediction System (COAMPS), fire model, FIRETEC, geographical information systems (GIS), high-gradient flow solver program (HIGRAD), Los Alamos National Laboratory, Lawrence Berkeley National Laboratory, National Atmospheric Release Advisory Center (NARAC), TeraCluster2000 supercomputer, wildfires.

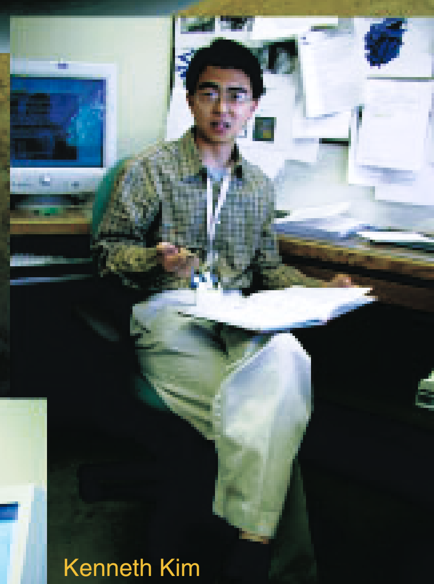
For further information contact Michael Bradley (925) 422-1835 (bradley6@llnl.gov).

The Best and the Brightest Come to Livermore

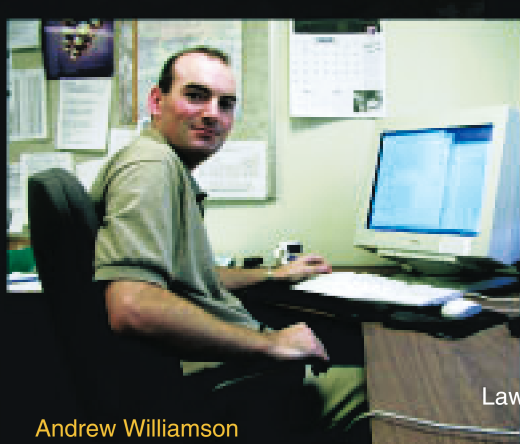
Fewer than 1 percent of applicants become Lawrence fellows at Livermore.



Shea Gardner



Kenneth Kim



Andrew Williamson

WOULD you apply to be a Lawrence fellow, knowing your chances were less than 1 in 100 of being accepted? For the applicants, the stakes are high. But the payoff is great for both the fellows and the Laboratory.

This postdoctoral program is formally known as the Lawrence Livermore Fellowship Program. Informally, it is called the Lawrence Fellowship in tribute to Ernest O. Lawrence, the cofounder of the Laboratory, who cultivated creativity and intellectual vitality in the scientists who worked with him. Lawrence Livermore National Laboratory strives to do the same.

The Laboratory has always been a place where postdoctoral fellows thrive. They can work on state-of-the-art equipment with leaders in their field, performing research in areas of high demand. While all postdoctoral fellows pursue independent research, most are hired by a particular program, usually to perform research for a specific project. Lawrence fellows have no programmatic responsibilities and are given the opportunity to select the group in which they want to work. The allure of freedom and an atmosphere that cultivates creativity, coupled with a competitive salary and Livermore's extensive resources, make the Lawrence Fellowship Program a prestigious opportunity. In exchange, it brings to Livermore some of the most sought-after Ph.D.s in the world.

The fellows produce remarkably creative research during their tenure. Many stay on as full-time career employees, continuing their work. Some leave Livermore to take positions at other institutions. But, as one fellow says, "The ones who leave are ambassadors for Livermore for the rest of their careers."


Olgica Bakajin

Solution to a Challenge

The Lawrence Fellowship Program was the brainchild of Jeff Wadsworth, former deputy director for Science and Technology. He initiated the program in 1997 in an effort to reverse the effects of the "dot-com" boom, which was leading many young scientists to choose the remuneration offered by private industry over employment with Department of Energy laboratories.

To help persuade the best and the brightest to come to Livermore, the Lawrence Fellowship offers an attractive salary and considerable research freedom. It was modeled after the J. Robert Oppenheimer Postdoctoral Fellowship Program at Los Alamos National Laboratory. In both programs, non-U.S. citizens may apply. Lawrence fellows are hired by the Director's Office, in cooperation with Livermore's University Relations Program.

The new program was first announced in the fall of 1997. Although some Lawrence fellows learn about the program through contacts with Laboratory employees, most applicants find out about it through advertisements in journals such as *Science* and *Nature* or on the Web at either fellowship.llnl.gov/ or www.llnl.gov/postdoc/.

"We are interested in finding people who weren't necessarily thinking about coming to Livermore or who didn't know about Livermore initially," says Harry Radousky, chair of the Lawrence Fellowship Program committee.


Julio Camarero

The fellows are chosen for 3-year appointments by a selection committee consisting of a representative from each of the Laboratory's scientific directorates. The criteria for acceptance are rigorous. Out of 1,849 applicants in the first 4 years of the program, only 15 have been accepted. More recently, 282 applications were received for the program's fifth year, and 2 applicants have been invited to participate.

Each application is read by the selection committee, which looks primarily for leadership of stellar research projects. Applicants must have received their Ph.D. within the last 5 years. The applicant pool is eventually reduced to 6 individuals who undergo a 2-day interview. On the first day, the fellowship finalist gives a seminar on his or her area of interest; has lunch with the committee, which serves as a question-and-answer session; and then meets with current fellows in the afternoon. On the second day, applicants have the opportunity to talk to Laboratory scientists with whom they might be interested in working.

The goal of this process is to find people who will succeed at the Laboratory. The likelihood of success is measured in several ways: by matching an applicant's field of interest with those of the Laboratory, examining the applicant's academic record and publications, and analyzing the research projects the applicant has initiated and the level of innovation those projects represent.

"We're not looking for management skills but at scientific leadership," says Radousky. "The object of the fellowships is to encourage intellectual vitality at the Lab and to recruit the best people in the world," he continues. "What we've discovered is that the application process is an excellent way to attract people to all kinds of positions. Many applicants who don't get into the Lawrence Fellowship Program are awarded postdoctoral fellowships to work in Laboratory programs or are hired as full-time employees."

Of the 15 individuals who have received Lawrence Fellowships thus far, 3 are now career employees, 2 left to become professors at the Massachusetts Institute of Technology (MIT), 1 went to the National Institute for Standards and Technology, another returned to his native Belgium, and the remaining 8 are still Lawrence fellows.

The Results of Freedom

Freedom to work on projects and with mentors of their choice is what most current Lawrence fellows say attracted them to the program. This freedom, coupled with the Laboratory's interdisciplinary atmosphere, also permits many fellows to move outside their initial area of specialization and investigate other scientific fields.

Wei Cai, for instance, a current Lawrence fellow from China, earned his Ph.D. from MIT. Midway through his graduate work, mentor Vasily Bulatov left MIT for the Laboratory. Bulatov encouraged Cai to apply for the program. Cai was a successful fellowship applicant and has worked not only with Bulatov but also with Malvin Kalos, the father of quantum Monte Carlo simulations. With Kalos, Cai has been investigating how to use Monte Carlo simulation codes more efficiently for modeling the microstructures of materials. Cai has amended some of Kalos's techniques and applied them to small-scale problems with great success. Now, together with Kalos, Bulatov, and other Livermore researchers, Cai is working on a project funded by the Laboratory Directed Research and Development (LDRD) program to apply these techniques to larger, more complex systems. Cai has also been working on a new massively parallel computer code for modeling dislocation dynamics. "What happened here has a lot to do with the academic freedom the fellowship provides," Cai attests.

This freedom also allowed Cai to work on a particularly exciting project far removed from his usual line of research. At the suggestion of Giulia Galli, leader of the Quantum Molecular Dynamics Simulations Group, Cai tried to solve a problem that Galli's group was facing: adding a means of modeling a magnetic field to the electronic structure simulation codes regularly used to model condensed matter systems. Cai devised a code that successfully modeled in two dimensions the behavior of small systems, such as isolated hydrogen atoms and molecules, under an arbitrary magnetic field. The next step will be to apply this method with the more powerful electronic structure codes used for large-scale calculations, such as the modeling of magnetic field effects on the dynamics of fluid hydrogen.

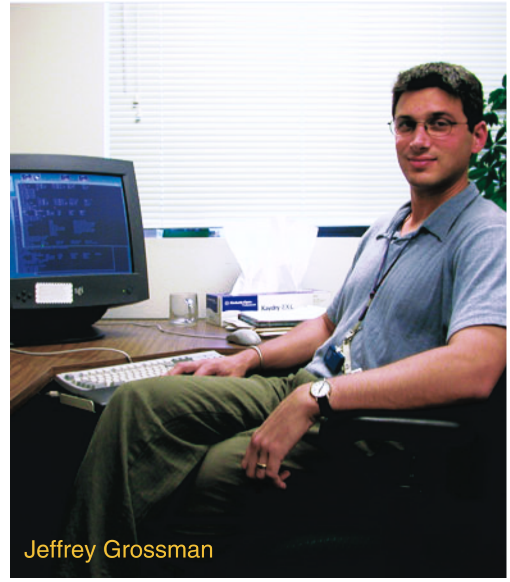
Cai notes that the freedom allowed in the Lawrence Fellowship Program can be almost disconcerting at times. "You need discipline and must be able to make decisions at critical times about what you want to study."

Working at the Nanoscale

Two computational physicists became a team as Lawrence fellows. Jeffrey Grossman, a Ph.D. from the University of Illinois at Champaign-Urbana, and Andrew Williamson, a Ph.D. from the University of Cambridge in England, had known each other for years and both were interested in working with Giulia Galli. Almost immediately after arriving at Livermore as fellows, they applied for LDRD funding to use quantum Monte Carlo simulations to learn more about the characteristics of nanostructures, atomic-scale dots 1,000 times smaller than the width of a human hair. (See *S&TR*, April 2002, pp. 4–10.)

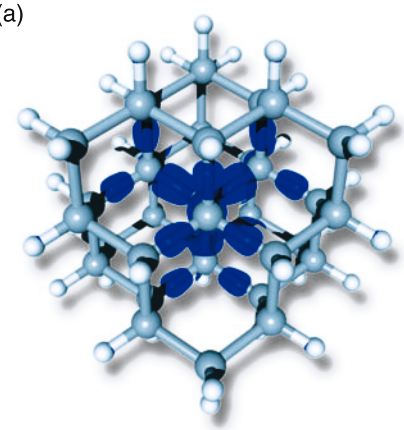
"Scientific interest in nanotechnology centers around one very simple concept," says Grossman. "When you make something really small, its characteristics change. At the nanoscale—just a few hundred atoms—a material's properties start changing and become really interesting. Those differences and the ability to control the size of the structures mean that all kinds of new devices could be made—new ways to deliver drugs, storage systems for hydrogen fuel, detectors that can recognize microscopic amounts of anthrax in the air."

Livermore's supercomputers were a major draw for this duo because quantum Monte Carlo simulations are computationally intensive. With Livermore's computers, they can do work that they couldn't do at most places.



Jeffrey Grossman

(a)



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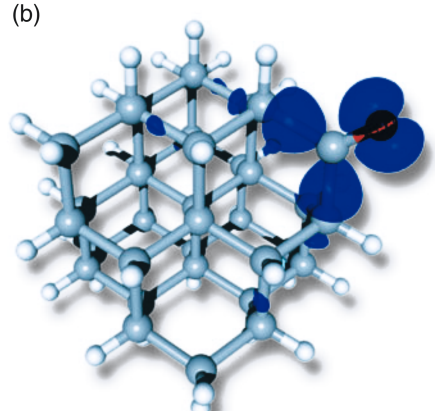


Lawrence fellows Jeffrey Grossman and Andrew Williamson are using quantum Monte Carlo simulations to research the characteristics of nanostructures such as these silicon quantum dots. (a) A 71-atom silicon quantum dot. Hydrogen atoms (white) bonded to the surface make the material less reactive. (b) When a more reactive oxygen atom replaces two hydrogen atoms, the electron charge cloud (purple) is drawn toward the oxygen atom, dramatically changing the optical properties (wavelength) of the silicon quantum dot.

Another selling point was that Galli's group was beginning a new project on nanoscience when Grossman and Williamson joined the Laboratory. "Part of what makes the Lawrence Fellowship Program so attractive," says Williamson, "is the opportunity to create something new and shape the direction that research takes, rather than trying to come in and fit into a slot that was shaped by someone else."

Experimental biologist Julio Camarero, who is also working at the nanoscale, saw the Lawrence program advertised in *Science* and *Nature* while a postdoctoral fellow at Rockefeller University in New York City. Camarero received his Ph.D. from the University of Barcelona.

At Livermore, he started out in the Biology and Biotechnology Research Program (BBRP) but moved to the Chemistry and Materials Science Directorate, where he continues to perform biological experiments. He is a member of a team that aims to use dip-pen nanolithography to create and probe ordered arrays of proteins and colloids. One of the many uses for dip-pen nanolithography is to create tiny sensors that will detect biological warfare agents.

"The Lab is interested in applying science and technology to create tools for national security," notes Camarero. "I think that the technology we have developed is very powerful and has many applications, not the least of which is protecting us from biological terrorism."

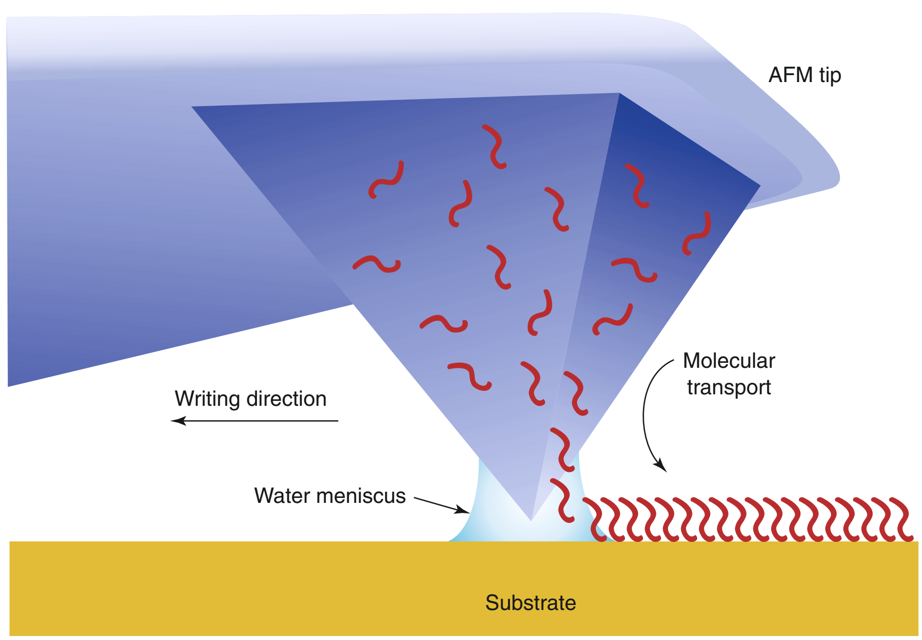
In dip-pen nanolithography, the tip of an atomic force microscope is dipped into either an organic or inorganic substance (the "ink") and then is used to "write" on the surface of an inorganic substrate. (See *S&TR*, December 2001, pp. 12–19.) As the tip moves across the surface, it creates a precise, orderly pattern, or template, of material that is in chemical contrast to the substrate surface.

The goal of Camarero's research is to form specific chemical patterns less than 10 nanometers wide on silicon dioxide and gold surfaces. The chemicals in this template will react with proteins, thus making the template a sort of "molecular Velcro" to which the proteins bind in ordered arrays. Use of these templates allows for total control over the orientation of the proteins.

Small, Complex Systems

Kenneth Kim was at the University of Cambridge as a Wellcome Trust fellow in the Applied Mathematics and Theoretical Physics Department when he learned about the Lawrence Fellowship Program from colleagues at the University of California at Berkeley and from Livermore's Web site. Kim works in BBRP's Computational and Systems Biology Division, led by Michael Colvin. "Traditionally, biology has been a qualitative discipline," Kim says. "But mathematics can play an important role in the biological sciences by providing a precise and powerful language to clarify underlying mechanisms and reveal hidden connections between seemingly disparate systems. Mathematical modeling may allow biology to become a predictive science alongside physics and chemistry."

Kim is applying the mathematical methods of statistical mechanics to the study of the astonishingly complex interactions and collective behavior of biological systems. He has studied the collective behavior of interacting bodies (inclusions) in an elastic medium (a cell membrane). The mathematical model that describes this behavior can be used to investigate the mechanism that causes protein inclusions in cellular membranes to distribute themselves into large, stable



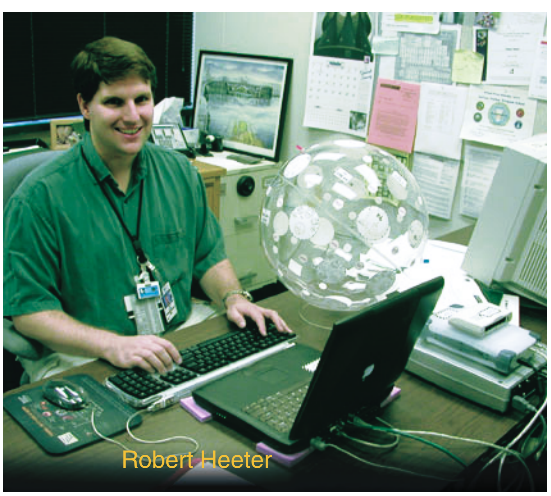
Lawrence fellows Julio Camarero and Aleksandr Noy—now a full-time Laboratory employee—are pursuing research using dip-pen nanolithography. This technology uses the tip of an atomic force microscope (AFM) dipped in molecules to "write" on an inorganic substrate. The molecules react with the substrate to create a pattern of nanostructures attached to the substrate. These nanostructures have a variety of scientific uses.

aggregates as a function of their global shape. This research illustrates the rich interplay between geometry and statistical mechanics that underlies biological and other complex systems.

Kim is also developing a mathematical model for gene regulatory networks. In a gene network, the protein encoded by a gene can regulate the expression of other genes, which in turn control other genes. A protein can also regulate its own level of production through feedback processes.

"This network of interacting genes is another concrete example of collective behavior exhibiting an amazing degree of complexity at many spatial and temporal scales," says Kim.

Olgica Bakajin of Yugoslavia is yet another fellow working at the nanoscale. Bakajin had completed her Ph.D. at Princeton University and was on her way to the National Institutes of Health (NIH) when Livermore called to inform her that she was a successful Lawrence fellow applicant. Since arriving at Livermore, she has worked on several projects related to the development of novel microstructures and nanostructures. She is designing and fabricating a fast microfluidic mixer for the study of proteins. Just 10 micrometers wide—a human hair is 80 micrometers wide—the mixer can cause proteins to fold and unfold when solution conditions in the mixer are changed quickly and precisely. Bakajin will be using the mixer to examine the kinetics of fast protein folding reactions (an LDRD-funded project) and to investigate the kinetics of the folding of single-protein molecules (a collaboration with NIH scientists).



Robert Heeter

Working with former Lawrence fellow Aleksandr Noy, Bakajin is using carbon nanotubes in microfabricated devices to separate biological molecules. In the future, these microdevices could be used as detectors of chemical and biological warfare agents. "The interdisciplinary atmosphere at the Lab has provided me with lots of research opportunities," says Bakajin. "Right now, I have more ideas for interesting projects than I have time to pursue them."

Here to Stay

Three former fellows are now full-time Laboratory employees, having exchanged some of the freedom of the Lawrence Fellowship for a staff position.

Theoretical biologist Shea Gardner, who studied population biology at the University of California at Davis, worked initially on several computational biology projects, one of which was a mathematical model to tailor chemotherapy treatments for individual cancer patients. Treatment strategies are based on the kinetics of the patient's particular tumor cells. Gardner has filed a provisional patent for this modeling approach and has been contacted about commercially developing the software.

Gardner also worked on biostatistics for the analysis of gene microarrays. A microarray is a glass microscope slide covered with "spots," each occupied by a different gene. (See *S&TR*, March 2002, pp. 4–9.) The entire slide is exposed to a stimulus such as a chemical or a change of temperature, and scientists note how each gene responds to the stimulus. "With microarrays, you can see the expression of over 12,000 genes at once, in a single run," Gardner notes. "Previously, you could look at just one gene at a time."

Gardner is now participating in bioinformatics work for the National Nuclear Security Administration's Chemical and Biological National Security Program, computationally identifying DNA signatures that could be used to detect biological pathogens. She hopes to continue with this research. "Mathematical modeling, biostatistics, and bioinformatics are really different," she says. "Where else would I have had the opportunity to work on all three?"

Aleksandr Noy, a physical chemist from Harvard University, came to Livermore in 1998 to work on high-resolution microscopy. To that end, he developed a new microscope system that combines the topographic capabilities of the atomic force microscope with the spectroscopy capabilities of a confocal microscope. (See *S&TR*, December 2001, pp. 12–19.)

"My interests morphed from just looking at tiny things to fabricating them and using them for nanoscience applications," he says. "Shifting focus like that would not have been possible if I had not been a Lawrence fellow." Noy has worked on several nanoscience projects, including some that use carbon nanotubes in unique ways. Much of his research requires his new microscope to make the results visible.

He now leads a group that is fabricating electroluminescent nanostructures by dip-pen nanolithography. The researchers "write" with a conjugated polymer that emits light when a voltage is applied. Nanowires made of conjugated polymer poly [2-methoxy, 5-ethyl [2´ hexy(oxy)] para-prenylene vinylene], or MEH-PPV, may some day serve as light-emitting nanodiodes. MEH-PPV nanowires are also highly sensitive to light and can serve as tiny optoelectric switches, which today are typically 1,000 times larger than tomorrow's MEH-PPV nanowires will be.

Plasma physicist Robert Heeter heard about the Lawrence Fellowship Program from Paul Springer, a group leader in Livermore's Physics and Advanced Technologies Directorate, who performs laboratory astrophysics experiments. Heeter has been working with Springer since coming to Livermore in 1999.

While at Princeton University earning his Ph.D., Heeter worked in England at the Joint European Torus, a magnetic fusion energy facility. But because of funding cuts, magnetic fusion research had fewer opportunities when Heeter was about to graduate. He was also interested in astrophysics, so he decided to apply for a Lawrence Fellowship at Livermore, which had active programs in both astrophysics and fusion energy.

Heeter became a Lawrence fellow and almost immediately got involved in photoionization experiments on Sandia National Laboratories' *Z* Accelerator in Albuquerque, New Mexico. Today, he continues his photoionization research. "I've also been doing other experiments in high-energy-density plasma physics," he adds. "I've stayed in the same group and in the same field that I was in as a fellow. High-energy-density physics experiments have numerous applications: in stockpile stewardship, in inertial fusion, and in astrophysics. And there's a lot of fundamental science to explore that hasn't been done before."

Laboratory Ambassadors

Not all Lawrence fellows stay on as full-time Laboratory employees. The most recent one to depart was metallurgist Christopher Schuh, who left in the summer of 2002 to become a professor at MIT. After completing his Ph.D. at Northwestern University, he came to Livermore to work on grain boundary engineering, in which conventional metallurgical processing is tailored to produce better metals. Grain boundaries—where crystals with different orientations come together—are the weak link in any material. Schuh examined ways to manipulate the orientation of crystals at grain boundaries to create metals with desirable properties such as less cracking, corrosion, and cavitation.

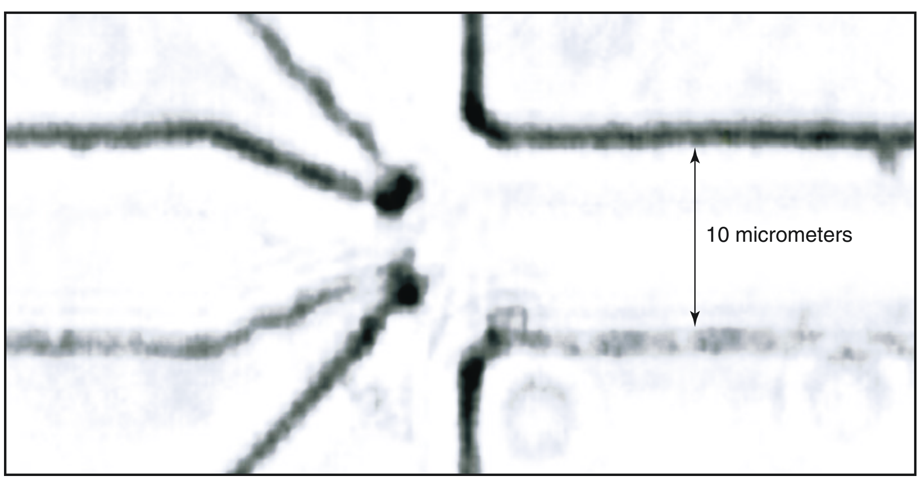
Schuh's research also took him beyond grain boundaries to the individual atoms in the crystals. "If you disturb the atoms in metals so much that the crystal structure no longer looks anything like that of traditional metals, the metals will have very different properties," says Schuh. "We're trying to understand how these changes affect the physics of the metal."

Schuh notes that postdoctoral fellows typically join a program with the understanding that they have been hired to work with someone on a certain project. "For Lawrence fellows," he says, "there's no such obligation. That gives you complete freedom and a lot of latitude."

Nicolas Hadjiconstantinou received his Ph.D. from MIT and immediately joined Livermore as a Lawrence fellow, deferring a teaching appointment at MIT for a year. While at Livermore, he helped to develop a code that extended the use of direct Monte Carlo calculation from the simulation of dilute gases to the simulation of dense fluids. With this code, Livermore researchers can simulate for the first time the phase change characteristics of a van der Waals fluid.

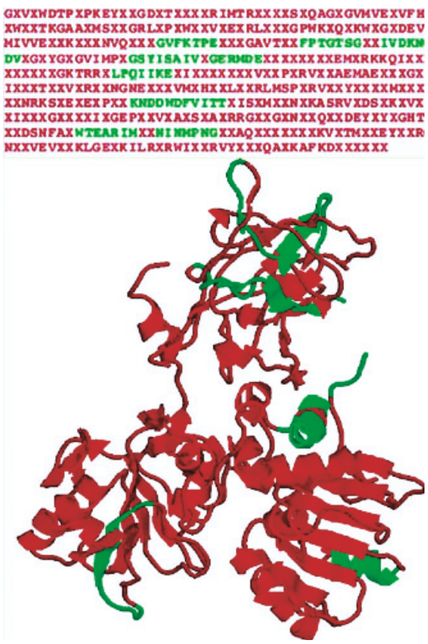
Joel Ullom, who completed his Ph.D. at Harvard, focused on the development of cryogenic detectors, which are small electrical circuits that produce a current or voltage pulse when hit by a photon or particle. The detector

Aleksandr Noy

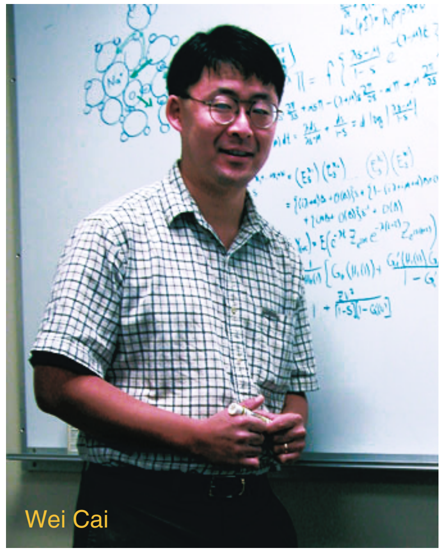


Olgica Bakajin is designing and fabricating this fast microfluidic mixer used for researching the kinetics of protein folding.

must be cooled to temperatures between 0.1 and 1 kelvin, so that the energy of a single photon will produce measurable heating. Ullom used cryogenic detectors to weigh the protein fragments dislodged from bacterial spores by a pulse of laser light. He also developed refrigeration technology to produce the ultralow temperatures needed for cryogenic detectors. Ullom became a Laboratory career employee before leaving for a position at the National Institute of Standards and Technology.



One of the research interests Shea Gardner pursued as a Lawrence fellow, which she continues today as a Laboratory employee, is modeling the DNA signatures of viral pathogens. These simulations contribute to technologies for detecting agents of biowarfare.



Wei Cai

Luc Machiels, a native of Belgium, received his Ph.D. from the Swiss Federal Institute of Technology. After a postdoctoral position at MIT, he came to the Center for Applied Scientific Computing, where he solved problems in continuum mechanics. With colleagues at MIT, he developed a new finite-element error control strategy for the version of the Navier–Stokes equation that describes the motion of an incompressible fluid. The technique, which is both accurate and efficient, calculates lower and upper limits for the output of a system, such as the temperature bounds at the surface of an electronic device. Before leaving Livermore, he also developed new techniques for the solution and modeling of partial differential equations.

A Resounding Success

Radousky has only good things to say about the Lawrence Fellowship Program. "We've learned that we can attract really top people to the Laboratory," he says. "This program has attracted the best young scientists to the Lab and promoted university collaborations. It is also an excellent way to do general recruiting."

When the program first started, more fellows were engaged in traditional physics research, while today more are studying biology and nanoscience. This shift is consistent with changes throughout the scientific community. Biological research leaped to the foreground with the success of the Human Genome Project. Many experts predict that the 21st century will be remembered for a revolution in biotechnology and medicine comparable to the advances made during the last century in physics.

Nanoscience is a similarly "hot" research topic. As all kinds of devices in our world become smaller and smaller, nanostructures of all types will find many uses.

All in all, the Lawrence Fellowship Program has been a resounding success in bringing new talent to the Laboratory and encouraging creativity and exciting science.

—Laurie Powers and Katie Walter

Key Words: Lawrence fellows, Lawrence Fellowship Program, postdoctoral positions.

For further information contact Harry Radousky (925) 422-4478 (radousky1@llnl.gov).

For information on the Lawrence Fellowship Program and other fellowship opportunities at the Laboratory, see these Web sites:

fellowship.llnl.gov/
www.llnl.gov/postdoc/

A View to a Kill

MILITARY strategists have dreamed for years of being able to stop an incoming missile in midair. Missile interception was the goal of the Strategic Defense Initiative of the 1980s and is a Department of Defense (DoD) goal today.

DoD has hired the Boeing Corporation as the lead system integrator for a weapons system to intercept an incoming ballistic missile. Boeing's interceptor for the Ground-Based Mid-Course Defense (GMD) program is currently being flight tested.

For the flight tests, a missile loaded with a "kill" vehicle is launched from Reagan Test Range at Kwajalein Atoll in the Pacific Ocean, to target the mock weapon-laden reentry vehicle of a missile launched from Vandenberg Air Force Base in California. Under contract to Boeing, a Livermore project has developed several sensors whose data help DoD determine whether the interceptor met the goal of killing the target missile.

Physicist Alex Pertica leads Livermore's Remote Optical Characterization Sensor Suite (ROCSS) project. Some of the ROCSS instrumentation has been developed by the Laboratory, and some is available commercially. Spectrometers examine the chemical makeup of the debris from the midair intercept while radiometers measure impact temperature and intensity. At the same time, high-speed cameras document the intercept event.

Livermore is one of several research organizations and companies responsible for monitoring the flight test program. "Our niche," says Pertica, "is the collection of spectral information as well as high-speed video to reveal the phenomenology of the intercept. Other organizations are tracking debris fragments and providing additional photo documentation of the intercept."

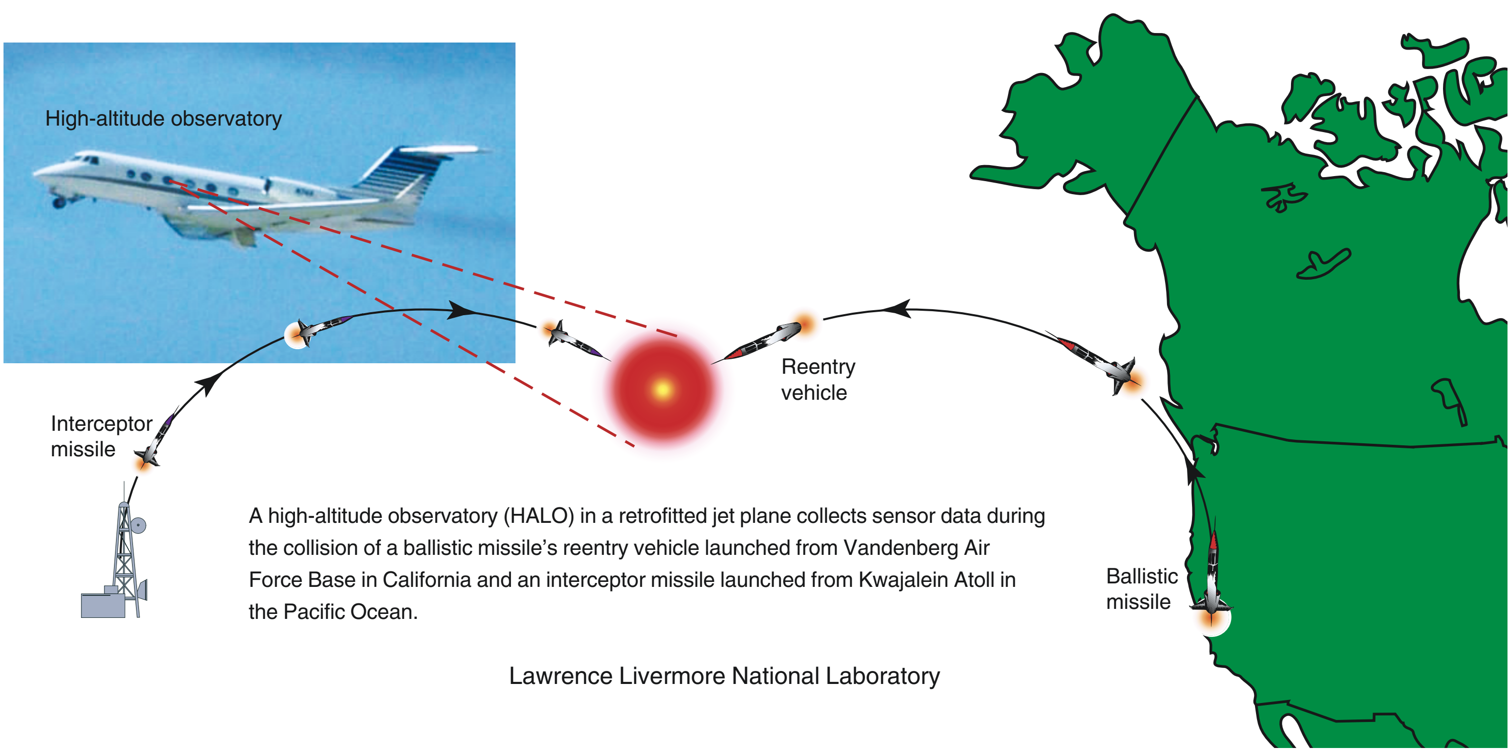
High-Flying Instruments

Livermore's sensors and cameras—as well as the instrumentation of other organizations—fly in a retrofitted business jet known as a high-altitude observatory (HALO). HALO flies at an altitude of about 14 kilometers, high above the weather. At least one Lawrence Livermore scientist is onboard each flight and must take Air Force high-altitude training before flying.

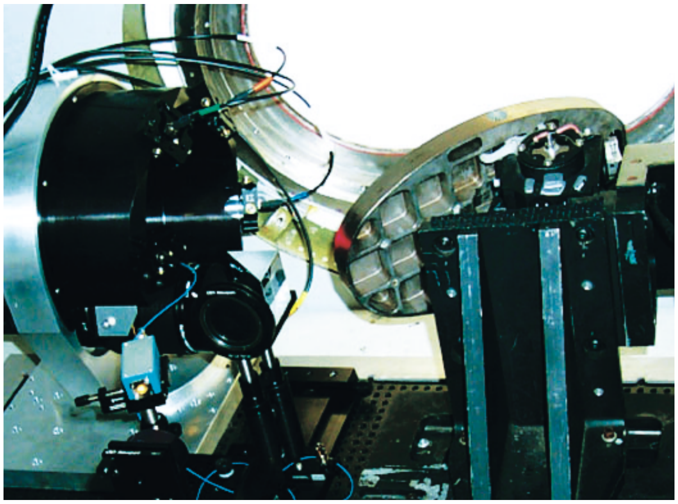
The HALO takes off from Reagan Test Range about 1 hour prior to the launch of the target missile from Vandenberg. Once in the air, HALO remains within 650 to 900 kilometers of the interceptor missile, also launched from Reagan Test Range, until the intercept occurs. A tracking mirror onboard the jet is guided by ground-based radar and tracks the trajectory of the interceptor missile.

The jet's high altitude not only keeps it above the weather but also provides for increased atmospheric transmission of infrared light. Many onboard sensors, including several of Livermore's, collect data in the infrared wavelengths. The ROCSS telescopes collect light through a window specially designed to transmit infrared light and channel it to the instruments via fiber-optic lines.

Five Livermore instruments fly onboard the HALO to collect data on the final boost of the interceptor rocket and then on the kill vehicle's collision with the reentry vehicle. A highly sensitive infrared echelle-grating spectrometer (EGS) detects the presence of gaseous chemical species in the effluent cloud. This instrument was developed at Livermore for another purpose entirely: to "sniff" the smokestacks of suspected chemical and nuclear facilities for tell-tale traces of weapon production.



A high-altitude observatory (HALO) in a retrofitted jet plane collects sensor data during the collision of a ballistic missile's reentry vehicle launched from Vandenberg Air Force Base in California and an interceptor missile launched from Kwajalein Atoll in the Pacific Ocean.



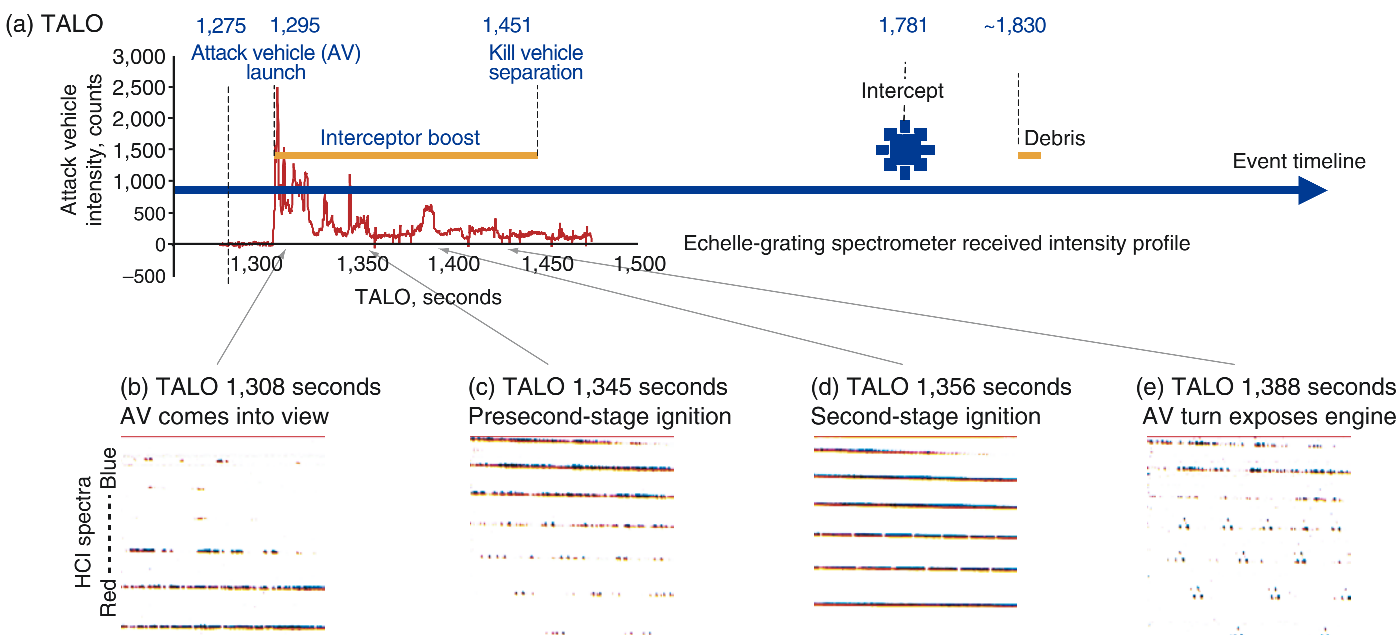
A tracking mirror (right) points out of a window of the high-altitude observatory (HALO) jet. The window is designed to admit infrared light for several of the onboard sensors. On the left is the front end of Livermore's instrumentation, whose fiber-optic lines carry data to individual sensors.

Another spectrometer operating in the visible wavelengths estimates temperatures and identifies materials produced by the interceptor's boost phase and by the collision of the interceptor with the target missile. It provides especially useful data about the first instant of the hit, just as the two vehicles are beginning to touch. A short-lived flash at that moment reveals the signatures of the metals that are crashing together.

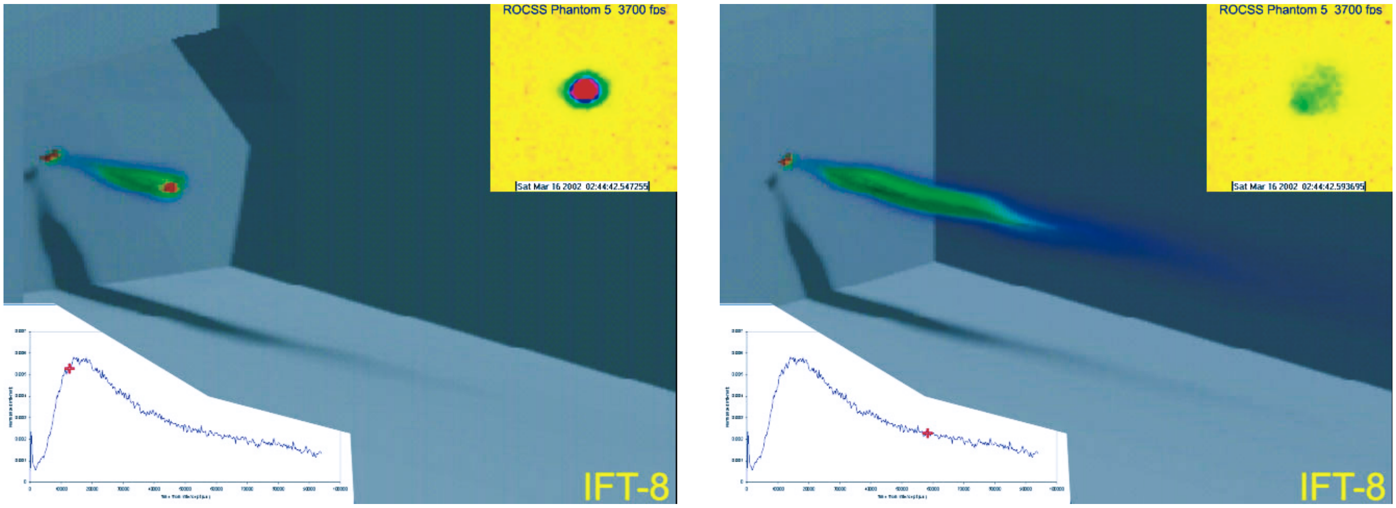
Radiometers operating in the visible, short-wavelength infrared, and mid-wavelength infrared spectral bands collect data on the temperature and intensity of the boost and the impact. A high-speed camera that captures 16,000 frames in 4 seconds records the evolution of the debris cloud created by the collision. A slower-speed videorecorder and another analog video system also record the collision.

Getting to the First Test Flight

The EGS was first applied to ballistic missile defense in September 1998. On the ground at the White Sands Proving Ground in New Mexico, the EGS successfully detected the exhaust chemicals from an Army Theater High Altitude Area



(a) The timeline shows events for the interceptor missile fired from Kwajalein in seconds after launch of the target missile (TALO) from Vandenberg Air Force Base. (b) During the boost of the interceptor rocket, the spectra for hydrogen chloride (HCl) are visible as the rocket comes into view, although light in the blue wavelengths is attenuated by atmospheric absorption. (c) Thirty-seven seconds later, with less atmospheric attenuation, HCl begins to dominate the spectrum. (d) Eleven seconds later, the practiced eye can see atmospheric methane absorption and a dense cloud of alumina particles from the rocket's exhaust. (e) Finally, as the missile turns, HCl again dominates the spectrum.



The high-speed camera captures 16,000 frames in 4 seconds from the moment that the kill vehicle collides with the reentry vehicle. The development of the "worm" of debris from the collision is shown in these two frames.

Defense (THAAD) rocket. The chemicals it detected, primarily hydrogen chloride, almost exactly matched the model for the rocket's exhaust materials. "We were quite pleased with that first test," says Pertica.

Numerous other tests from 1999 to 2001 were equally successful. One took place in Livermore's High Explosives Application Facility with an explosion designed to simulate an intercept. In June 2001, Livermore's ROCSS instrumentation was integrated into the HALO jet. In the first flight of the ROCSS instrumentation, HALO followed a rocket launched from Vandenberg Air Force Base to detect chemical effluents in the rocket's exhaust. In a similar test, the jet trailed an Atlas 3B rocket launched from Kennedy Space Center in Florida.

The first actual intercept test for ROCSS was Intercept Flight Test 8 (IFT-8) at Kwajalein in March 2002. During an 80-second period, from 1,308 to 1,388 seconds after launch of the target missile, the EGS data reveal first hydrogen chloride in the rocket's emissions as the interceptor comes into view, then increased hydrogen chloride as atmospheric attenuation lessens, and later, hydrogen chloride mixed with atmospheric methane and a dense exhaust of alumina particles. (See the figure at the bottom of p. 20.) In the final spectrum, the hydrogen chloride is clear again as the interceptor turns to expose its engine.

This spectral information can also indicate temperatures of the exhaust using the line intensities from the two isotopes of hydrogen chloride: hydrogen chloride-35 and hydrogen chloride-37. If the intercept involves an enemy missile, chemical and temperature data can be used as a diagnostic tool to determine the type incoming rocket.

"Also," adds Pertica, "if a rocket isn't performing as expected, temperature information is especially useful for indicating possible problems."

Images from the high-speed camera during the intercept reveal the growth of what Pertica calls a worm of debris. The worm begins its growth at the first instant of the kill vehicle's collision with the ballistic missile's reentry vehicle and continues to develop until the debris cloud dissipates.

What Lies Ahead

With that first flight test, Livermore completed the development phase of this project. The next phase is deployment, which is planned to continue through 2008 and IFT-26. The next flight test, IFT-9, is scheduled for late in 2002.

The ROCSS team plans to upgrade the EGS to include the full mid-wavelength infrared range, almost doubling its spectral coverage. This spectrometer and other ROCSS instrumentation may begin supporting future development tests of the new GMD booster, in addition to the intercept flight tests.

Pertica hopes to develop a broader capability for monitoring intercepts with instrumentation mounted either on satellites or flying along on the kill vehicle's booster rocket, paving the way for eventual kill assessment of intercepts from real enemy missiles.

—*Katie Walter*

Key Words: ballistic missile interceptor, Ground-Based Mid-Course Defense (GMD), high-altitude observatory (HALO), high-speed camera, infrared spectrometry, Remote Optical Characterization Sensor Suite (ROCSS).

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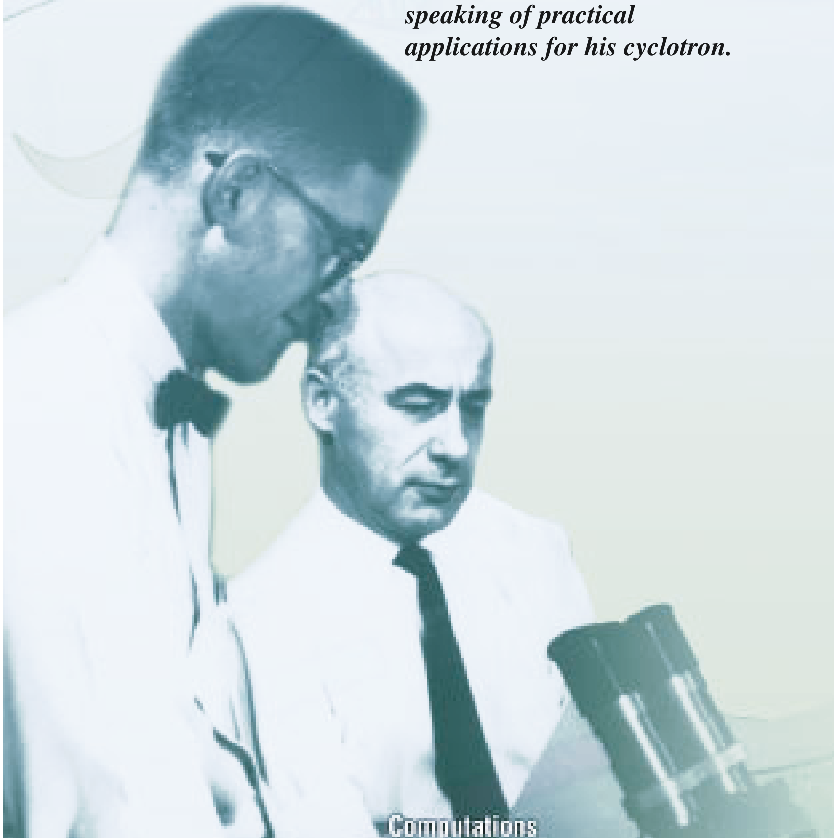
Biological Research Evolves at Livermore

"We count it as a privilege to do everything we can to assist our medical colleagues in the application of these new tools to the problems of human suffering."

—Ernest O. Lawrence, in his acceptance speech for the 1939 Nobel Prize for Physics, speaking of practical applications for his cyclotron.



As the Laboratory celebrates its 50th anniversary, its biological research program begins its 40th year. Established in May 1963 by the Atomic Energy Commission, the program's original mission was to investigate the effects of ionizing radiation on humans.

Today, Livermore's biological research extends far beyond studying the effects of radiation. A primary emphasis is countering the terrorist threat that grips our nation. The anthrax scares in the fall of 2001 alerted us to the danger of bioterrorism and heightened the need for fast, accurate, inexpensive methods to detect biological warfare agents. Fortunately, long before last fall, Livermore was a leader in developing innovative methods and technologies for early detection of bioterrorism threats. Since the attack, the Laboratory has intensified its efforts in this area so vital to national security.

Radiation effects and bioterrorism response have more in common than might at first be apparent. The link is DNA, the genetic code of all living things. Technologies developed during Livermore's studies of how radiation affects DNA contributed to the founding of the Human Genome Project, the largest biological research project ever undertaken. Since the working draft of the human genome was completed in 2000, the genomes of many other animals and microbes have been sequenced. Sequencing the DNA of bioagent microbes supplies the basis for DNA signatures that are being put to work in new detectors.

Livermore's early analysis of DNA damage has evolved into long-term research in several areas important to human health. Research on radiation exposure resulted in new assays that were first used to evaluate genetic changes in atom bomb survivors in Japan and later applied to understanding the exposures incurred by workers who cleaned up the Chernobyl nuclear power plant after the 1986 accident. Several of these tools have broad application in bioscience. Another research area focuses on how DNA repairs itself. One project analyzes the ways that damaged DNA affects sperm during critical stages of reproduction. Another examines how cooking certain foods produces chemicals that damage DNA. Along the way,

Livermore bioresearchers have pioneered many new tools and methods for bioscience research, often collaborating with physicists, chemists, engineers, and computer scientists.

In 1972, Roger Batzel, then Laboratory director, said, “I personally view Bio-Med as an area which could well grow. It’s been a relatively small program, but I think it could develop into one of the strengths of the Laboratory.”

Batzel could hardly imagine how dramatically Livermore’s nascent biomedical program would grow and change. The recent proposal to establish a homeland security center of excellence at Livermore owes much to the distinguished efforts over the years of many Livermore biological research scientists.

During the 1983 celebration of the 20th anniversary of biomedical research at Livermore, then Laboratory Director Roger Batzel, Associate Director Mort Mendelsohn, and former Program Director John Gofman viewed the work of bioscientist Laurie Gordon.

Of Chromosomes and DNA

Biological studies at Livermore have two major origins. One was the advent of thermonuclear testing in the Pacific Ocean during the mid-1950s. The other was Project Plowshare, which was devoted to the peaceful uses of nuclear weapons for stimulating underground natural gas production, mining, blasting out harbors, and perhaps even creating a new Panama Canal. Testing in the Pacific and in the Soviet Union had made radioactive fallout a major public issue. With Plowshare’s vision of nuclear explosions near populated areas for routine engineering tasks, nuclear contamination became a more direct concern.

John Gofman, a professor of medical physics at the Donner Laboratory of the University of California at Berkeley, was recruited to set up the new program. As it happened, Project Plowshare was largely shelved by the time Gofman started working. “But he studied the dose to humans anyway, with an emphasis on radiation safety,” says Mort Mendelsohn, who followed Gofman as leader of the biomedical research program.

By 1963, the scientific community suspected that DNA was the cellular part most sensitive to radiation damage. Gofman had already become involved in cytogenetics, the study of chromosomes, a field that was making major advances at the time. According to Mendelsohn, “Gofman wanted to measure chromosomes for a reason that was way ahead of its time.” Many researchers were growing cancer cells in culture, and Gofman suggested examining the chromosomes in these cells to see what changes they had in common. He developed a method of analyzing chromosomes by measuring their length. It proved to lack adequate sensitivity, but his work set the stage for future cytogenetics progress at Livermore.

In 1974, two years after Mendelsohn’s arrival, Livermore scientists made history when they successfully measured and sorted hamster chromosomes using flow cytometry. In humans and other complex organisms, DNA is packaged into chromosomes. Humans have 23 pairs, or 46 total. With flow cytometry, researchers could for the first time automatically

identify and sort individual chromosomes or whole cells for subsequent assessment.

During the 1970s and 1980s, the Laboratory made rapid advances in flow cytometry and was for many years a premier institution for cytometric research. In fact, Mendelsohn and other Livermore scientists founded the Society for Analytic Cytology, now the International Society for Analytic Cytology. The journal *Cytometry*, first issued in 1980, was published from Livermore for many years. More recently, Livermore engineers miniaturized flow cytometry in microfluidic systems that support medical devices and detectors for biological and chemical agents. (See *S&TR*, November 1999, pp. 10–16.)

By 1979, scientists had learned how to sort human chromosomes, which are much smaller and more varied than the hamster's. By 1984, says Mendelsohn, "We had increased our proficiency and confidence in flow cytometry such that we could separately identify and study each of the human chromosomes." This ability, combined with worldwide developments in recombinant DNA technology, led to the Livermore–Los Alamos project to build human chromosome-specific DNA libraries.

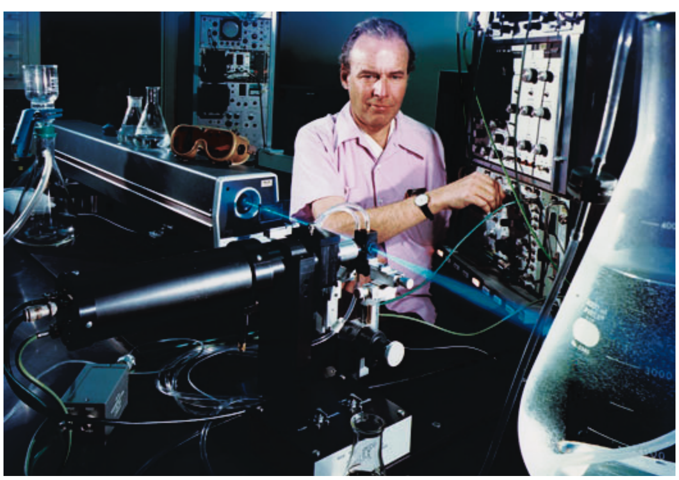
"The development of chromosome-specific libraries was important," continues Mendelsohn. "At that time, sequencing technology was slow and primitive. The thought of sequencing the entire human DNA was overwhelming. But when the sequencing process could be broken down into smaller pieces—chromosomes—it became a possibility."

At a 1984 meeting, molecular geneticists from around the world brainstormed the potential for DNA-oriented methods to detect heritable mutations in the children of people who survived the atom bombs in Japan. Many of the questions were so challenging that large-scale, detailed genomic sequence analysis would be needed to even attempt to answer them. (To this day, the basic question of how often heritable mutations occur remains unanswered.) Recognizing the classes of problems that require large-scale, detailed sequence data helped inspire the idea of sequencing the entire human genome.

In 1986, the Department of Energy launched a major initiative to completely decipher the human genetic code. A year later, Livermore researchers began to study chromosome 19, which they had earlier learned was home to several genes important for DNA repair. DOE joined forces with the National Institutes of Health in 1990 to kick off the Human Genome Project.

In 1992, Anthony Carrano became associate director of biomedical research. Carrano, who had been studying chromosomes and DNA since arriving at Livermore in 1973, was instrumental in building the Laboratory's human genome efforts, particularly sequencing. In 1996, he helped form the Joint Genome Institute (JGI). This collaboration of the Livermore, Berkeley, and Los Alamos national laboratories pooled resources to form a production facility to sequence human chromosomes 5, 16, and 19 for the international Human Genome Project.

During the 1990s, sequencing technologies matured, becoming ever more automated. Sequencing speed increased rapidly. A working draft of the three chromosomes was completed in April 2000, a year ahead of a greatly accelerated



Marv Van Dilla, an expert in flow cytometry, came to Livermore from Los Alamos in 1972. Shown here in 1973, Van Dilla was instrumental in establishing the Laboratory's preeminence in cytometric research. Livermore was the first to use flow cytometry to sort chromosomes.

Bioscientists Anthony Carrano, who later became associate director, and Larry Thompson in 1978. They had just developed a quick and efficient test to detect damage to genes. The test was based on a finding by Livermore scientists that there is a direct relationship between hard-to-spot gene mutations and an easily recognized process that occurs during cell division. Today, Thompson performs research on DNA repair processes.

schedule set just 18 months earlier. (See *S&TR*, April 2000, pp. 4–11.) This accomplishment was a major step toward understanding DNA and its functions and a significant contribution to the completion of draft sequences of the entire genome in June 2000.

Still Much to Learn

In the excitement over the completed sequence of the human genome, it is easy to forget that this step is just a prologue. The next step is to identify all of our genes and determine what they do and how they do it. Comparative genomics—in which the genomes of different species are compared—is helpful. Mouse DNA is useful because about 99 percent of a mouse's genes are similar to human genes. Comparing how these genes work in mice and how they are activated under different conditions tells us much about our own genes. A JGI team led by Livermore biologist Lisa Stubbs compared human chromosome 19 with similar sections of the mouse DNA to understand the functional significance of DNA sequences. (See *S&TR*, May 2001, pp. 12–20.) Stubbs notes, "Imagine taking human chromosomes, shattering them into pieces of varying lengths, and putting them back together in a different order. That's what mouse chromosomes look like." The Japanese pufferfish (fugu) has also been sequenced because its genome is a compact version of our own.

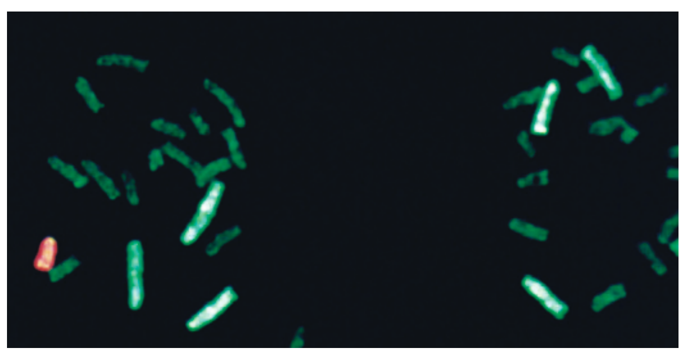
Another outgrowth of the Human Genome Project is proteomics, the study of the 100,000 or so proteins that are generated by our DNA. Proteins are the building blocks of our cells and of the molecular machinery that runs our tissues, organs, and bodies. Understanding how proteins operate is essential to understanding how biological systems work.

X-ray crystallography and nuclear magnetic resonance spectroscopy are two tools Livermore is using to determine the three-dimensional structure of proteins at the atomic level. From that structure, computational methods can attempt to model a protein's function. But determining the structure protein by protein would take years of research to complete. Instead, Livermore scientists are using the minimal data available in computational models to try to predict a protein's structure.

Measuring Radiation Effects

In the first 10 years of Livermore's biological research program, scientists searched for biological measurements that would indicate the radiological dose to which an individual had been exposed. Livermore developed several biological dosimeters to detect and measure changes in human cells,

Researcher Laura Chittenden is shown with a mouse. Mouse DNA, 99 percent of which is similar to human DNA, is being compared to human DNA to help uncover clues to gene regulation and control.



Chromosome painting is the process scientists use to fluorescently label small pieces of DNA from a chromosome-specific library. These chromosome-specific fluorescent probes bind to complementary sequences of the target chromosome and, when viewed under a microscope using fluorescent light, can reveal a targeted gene along a chromosome. This photo is of chromosomes from one-day-old mouse embryos. The bright green chromosomes are chromosomes 1, 2, 3, and X. The orange one is chromosome Y.

significantly advancing the study of human radiation biology and toxicology. The first was the glycophorin-A assay that detects residual mutations in human red blood cells from exposure to radiation decades earlier. Its first use was on atom bomb survivors in Japan.

Work on the glycophorin-A assay begat one of Livermore's first biotechnology projects. In the late 1970s, Laboratory biologists needed antibodies that recognize the subtle distinction between normal and mutant red blood cells. Researchers rolled up their sleeves and began to produce these and many other made-to-order monoclonal antibodies (antibodies derived from a single cell) with a range of potential uses—from detecting sickle cell anemia to evaluating how fast cancer cells are growing. Livermore is no longer in the production mode, but many of its monoclonal antibodies were commercially produced and used by others.

Another important technology developed at Livermore in the mid-1980s is chromosome painting. Scientist Dan Pinkel was instrumental in developing this technology, and the patent for this work has been one of the most lucrative in Livermore's patent portfolio for the past several years.

When first developed, chromosome painting was used to identify DNA damage in which the ends of two chromosomes break off and trade places with each other. These "reciprocal translocations" are one of the distinguishing effects of radiation damage to DNA. Using chromosome painting, scientists can see and count translocations between two differently painted chromosomes to determine a person's likely prior exposure to ionizing radiation. This method of identifying translocations is 10 to 100 times faster than it was before, with greatly increased reliability.

Biology Meets the Computer—The Early Days

Throughout its 50-year history, the Laboratory has pioneered the use of powerful computers to solve complex scientific problems. Challenges in biological research were no exception.

In the mid-1960s, new work on the dynamics of cell multiplication made use of computer codes first developed for Livermore's weapons program. Part of an effort to design an optimal radiation dosage program for cancer therapy, the study included an ingenious calculation system using computer codes to simulate cell activity.

A remarkable combination of an electron microscope and a computer in 1968 produced dramatic three-dimensional images of organelles, tiny working parts within the cell nucleus. Using essentially the same process the human brain uses to produce three-dimensional images from two flat pictures—one taken with each eye—the computer took 12 electron microscope shots, integrated the information, and created three-dimensional images of the organelles that were 50,000 times their real size. The feat had never before been accomplished.

By 1973, Livermore's cytophotometric data conversion system (CYDAC) was attracting interest when it showed that it could measure the DNA in individual chromosomes to great sensitivity. CYDAC studies showed unsuspected small differences in chromosomal DNA content among supposedly normal individuals.

In its first clinical application in 1974, CYDAC confirmed a suspected chromosome abnormality in a patient with chronic myelogenous leukemia (CML). In the early 1960s, scientists discovered that CML was invariably associated with a loss of genetic material from a portion of chromosome 22. This aberration was rarely found otherwise. About 10 years later, researchers at the University of Chicago found an excess of chromosomal matter on chromosome 9 in the same patients. They suspected that the lost material from chromosome 22 had been captured by chromosome 9. It took CYDAC's unprecedented precision to confirm that hypothesis and set cancer researchers on the track of other DNA translocations.

Bioengineers at Livermore combined mechanical skills with an understanding of biology to design the cytophotometric data converter (CYDAC), a highly sensitive diagnostic instrument that measures the amount of DNA in chromosomes. In this 1976 photograph, bioresearcher Linda Ashworth uses CYDAC to scan chromosomes from a mammalian cell.

A third dosimetry method measures the frequency of mutations in the hypoxanthine phosphoribosylantransferase (HPRT) gene in lymphocytes. This assay was developed elsewhere, but since the 1980s, researchers led by biological scientist Irene Jones have greatly expanded understanding of the assay's ability to detect DNA damage from ionizing radiation.

Immediately after the 1986 Chernobyl nuclear accident, the glycophorin-A assay was put to work to screen cleanup workers for their exposures. Years later, bioscientists used the HPRT assay and chromosome painting to measure mutations and alterations in lymphocytes to reconstruct the doses received. (See *S&TR*, September 1999, pp. 12–15.)

To Your Health

A natural extension of studying the effects of ionizing radiation on humans was to explore how radiation and chemicals interact with human genetic material to produce cancers, mutations, and other adverse effects.

In the face of damaging toxins, DNA is able to repair itself—up to a point. How DNA repairs itself has been a focus of ongoing research under bioscientist Larry Thompson almost since the Laboratory began to study DNA damage. Livermore chose to sequence chromosome 19 as part of the Human Genome Project because its properties suggested that it was gene-rich, which proved to be an accurate prediction. Chromosome 19 has the highest gene density of any human chromosome. It was also an apt choice because Livermore researchers had earlier discovered that three genes on chromosome 19 are involved in the repair of DNA damaged by radiation or chemicals. In studies of the Chernobyl cleanup workers, a goal has been to understand why the same dose of radiation has different effects on the cells of individuals. Identifying the differences in DNA repair gene sequence and function for different individuals is key.

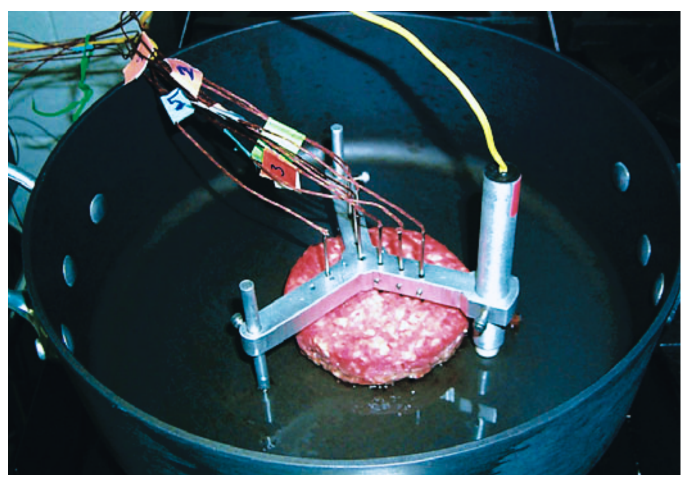
In the 1970s, Livermore's growing expertise in flow cytometry enabled researchers to analyze and sort sperm for the first time. Using this approach, scientists could begin to study the effects of pollutants on DNA during critical stages of sperm formation. Under the leadership of biophysicist Andrew Wyrobek, Livermore has developed several powerful molecular methods to visualize individual chromosomes in sperm and to detect genetic defects in embryos. (See *S&TR*, November/December 1995, pp. 6–19.) These research methods, combined with animal models, have broad implications for screening males for chromosomal abnormalities and genetic diseases, for studying the effects of exposure to mutagenic agents, and for assessing genetic risks to embryos and offspring.

Even the food we eat can damage our DNA. Both 2-amino-1-methyl-6-phenylimidazo [4,5-b] pyrinidine (PhIP) and 2-amino-3,8-dimethylimidazol [4,5-f] quinoxaline (MeIQx) are heterocyclic aromatic amines that appear in meat when it is cooked at high temperature. These compounds and others produced when they are digested form adducts, which are molecules that attach to DNA strands and may interfere with their function. Jim Felton, who is now deputy associate director for Biology and Biotechnology Research Program (BBRP), led a group studying food mutagens for almost two decades.

PhIP and MeIQx have been shown to cause cancer in laboratory animals when administered at high doses. More recently, researchers wanted to know whether DNA and protein adducts can be detected in laboratory animals and humans when they take in a smaller, more typical dietary amount of these substances. In numerous experiments using carbon-14-tagged PhIP and MeIQx molecules, the team has confirmed not only that adducts can be detected at low doses, but also that humans may be more sensitive to these substances than mice or rats.

Such experiments would not have been possible without Livermore's Center for Accelerated Mass Spectrometry. Physics-based accelerator mass spectrometry (AMS) is so sensitive that it can find one carbon-14 atom among a quadrillion other carbon atoms. It can observe the interaction of mutagens with DNA in the first step in carcinogenesis. Livermore is one of just a few institutions in the world using AMS routinely for biomedical and pharmaceutical applications, and it is a recognized leader in the field. (See *S&TR*, July/August 2000, pp. 12–19.)

Continuing a long tradition of collaboration with universities, Livermore joined forces with the University of California at Davis Cancer Center in October 2000 to fight



Meat cooked at high temperatures produces mutagens, which are compounds that can damage DNA. Here, a fully instrumented hamburger patty is fried to determine its temperature as a function of depth as well as the corresponding concentrations of food mutagens. The data are used to develop computer simulations of the cooking process and to predict the formation of mutagens.

cancer, the nation's second leading killer. Together, they are researching cancer biology, prevention, and control as well as new cancer detection and treatment techniques. In July 2002, the center attained National Cancer Center status from the National Cancer Institute. AMS is a key technology in this collaboration's research.

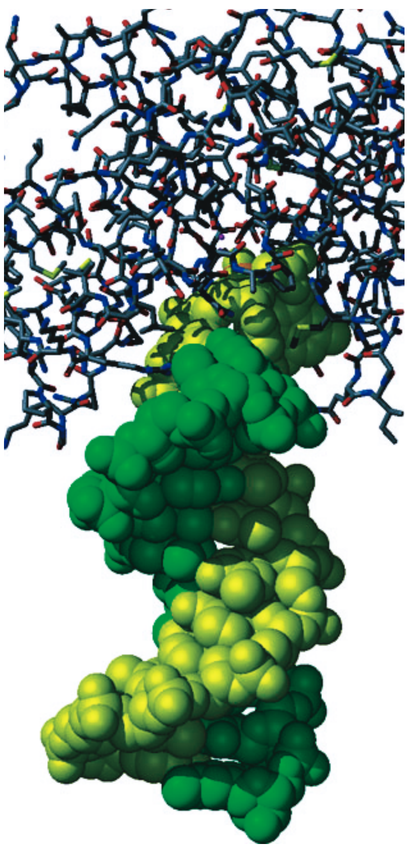
Putting the Computer to Work

Computers have played an integral role in biological research at Livermore for years (see the box on p. 26). In fact, the biomedical program was the first one at Livermore to purchase a personal computer for scientific use. The Procurement Department looked on this purchase with considerable suspicion, viewing a personal computer only as a means to play "Pong." But that little PC automated what had been a tedious manual cell-counting process, and it is impossible to imagine the Laboratory without desktop computers today.

Using both mainframe and personal computers, the Laboratory has pioneered many new ways to use the computer in a biological research setting. Bioinformatics is an area of special strength. In bioinformatics, computer scientists organize the results of molecular biologists' work, developing databases and new analytical tools so that the data can be put to good use. Livermore's leading role in the Human Genome Project would not have been possible without the efforts of BBRP's bioinformatics team. Computer scientist Tom Slezak started this group almost 25 years ago and still leads it.

"Our work is 'bottom of the iceberg' stuff and invisible to most people," says Slezak. "But it's really important. In sequencing the human genome, the flood of data was enormous. As other organisms are sequenced and as the field of comparative genomics takes off, we try to leverage our computational capabilities to stay a step or two ahead."

Computational biology, a relatively recent research area, builds on the Laboratory's strength in computations. According to Michael Colvin, who leads the Computational Biology Group at Livermore, "The emerging explanation of biological functions in terms of their underlying chemical processes is creating an important role for predictive chemical simulations in biological research."



This classical molecular dynamics simulation examines the motion of 1 of 10 proteins of *Escherichia coli* polymerase III, the major DNA replication enzyme in *E. coli* bacteria. This protein's function is to "proofread" a newly synthesized DNA strand by excising any incorrect bases immediately after they are added to the DNA. The goal of this simulation is to understand the chemical mechanism of the proofreading function. Shown as sticks is the proofreading protein. The yellow and green spheres simulate the double-stranded DNA being proofread.

The Handheld Advanced Nucleic Acid Analyzer can detect biological pathogens in the field. It examines the DNA of a sample and compares it with the known DNA sequence of various pathogens such as anthrax and plague. Rapid detection of agents of biological warfare could help save lives because the diseases resulting from many such pathogens are highly treatable if detected early.

Livermore scientists are at the forefront of integrating computation and experiment in bioscience. Ongoing computational biology projects include studying the action of anticancer drugs, DNA-binding properties of mutagens in food, the binding of ligands to selected sites on proteins, the mechanisms of DNA repair enzymes, and the biophysics of DNA base pairing. (See *S&TR*, April 2001, pp. 4–11.)

A particularly exciting tool in computational biology is first-principles quantum mechanics methods to describe the electronic structure of atoms and their chemical properties. Computerized quantum simulations permit researchers to "see" inside biochemical processes to learn how reactions are taking place on a molecular and even atomic level. Such simulations are highly intensive computationally and had to await the arrival of massively parallel computers before they could be performed. (See *S&TR*, April 2002, pp. 4–10.)

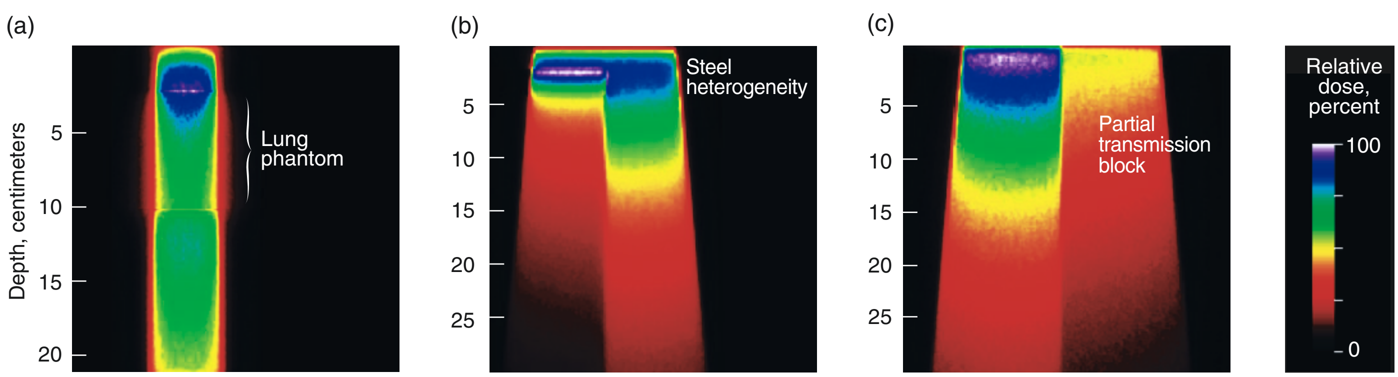
Fighting Bioterrorism

Bacteria, viruses, biological toxins, or genetically altered organisms could be used to threaten urban populations, destroy livestock, and wipe out crops. These agents are difficult to detect and to identify quickly and reliably. Yet, early detection and identification are crucial for minimizing their potentially catastrophic human and economic cost. At Livermore, developing technologies to detect agents of biological warfare has been under way for a decade. Livermore researchers pioneered technologies for rapid detection of tiny amounts of DNA. Equally important has been identifying specific DNA sequences that can be targeted with our detectors. With the recent anthrax attacks and the resulting awareness of bioterrorism threats, Livermore has stepped up its efforts to optimize stationary and portable equipment to detect biological agents.

The foundation for this research was laid during the early years of the program and studies of DNA. For example, by computationally comparing the DNA sequence of *Yersinia pestis*, the bacterium that causes bubonic plague, with the sequence of its close relatives and other bacteria, Livermore has been able to develop unique DNA signatures that allow *Yersinia* to be quickly detected. (See *S&TR*, May 2000, pp. 4–12.)

An entirely new sequencing analysis technique, developed by Livermore's bioinformatics team, recently won one of two 2002 Lawrence Livermore Science and Technology Awards. Using their experience from many years on the Human Genome Project, the team members found a novel way to perform whole genome analysis to compare genomic sequences. With it, they can rapidly determine unique DNA signatures of biowarfare pathogens. They are the first to apply whole genome analysis to pathogens.

Several DNA-detection technologies have been licensed to industry, most recently the Handheld Advanced Nucleic Acid Analyzer (HANAA). Some of these devices depend not only on accurate DNA signatures but also on microfluidics—the miniaturization of piping systems through which fluids flow. In a collaboration with Los Alamos National Laboratory, Livermore's DNA analysis capabilities were used to develop the analysis core of the Biological Aerosol Sentry and Information System, which was deployed at the 2002 Winter Olympics in Salt Lake City, Utah.



PEREGRINE is an innovative radiation planning technology developed at Livermore. Taken by the staff at the University of California at San Francisco, these images of PEREGRINE measurements demonstrate how effectively PEREGRINE can handle different materials and shapes, including (a) heterogeneous materials such as soft tissue and air in the lung, (b) a steel prosthesis, and (c) a partial transmission block that protects healthy tissue from radiation treatment.

Another technique for detecting biological agents focuses on detecting the proteins that DNA generates. Protein detection techniques are typically fast and easy to use but are not as sensitive and specific as DNA detection methods. Livermore is designing seek-and-destroy, antibodylike molecules, called high-affinity ligands, that target specific proteins in biological agents. The development of ligands for detecting tetanus toxin is almost complete. This detection methodology promises to be fast and easy to use as well as highly sensitive and specific. (See *S&TR*, June 2002, pp. 4–11.)

Physics to Biology

Many threads link physics advances and bioresearch progress. Ernest O. Lawrence, founder of the Laboratory, set the precedent for applying tools developed in the course of physics research to fighting human disease. After Lawrence built the cyclotron, he put it to use as a medical tool as quickly as he could. In 1937, Lawrence's mother Gunda was told by many specialists that she had an inoperable tumor. But her life was saved by radiation treatment with the only megavolt x rays then available in the world, using a device developed by her son. She was still living in Berkeley when he died 21 years later.

In this tradition, Livermore recently developed an innovative tool for analyzing and planning radiation treatment for tumors. In the early 1990s, researchers began combining Livermore's huge storehouse of data on nuclear science and radiation transport with Monte Carlo statistical techniques. The result was PEREGRINE, a radiation planning technology that has been licensed to a private company and was approved for use by the U.S. Food and Drug Administration in September 2000. (See *S&TR*, June 2001, pp. 24–25.)

Mrs. Lawrence's treatment and PEREGRINE bring the results of physics research to bear on a pressing medical challenge. Weapons materials have also been used in artificial hip joints designed at Livermore. X-ray tomography developed to examine the inner components of nuclear weapons has revealed the bone weakening of osteoporosis. Quantum simulations, a physics tool that can describe the fundamental interactions of weapons materials, are exposing the inner workings of biochemical processes important to human health. X-ray diffraction using synchrotron light sources, another physics tool, illuminates proteins to help define their function.

The next step in biological research will depend on another tool made possible by advanced physics research—even more powerful computers than are available today. "Where we're going next," says Bert Weinstein, acting associate director for BBRP, "is to understand the whole system of genes. Not just genes as individual parts but as an integrated, intermeshed set of molecular machines, working together to produce the miracle of life."

—*Katie Walter*

Key Words: accelerator mass spectrometry (AMS), biological warfare agent detectors, chromosome painting, comparative genomics, computational biology, DNA repair, dosimetry, flow cytometry, food mutagens, glycophorin-A assay, Human Genome Project, Joint Genome Institute (JGI), PEREGRINE, proteomics, sperm mutations.

For more information about Biology and Biotechnology Research Program Directorate:

www-bio.llnl.gov/

For details about the history of biology research at Livermore:

www-bbrp.llnl.gov/50_year_anniversary/

For frther information about the Laboratory's 50th anniversary celebrations:

www.llnl.gov/50th_anniv/

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

Patents

Compact Multiwavelength Transmitter Module for Multimode Fiber Optic Ribbon Cable

Robert J. Deri, Michael D. Pocha, Michael C. Larson, Henry E. Garrett
U.S. Patent 6,419,404 B1
July 16, 2002
A compact, multiwavelength transmitter module for multimode fiber-optic ribbon cable. The module couples light from an M × N array of emitters onto N fibers, where the M wavelength may be distributed across two or more vertical-cavity, surface-emitting laser (VCSEL) chips. It combines emitters and multiplexer into a compact package that is compatible with placement on a printed circuit board. A key feature of this invention is bringing together two emitter arrays fabricated on different substrates—each array designed for a different wavelength—into close physical proximity. Another key feature is to compactly and efficiently combine the light from two or more clusters of optical emitters, each in a different wavelength band, into a fiber ribbon.

Optical Coherence Tomography Guided Dental Drill

Luiz B. Da Silva, Bill W. Colston, Jr., Dale L. James
U.S. Patent 6,419,484 B1
July 16, 2002
A dental drill that has one or multiple single-mode fibers used for imaging in the vicinity of the drill tip. Imaging below the surface being drilled is valuable for minimizing damage to vital or normal tissue. Identifying the boundary between decayed and normal enamel (or dentine) would reduce the removal of viable tissue, and identifying the nerve before getting too close with the drill could prevent nerve damage. An improved dental treatment device results from surrounding a drill with several optical fibers that can be used by optical coherence domain reflectrometry to image several millimeters ahead of the ablation surface.

DNA Attachment to Support Structures

Rodney L. Balhorn, Christopher H. Barry
U.S. Patent 6,420,112 B2
July 16, 2002
Microscopic beads or other support structures are attached to nucleic acids (DNA) using a terminal transferase. The transferase adds labeled dideoxy nucleotide bases to the ends of linear strands of DNA. The labels, such as the antigens digoxigenin and biotin, bind to the antibody compounds or other appropriate complementary ligands that are bound to the microscopic beads or other support structures. The method does not require the synthesis of an oligonucleotide probe. The method can be used to tag or label DNA even when the DNA has an unknown sequence, has blunt ends, or is a very large fragment (for example, greater than 500,000 base pairs).

Flat Panel Display Using Ti–Cr–Al–O Thin Film

Alan F. Jankowski, Anthony P. Schmid
U.S. Patent 6,420,826 B1
July 16, 2002
Thin films of titanium–chromium–aluminum–oxygen (Ti–Cr–Al–O) are used as a resistor material. The films are radiofrequency-sputter-deposited from ceramic targets using a reactive working gas mixture of argon and oxygen. Resistivity values from 10 thousand to 10 billion ohm-centimeters have been measured for Ti–Cr–Al–O film less than 1 micrometer thick. The film resistivity can be discretely selected through control of the target composition and the deposition parameters. The application of Ti–Cr–Al–O as a thin-film resistor has been found to be thermodynamically stable, unlike other metal-oxide films. The Ti–Cr–Al–O film can be used as a vertical or lateral resistor, for example, as a layer beneath a field emission cathode in a flat-panel display, or used to control surface emissivity, for example, as a coating on an insulating material such as vertical wall supports in flat-panel displays.

Constant Volume Gas Cell Optical Phase-Shifter

Donald W. Phillion
U.S. Patent 6,421,130 B1
July 16, 2002
A constant-volume gas-cell optical phase shifter, particularly applicable for phase-shifting interferometry, contains a sealed volume of atmospheric gas at a pressure somewhat different from atmospheric. An optical window is present at each end of the cell, and as the length of the cell is changed, the optical path length of a laser beam traversing the cell changes. The cell comprises movable coaxial tubes with seals and a volume-equalizing opening. Because the cell is constant volume, the pressure, temperature, and density of the contained gas do not change as the cell changes length. This produces an exactly linear relationship between the change in the length of the gas cell and the change in optical phase of the laser beam traversing it. Because the refractive index difference between the gas inside and the atmosphere outside is much the same, a large motion is needed to change the optical phase by the small fraction of a wavelength required for phase-shifting interferometry. This motion can be made to great fractional accuracy.

Compact, Flexible, Frequency Agile Parametric Wavelength Converter

Stephan P. Velsko, Steven T. Yang
U.S. Patent 6,421,166 B1
July 16, 2002
This improved frequency agile optical parametric oscillator (FA-OPO) provides near on-axis pumping of a single quasi-phase-matched crystal with a tilted, periodically poled grating so that finding a particular crystal that will permit collinear birefringence is not necessary for obtaining a desired tuning range. A tilted grating design and the elongation of the transverse profile of the pump beam in the angle tuning plane of the FA-OPO reduces the rate of change of the overlap between the pumped volume in the crystal and the resonated and nonresonated wave mode volumes as the pump beam angle is changed. A folded mirror set relays the pivot point for beam steering from a beam deflector to the center of the FA-OPO crystal. This setup reduces the footprint of the device by as much as a factor of two over that obtained when using the refractive telescope design.

High-Speed Pulse-Shape Generator, Pulse Multiplexer

Scott C. Burkhart
U.S. Patent 6,421,390 B1
July 16, 2002
The invention combines arbitrary amplitude high-speed pulses for precision pulse shaping for the National Ignition Facility (NIF). The circuitry combines arbitrary height pulses that are generated by replicating scaled versions of a trigger pulse and summing them delayed in time on a pulse line. The combined electrical pulses are connected to an electrooptic modulator that modulates a laser beam.

The circuit can also be adapted to combine multiple channels of high-speed data into a single train of electrical pulses that generate the optical pulses for very high-speed optical communication. The invention has application in laser pulse shaping for inertial confinement fusion, in optical data links for computers and telecommunications, and in laser pulse shaping for atomic excitation studies. It also can be used to effect at least a 10-fold increase in all fiber communication lines and allows a greatly increased data transfer rate between high-performance computers. The invention is inexpensive enough to bring high-speed video and data services to homes through a supermodem.

Amplification of Chromosomal DNA In Situ

Allen T. Christian, Matthew A. Coleman, James D. Tucker
U.S. Patent 6,432,650 B1
August 13, 2002
Method for amplifying chromosomal DNA in situ to increase the amount of DNA associated with a chromosome or chromosome region. The amplification of chromosomal DNA in situ provides for the synthesis of fluorescence in situ hybridization painting probes from single dissected chromosome fragments, the production of cDNA libraries from low-copy mRNAs, and the improvement of comparative genomic hybridization procedures.

Metals Removal from Spent Salts

Peter C. Hsu, Erica H. Von Holtz, David L. Hipple, Leslie J. Summers, William A. Brummond, Martyn G. Adamson
U.S. Patent 6,436,358 B1
August 20, 2002
A method and apparatus for removing metal contaminants from the spent salt of a molten salt oxidation reactor. Spent salt is removed from the reactor and analyzed to determine the contaminants present and the carbonate concentration. The salt is dissolved in water, and one or more reagents may be added to precipitate the metal oxide and/or metal as metal oxide, metal hydroxide, or salt. The precipitated materials are filtered, dried, and packaged for disposal as waste or can be immobilized as ceramic pellets. More than about 90 percent of the metals and mineral residues (ashes) present are removed by filtration. After filtration, salt solutions having a carbonate concentration of greater than 20 percent can be spray-dried and returned to the reactor for reuse. Salt solutions containing a carbonate concentration of less than 20 percent require further cleanup using an ion exchange column, which yields salt solutions that contain less than 10 parts per million of contaminants.

Awards

Secretary of Energy Spencer Abraham has announced the seven winners of the **E. O. Lawrence Award**. The winners from Lawrence Livermore are **Bruce T. Goodwin** and **Benjamin D. Santer**.

Other winners are Jeffrey Brinker of Sandia National Laboratories and the University of New Mexico at Albuquerque; Claire M. Fraser, the Institute for Genomic Research, Rockville, Maryland; Keith O. Hodgson, Stanford University and the Stanford Linear Accelerator Center, Stanford, California; Saul Perlmutter, Lawrence Berkeley National Laboratory, Berkeley, California; and Paul J. Turinsky, North Carolina State University at Raleigh.

Goodwin receives the award in the national security category for his research on the complex dynamics of the fission triggers of thermonuclear weapons. He is associate director for Defense and Nuclear Technologies at the Laboratory.

Santer is honored in the environmental science and technology category for his contributions to understanding the effects of human activities on Earth's climate. He is a physicist in the Laboratory's Energy and Environment Directorate.

The E. O. Lawrence Award was established in 1959 to honor the inventor of the cyclotron particle accelerator, winner of the 1939 Nobel Prize for Physics, and founder of both Lawrence Livermore and Lawrence Berkeley national laboratories.

The award is given for outstanding contributions in the general field of atomic energy in seven categories—chemistry, biology, national security, materials research, life sciences, physics, environmental science and technology, and nuclear technology.

Each winner received a gold medal, a citation, and $25,000 at a ceremony in Washington, D.C., on October 28, 2002.

This Model Can Take the Heat

A Livermore–Los Alamos team is developing a computer simulation system that can accurately predict wildfire behavior based on existing weather conditions, types of vegetation, and terrain. The team's goal is to help emergency response managers to plan for fires, anticipate where and how quickly an existing fire will spread, and evaluate the effectiveness of alternative firefighting strategies. With this program, fire managers could use their limited resources much more effectively, thereby saving lives, property, and irreplaceable resources. The program combines a physics-based wildfire model developed at Los Alamos with the extensive emergency response capabilities of the National Atmospheric Release Advisory Center at Livermore, including its weather prediction and smoke transport codes. The team has been validating the program by simulating well-documented wildfires. An early simulation successfully re-created a wildfire that occurred in Calabasas, near Malibu, California, in 1996. A more exhaustive validation of the program's capabilities has been to reconstruct the first half-hour of the catastrophic 1991 fire in the hills of Oakland and Berkeley, California.

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The Best and the Brightest Come to Livermore

Livermore's prestigious Lawrence Fellowship Program recently completed its fourth year with 15 fellows having been selected from among 1,849 applicants. The fellows' specialties run the gamut from mechanical engineering theory to advanced microscopy, sensors, plasma physics, theoretical biology, Monte Carlo simulations, materials science, and theoretical biophysics. Two more fellows recently began their three-year tenure. The Lawrence program has numerous advantages for both its fellows and the Laboratory. Fellows enjoy a great deal of freedom in their choice of research areas. They can pursue the latest advances in their field and be mentored by internationally recognized senior staff scientists. Or they can choose to do research in a new and different area where Livermore excels. The Laboratory benefits by attracting promising young scientists from around the world, whether they become one of the few Lawrence fellows, accept one of the many other fellowship opportunities available at Livermore, or become a full-time employee.

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Livermore Begins Its Next 50 Years

Multidisciplinary teams are finding innovative solutions to support the near- and long-term needs of Livermore's national security mission, from stockpile stewardship to homeland security.

Also in December

- ***The ability to control molecules could lead to new microdevices.***
- ***Laser technology is meeting long-distance communication needs at gigabit rates.***

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