Science & Technology REVIEW

March 2002

National Nuclear Security Administration's
Lawrence Livermore National Laboratory

Studying Plague to Understand Virulence

Also in this issue:

- New Decontaminant for Chemical and Biological Agents
- Faster Technique for Inspecting Laser Glass
- 50th Anniversary Highlight: Achievements in Computation

Lawrence Livermore National Laboratory

Making History Making a Difference

1952-2002

About the Cover

The flea is a host to plague bacteria (shown in background) and helps transmit the disease. Under the auspices of the National Nuclear Security Administration's (NNSA's) Chemical and Biological National Security Program, researchers at Livermore and other NNSA laboratories are investigating what causes virulence in *Yersinia pestis*—the plague bacterium. The article beginning on p. 4 describes how the researchers are studying plague as a prototype for pathogenic agents that could be used in biological terrorism. Research is also continuing on DNA signatures that can be used to quickly detect and identify plague outbreaks.

Cover design: Lew Reed

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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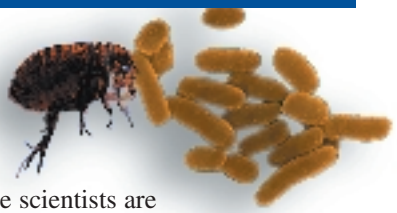

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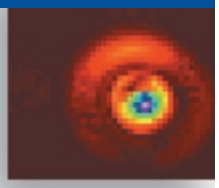

50th Anniversary Highlight

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Faster detection of salmonella

Biomedical scientists Peter Agron and Gary Andersen have developed a DNA-based detection system for identifying the presence of the salmonella pathogen, a major cause of food poisoning in humans. In a paper published in November 2001 in *Applied & Environmental Microbiology*, Agron and Andersen described their work to develop a DNA signature that will cut down the time usually taken to identify *Salmonella enteritidis*—the strain that causes bacterial infections—from as long as 2 weeks to as short as 2 hours.

During a year-long research effort, Agron and Andersen identified unique segments of DNA in *S. enteritidis*. They used a technique called suppression subtractive hybridization to compare the DNA of similar strains of *Salmonella* and determine what fragments of the DNA of *enteritidis* were unique and therefore the basis of its signature. Then they designed primers, or DNA markers, of the unique *enteritidis* regions. The primers were replicated many times using the polymerase chain reaction, and the replicated regions were processed to identify and characterize *S. enteritidis* unambiguously.

Coauthoring the journal article with Agron and Andersen were Jessica Wollard, also of Lawrence Livermore; Richard Walker, Sherilyn Sawyer, and Dawn Hayes of the California Animal Health and Food Safety Laboratory in Davis, California; and Hailu Kinde of the California Animal Health and Food Safety Laboratory in San Bernardino, California.

Contact: Peter Agron (925) 423-1284 (agron1@llnl.gov) or Gary Andersen (925) 423-2525 (andersen2@llnl.gov).

Need for explosives simulants increases

A California company with ties to the Laboratory predicts that its business will grow as a result of the September 11 attacks.

Van Aiken International, located outside Los Angeles, expects that the need to train more dogs to detect explosives and the increased screening of airline baggage for explosives will put a high demand on the explosives simulants that it is manufacturing under license from Lawrence Livermore.

Some 6 years ago, researchers at Livermore began developing high-explosive simulants, primarily to train bomb-sniffing dogs in real-life situations without posing a hazard. John Kury, project leader of the program, said that he and his team were trying to develop a full suite of simulants to match commercial explosives, gunpowders, and plastic explosives similar to those used to down the Pan Am flight over Lockerbie, Scotland.

Kury said that the simulant developed at the Laboratory contains just 8 percent of explosive, has passed all Department of Transportation tests, and is not classified as hazardous. It can be detected by trained dogs, and it looks like an explosive to an x-ray machine because it has the same density and average atomic number as real explosives.

Contact: John Kury (925) 422-6311.

Volcanic eruptions affected global temperature

Satellite measurements of temperature, which began to be collected in 1979, have shown little or no warming in the lower troposphere. These data have been cited to support skepticism of global warming. But recent research by atmospheric scientists has explained the apparent difference in warming rates at Earth's surface and in its lower troposphere.

In a paper published in November 2001 in the *Journal of Geophysical Research–Atmospheres*, these scientists presented their discovery that large volcanic eruptions cooled Earth's lower troposphere more than the surface and likely masked the actual warming of the troposphere.

The conclusion is presented in "Accounting for the Effects of Volcanoes and ENSO in Comparisons of Modeled and Observed Temperature Trends." The work was performed by Laboratory researchers Benjamin Santer, Charles Doutriaux, James Boyle, Sailes Sengupta, and Karl Taylor, who teamed with scientists from the National Center for Atmosphere Research; National Aeronautics and Space Administration/Goddard Institute for Space Studies; the Climatic Research Unit at the University of East Anglia, United Kingdom; and the Max Planck Institute for Meteorology, Germany.

The scientists used a statistical procedure to quantify the volcanic influences on surface and tropospheric temperatures. To do so, they also had to separate out the effects of El Niño events, which coincided with both of the eruptions they were studying—El Chichón in Mexico in 1982 and Mount Pinatubo in the Philippines in 1991.

"Our recent work shows that some of the differences between warming rates at the Earth's surface and in the lower troposphere are due to the effects of volcanic eruptions and stratospheric ozone depletion," said Santer, the lead author. "Both of these factors probably cooled the lower troposphere by more than the surface, for physical reasons that are well understood. Without ozone depletion and the recent eruptions of El Chichón and Pinatubo, it is highly likely that the lower troposphere would have warmed over the last two decades." These conclusions were reinforced by results from numerical models of the climate system.

Contact: Benjamin Santer (santer1@llnl.gov).

Counterterrorism Is One Part of the Threat Reduction Picture

SINCE the terrorist attacks of September 11, 2001, the news has been filled with stories about the events and their aftermath. Many of the stories have focused on what the U.S. government is doing to combat terrorism and ensure homeland security. And much of what the government is doing is made possible by Lawrence Livermore and its sister national security laboratories.

National security rests on two important actions: reducing threats by stemming and countering the proliferation of weapons of mass destruction, and deterring aggression against the U.S. through diplomacy, treaties, and military strength.

Threat reduction is an extremely complex challenge. It entails preventing the proliferation of weapons of mass destruction, most critically by keeping weapons-usable nuclear materials out of the hands of potential proliferants and terrorists. It also involves myriad efforts to detect proliferation-related activities and to counter them through diplomatic or military channels. Furthermore, threat reduction requires capabilities to defend against the new breed of terrorist, bent on causing widespread destruction and mass casualties without regard to personal preservation. The proliferation and terrorism threats are highly interconnected and must be addressed through an integrated program that tackles the threats in all of their various guises, stages, and aspects.

At Livermore, our threat reduction activities are conducted under the aegis of the Nonproliferation, Arms Control, and International Security (NAI) Directorate. Each of the four divisions in NAI focuses on a different stage of the threat reduction problem. The Proliferation Prevention and Arms Control (PPAC) Program addresses the front end of threat reduction, with particular emphasis on providing assistance to the former Soviet Union to improve the security of its vast stocks of weapons-usable nuclear materials. The Proliferation Detection and Defense Systems Program (Q Division) develops technologies to remotely detect proliferation activities and tools to assess options to reverse those activities. The Counterterrorism and Incident Response Program (R Division) devises new instruments and procedures for responding to and minimizing the effects of nuclear, chemical, or biological terrorism. NAI's International Assessments Program (Z Division) conducts all-source assessments related to the weapons capabilities, intentions, and motivations of other countries and subnational groups.

Two articles in this issue highlight projects focused on the response phase of threat reduction. The article beginning on p. 4 describes research to elucidate the genome of the various strains of *Yersinia pestis*, the pathogen that causes plague, and uncover the mechanism of its virulence. Building on the Laboratory's expertise in DNA sequencing, the researchers are searching for the DNA signatures that are unique to *Y. pestis* (but not any close relatives, such as *Y. pseudotuberculosis*), yet are found in every one of its thousand-some strains. This work is conducted for the National Nuclear Security Administration's Chemical and Biological National Security Program and its thrust in biofoundations.

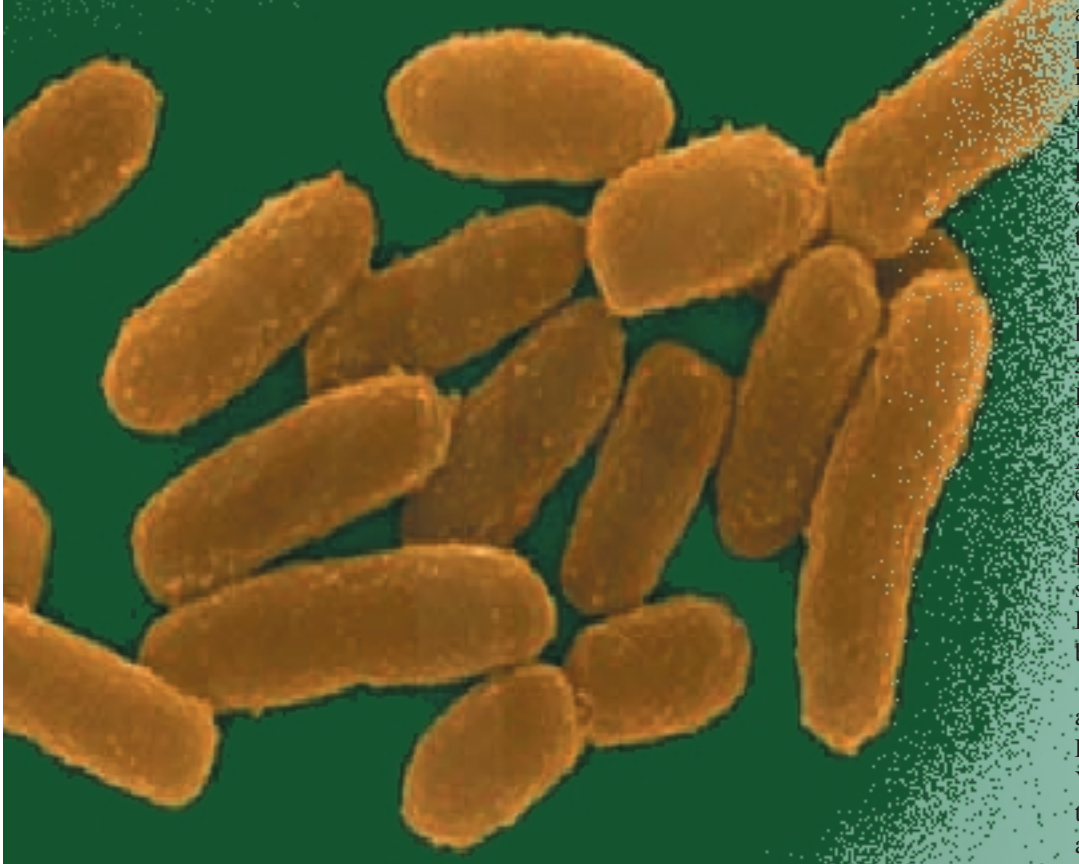
The article beginning on p. 10 summarizes work to develop an easy-to-use reagent for detoxifying or degrading chemical and biological warfare agents. The Livermore reagent, called L-Gel, has demonstrated its effectiveness in laboratory and field tests, and testing by analytical laboratories certified by the California Environmental Protection Agency has shown that the residual materials resulting from L-Gel decontamination are nonhazardous. L-Gel technology is being transferred to private industry, and commercial product should be available within the year.

The fact that Livermore has been able to provide advanced technology and expert assistance to the recently declared war on terrorism is testament to the importance of our threat reduction activities. Researchers in NAI have had the foresight to prepare for the "catastrophic maybe" of terrorism practiced with weapons of mass destruction. The war against terrorism will be fought for many years; indeed, it will likely never completely end. Thus, homeland security and counterterrorism are enduring national security missions, and Livermore's threat reduction activities will be even more critical in the years to come.

■ Wayne Shotts is associate director for Nonproliferation, Arms Control, and International Security.

Tracking Down Virulence in Plague

How do the plague pathogen and its host interact? Scientists will apply the answer to understanding a larger set of possible agents of biological terrorism.



PLAGUE is potentially a deadly agent of bioterrorism. Unlike anthrax, which has been so much in the news lately, plague is highly infectious and can be readily passed from one person to another. The bite of a plague-infected flea or the inhalation of just a few cells of plague bacterium can kill. Like smallpox, plague can spread and kill large numbers of people very quickly. Fortunately, it can usually be treated with antibiotics.

History tells us how devastating a plague epidemic can be. In what is known as the Justinian epidemic, from 540 to 590 AD, plague spread from Lower Egypt to Alexandria to Palestine and on to the Middle East and Asia. At its peak, 10,000 deaths occurred every day in Byzantium. Eight hundred years later, in 1347, plague came to Italy from Asia or Africa, probably by ship. By 1351, fully one-third of Europe's population had died from bubonic plague.

This European epidemic is known as the Black Death or the Great Pestilence. In 1894, when Andre Yersin identified the tiny bacterium that causes plague, he named it *pestis* after the Great Pestilence. He tried to

name the genus *Pasteurella* after his mentor, Louis Pasteur. But *Yersinia*, after its discoverer, is the name that stuck.

Today, *Yersinia pestis* is one of several infectious diseases and agents of bioterrorism that researchers across the Department of Energy complex are studying as part of the Chemical and Biological National Security Program. This program comes under the purview of DOE's National Nuclear Security Administration (NNSA). At Livermore, the work on *Y. pestis* also receives support from Laboratory Directed Research and Development.

Scientists at Livermore have developed DNA signatures for *Y. pestis* that can be used to quickly detect and identify plague outbreaks. (See "Uncovering Bioterrorism," *S&TR*, May 2000, pp. 4–12.) Signatures for nine strains of the disease have been submitted to the Centers for Disease Control and Prevention in Atlanta, Georgia, where they are undergoing a rigorous validation process.

Livermore's DNA-based detection method proved its mettle in northern Arizona last June when it was used to identify a plague outbreak in prairie dogs in just four hours. Standard detection processes, which require growing the suspected bacteria in a laboratory, take 36 to 48 hours.

For a plague detector to be truly effective, it must do more than simply indicate the presence of a specific organism known to cause plague, says Pat Fitch, who leads Livermore's Chemical and Biological National Security Program. The detector also must be able to identify the specific traits found in atypical plague-causing organisms. Scientists know of several hundred strains (or isolates) of *Y. pestis*, and they do not all behave in precisely the same way. A few strains are believed to have been genetically modified or engineered to be more deadly. There have also been two clinical cases of naturally occurring antibiotic-resistant plague. Knowing the precise identity of a strain of plague—or of any infectious disease, for that matter—could help physicians treat a patient properly.

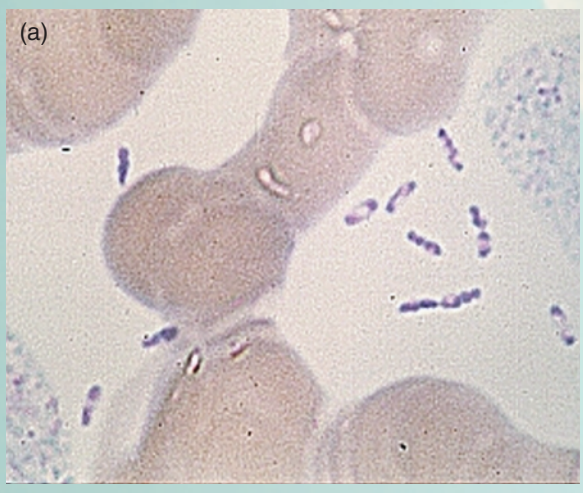
Plague research at Livermore currently is focusing on what makes *Y. pestis* so virulent and able to overcome the defenses of a host organism. Fitch is leading the Pathogen Pathway Project, using plague as a prototype for the functional genomics of a larger set of pathogenic agents that could be used in biological terrorism. (See the box on p. 6 for more information on functional genomics.)

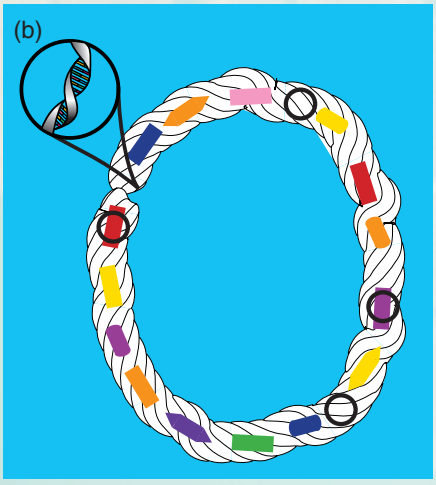
Besides building better detectors, work on the *Y. pestis* genome will also lead to a better understanding of pathogenicity and better vaccines and treatments for the disease. The ultimate goal, says Fitch, "is to produce a computer model that simulates the workings of a cell so that we can better manage exposure to pathogens."

Plague as Prototype

The highly contagious *Y. pestis* is an excellent model for studying the interactions of a pathogen and its host. In the case of *Y. pestis*, the host may be a flea, a rodent, or a human. Fleas carry plague bacteria and help transmit the disease. Once an infected flea bites a rodent or human, the bacteria begin to multiply in the new host, and their virulence shifts into high gear. *Y. pestis* circumvents the host's defenses by injecting into host cells a series of virulence factors that inhibit the response of the immune system.

Earlier research has shown that when *Y. pestis* is grown at the body temperature of a flea (26°C), its cells divide, but it does not express (turn on) many of the genes that make it virulent in rodents and humans. When the





(a) *Yersinia pestis*, which causes plague, is a pathogen likely to be used by terrorists. (b) Its DNA forms loops, unlike human DNA, which forms strands. Scientists studying it screen between two to five million of its nucleic acid bases to find unique regions (circled). Using polymerase chain reaction technology, the unique regions can be amplified thousands of times and processed to identify and characterize *Y. pestis*.

temperature increases to 37°C (human or rodent body temperature), the bacterium begins to produce the proteins essential to its virulence. This virulence mechanism can be induced in the laboratory, making plague relatively easy to study.

Examination of the *Y. pestis* genome before and after virulence has been induced shows what genes have been turned on. But that information is not enough to show precisely which genes are responsible for various aspects of virulence.

For comparative purposes, a Livermore team led by microbiologist Emilio Garcia collaborated with the Institut Pasteur in France to sequence *Y. pseudotuberculosis*, the parent organism of *Y. pestis*. Although their DNA sequences are about 95 percent identical, *Y. pestis* and *Y. pseudotuberculosis* behave differently. *Y. pseudotuberculosis* lodges in the intestine and causes flulike intestinal distress. *Y. pestis* is also closely related to the mild-mannered *Y. enterocolitica*, an intestinal bug that is itself very much like *Y. pseudotuberculosis*. *Y. enterocolitica* is currently being sequenced by the Sanger Center in Great Britain.

"Bacteria evolve very efficiently and make use of about 80 percent of their DNA," says Fitch. By comparison, humans use only about 30 percent of their DNA. Aiding speedy evolution are the many insertion sequences in a bacterial genome. Insertion sequences are bits of DNA that allow large regions of DNA to replicate themselves and move around the genome, relocating themselves somewhere else. When an insertion sequence lands within a gene, it deactivates that gene. These transfers can also occur across species, and it is not difficult for a bacterium to grab DNA from another bacterium.

Y. pestis evolved from *Y. pseudotuberculosis* within the past 15,000 years, a rapid evolution even for bacteria. "Something happened then to cause *Y. pestis* to learn how to live in a flea," says Garcia.

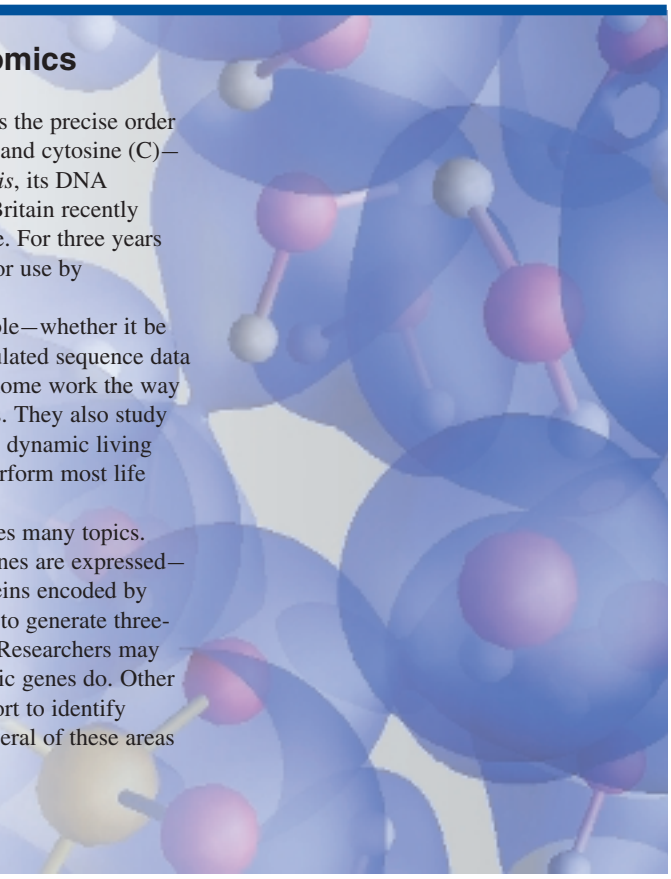
In addition to their normal chromosomal DNA, bacteria may have smaller circles of DNA known as plasmids. Plasmids replicate separately from chromosomal DNA and often

From Sequencing to Functional Genomics

DNA decoding, known as sequencing, is the process that determines the precise order of the four nucleic acid bases—adenine (A), thymine (T), guanine (G), and cytosine (C)—that comprise the DNA of all living things. In the case of *Yersinia pestis*, its DNA sequence comprises 4.66 million bases. The Sanger Institute in Great Britain recently published the complete and annotated sequence of the *Y. pestis* genome. For three years before that, a preliminary version of the sequence had been available for use by researchers throughout the world.

As the DNA genome, or parts list, for an organism becomes available—whether it be for plague, mice, or humans—researchers begin to examine the accumulated sequence data very closely. They are trying to identify what makes this particular genome work the way it does—its wiring diagram, so to speak. They search for specific genes. They also study how DNA works with proteins and the environment to create complex, dynamic living systems. Proteins are large molecules composed of amino acids that perform most life functions and make up the majority of cellular structures.

Functional genomics, as this field of research is known, encompasses many topics. Some researchers examine when, where, and under what conditions genes are expressed—that is, turned on. Others study the expression and function of the proteins encoded by certain genes. Still others use x-ray crystallography and other methods to generate three-dimensional structures of proteins, which offer clues to their function. Researchers may inactivate or knock out genes and study the results to learn what specific genes do. Other researchers compare the DNA sequence of several organisms in an effort to identify unique genes and interpret their function. Research is under way in several of these areas as Livermore examines what makes *Y. pestis* so virulent.



house genes that encode enzymes critical to the host cell or organism. For example, when a bacterium has become resistant to antibiotic drugs, it is usually because the bacterium has acquired a new plasmid.

One *Y. pestis* plasmid encodes at least two genes that allow *Y. pestis* to survive in fleas. Another plasmid is home to the gene that activates the disease's invasiveness. Researchers have found that *Salmonella* has a similar plasmid, which one bacterium probably obtained from the other.

"The interesting thing is that if you insert the three *pestis* plasmids into *Y. pseudotuberculosis* or *Y. enterocolitica*, you don't get *pestis*," says Garcia. "So something else is going on. Unfortunately, it's never simple."

Once its virulence genes have been turned on, plague infects its host using what is known as Type III secretion, an injection mechanism more colorfully called "*Yersinia's* deadly kiss." *Salmonella typhi*, enteropathogenic *Escherichia coli*, *Chlamydia psittaci*, various species of *Bordetella*, and other pathogenic bacteria appear to share this syringelike injection mechanism. This common trait may indicate another area of transferred genomic material.

Before Livermore's research on plague started, many of the genes critical for virulence had been identified but were poorly understood. The same was true for the underlying mechanisms of virulence. There was also little understanding of the gene and protein interactions that take place between the pathogenic bacteria and its host.

The Pathogen Pathway Project is using functional genomics tools to identify genes important to virulence and understand the pathways of virulence. The team's hypothesized pathway, from DNA to the host organism, is shown in the bottom figure at right.

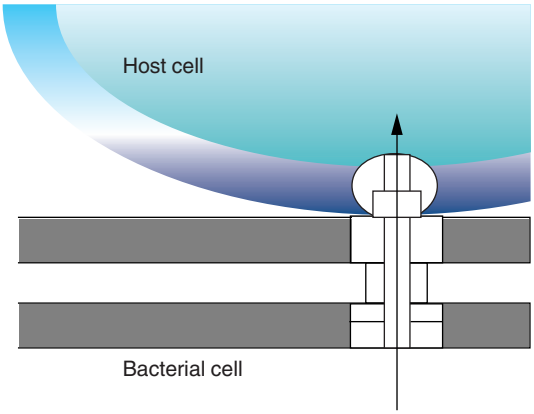
Expression and Function

An early task for Livermore bioscientists and computations experts was to develop a relational database of the DNA sequence of *Y. pestis*. In collaboration with the DOE Genome Consortium at Oak Ridge National Laboratory, these data were used to computationally predict where the 4,500 genes in *Y. pestis* are located and which genes might be associated with virulence.

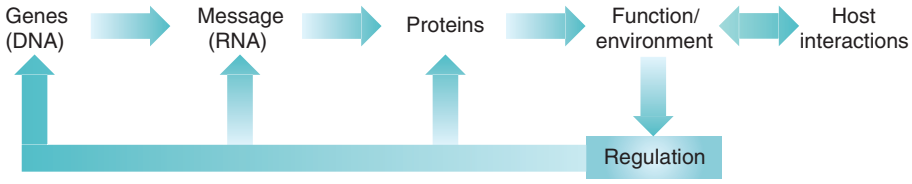
Next, Livermore bioscientist Vladimir Motin and colleagues designed chemical reagents for extracting over 300 genes from *Y. pestis* DNA, including all known virulence-associated genes on the plasmids. In an initial test, they extracted 85 genes associated with virulence and spotted them on a glass microscope slide alongside 11 control spots, making up a 96-spot microarray.

A microarray permits scientists to study the response of thousands of genes or other pieces of DNA quickly and efficiently in a process known as transcript profiling. In the process, each gene receives some kind of stimulus, causing it to turn on and produce messenger RNA (mRNA). In the case of plague, the stimuli are changes in temperature and calcium concentration. The production of mRNA leads, in turn, to the synthesis of unique proteins. The level of mRNA can be measured for each individual gene. The more active or expressed genes there are, the more mRNA will be present.

For the 96-spot microarray, the team developed a protocol to study the response of *Y. pestis* genes under conditions that mimic the infection process: at both flea and human/rodent body temperatures, 26°C and 37°C, and



The Type III secretion, a syringelike injection mechanism more colorfully called "*Yersinia's* deadly kiss," which is how plague infects a host once its virulence genes have been turned on.



A schematic diagram of information that is hypothesized to describe the pathways of virulence in a pathogen. The regulatory (feedback) loop is often nonlinear, and there can be multiple feedback paths with complex interactions.

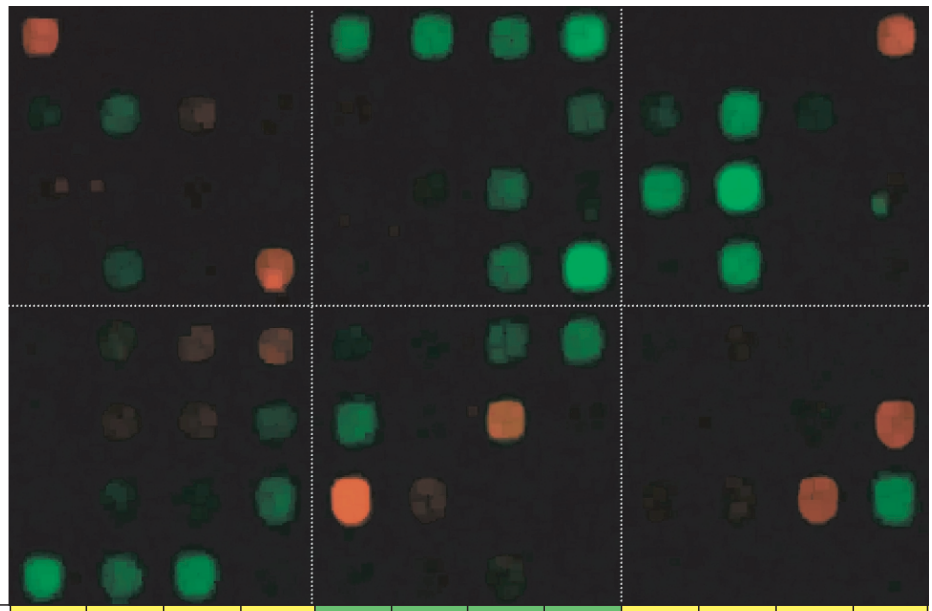
at calcium levels that correspond to those of blood (higher level) and organs (lower level), the latter location being where more virulence genes are expressed.

More recently, they developed a microarray for all 4,500 *Y. pestis* genes. All of the genes are being mapped at six time intervals as temperature rises and calcium concentration drops. The team is thus beginning to establish a timeline for how and when genes change and are expressed while the plague bacterium is infecting a human host. Some genes are expressed early, while others are late-onset genes. A detailed picture of how the bacterium behaves during the infection process will provide useful information for the development of diagnostic techniques and treatment methods.

Garcia and other researchers also completed a detailed analysis of three *Y. pestis* plasmids, which allowed them to confirm the location of several known virulence genes and to uncover four novel ones believed to contribute to virulence. Computerized comparisons with other genomic databases indicated the presence of a large number of virulence-related genes that are similar in both closely related bacteria such as *Y. pseudotuberculosis* and distantly related bacteria such as *E. coli*. The team also found numerous gene coding regions whose function they could not determine.

Using a proteomic approach of protein separation techniques and mass spectrometry (MS), Livermore researchers led by Sandra McCutchen-Maloney are analyzing complex mixtures of proteins isolated from *Y. pestis*. By comparing samples grown at the two physiological conditions mimicking the flea and the human (at 26°C and 37°C, respectively) and at low calcium concentration to induce virulence, the team is detecting differential protein expression to identify candidate proteins important for *Y. pestis* pathogenicity. Comparisons are also being made between human cells that have and have not been exposed to *Y. pestis* in order to understand the host immune response. Because it is the proteins that are actually responsible for virulence effects, the group is also working to correlate their proteomic data with genomic data obtained from microarray experiments. To learn more about the individual proteins responsible for virulence, the team is using various biochemical assays to test functional models of the candidate virulence

A 96-spot microarray for transcript profiling of 85 genes of *Yersinia pestis*; 11 of the spots are controls. Genes tagged with fluorescent dyes change color in response to various stimuli.



A	A	BRCA	XRCC	PKC	ypkA	yscC	yscO	lcrV	PKC	XRCC	BRCA	A
B	yopE	caf1A	sodA	envZ	ompR	yenI	rpoE	yopJ	yscB	lcrH	sycE	caf1R
C	tpx	rfaH	phoP	yenR	g6pd	rpoN	yopH	lcrF	lcrE	yopB	sycH	luxS
D	oxyR	psaA	glts	rpoS	lcrQ	yscW	tyeA	yopD	yadA	katY	hemF	toxR
E	rstB	nqrA	dha4	rpoH	yscL	yscU	sycN	yopM	pst	hns	cbl	flhC
F	nhaB	nadB	rpoD	yscH	lcrD	sycT	pla	catA	gcvA	copR	araC	nhaC
G	dam	yscG	lcrR	yopT	ymt	sodC	lysR	ilvY	tsaA	caf1	tuf	yscD
H	yscP	lcrG	yopK	caf1	sodB	crp	nhaR	fliA	h5	RAD	CDC2	Empt
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factors. In addition, McCutchen-Maloney's group is looking at host–pathogen interactions by using surface-enhanced laser desorption ionization (SELDI) MS to study various protein–DNA and protein–protein interactions within *Y. pestis* and between *Y. pestis* and the human host. For example, regulatory proteins that bind to genes and control differential expression are under investigation, as are the specific protein–protein interactions of suspected virulence factors. These molecular interactions are key to the genetic feedback that occurs as a pathogen infects its host, as shown in the bottom figure on p. 7.

Differences Are Key

Before Garcia's team completed its comparative sequencing of *Y. pseudotuberculosis*, microbiologists Gary Andersen, Lyndsay Radnedge, and others examined the differences between *Y. pseudotuberculosis* and *Y. pestis* using a different technique. This process, developed in Russia, is known as suppression subtractive hybridization (SSH). SSH identifies regions of DNA that are present in one species but absent in another.

SSH has the advantage of requiring only small amounts of genomic DNA. It can be used with any genome, even one that has not yet been characterized. It is especially useful for identifying the large genomic differences typically found between bacterial genomes. For example, SSH identified the genetic material that causes Kaposi's sarcoma, a skin lesion associated with HIV and AIDS. At Livermore, SSH has been useful for finding differences among anthrax strains and other potential agents of bioterrorism.

Comparison of *Y. pestis* and *Y. pseudotuberculosis* revealed seven DNA regions in *Y. pestis* that do not occur in *Y. pseudotuberculosis*. Four of them occur very closely to one another on the *Y. pestis* genome. "It is fair to assume that *pestis* acquired this region during its evolution from *Y. pseudotuberculosis,*" says Radnedge.

To learn more about the function of genes in these areas, Garcia and others are beginning "knock-out" studies. They will inactivate, or knock out, one gene at a time and test the resulting bacterium on an animal to see how the host and its genes respond. This is slow, laborious work, but it will help to determine what the function of each *Y. pestis* gene is, if any, and what gene or genes in the host are expressed as a response. This detailed examination of pathogen–host interaction for plague will be the first of its kind.

Being Prepared

Research to date on plague lays the groundwork for additional work planned at Livermore in the areas of microbiology, proteomics (the global study of proteins), bioinformatics (the integration and analysis of biological data), and biological modeling for the NNSA's Chemical and Biological National Security Program. Some of the research will elaborate on plague, some will examine a broader spectrum of human pathogens, and some will further the development and use of biodetectors, mass spectrometry, and other technologies.

In the U.S. today, plague pops out of the rodent population and into the human populace occasionally in the desert Southwest. It is a larger problem in a few other countries. But the real fear is that plague could be used as an agent of mass destruction. At least in industrialized countries, it is unlikely that plague would cause the huge number of deaths that occurred during earlier epidemics. Better sanitation, a more educated populace, and a far superior medical system would likely prevent that. But the world needs to be prepared.

—Katie Walter

Key Words: bioterrorism agents, Chemical and Biological National Security Program, plague, surface-enhanced laser desorption ionization mass spectrometry (SELDI-MS), suppression subtractive hybridization (SSH), virulence, *Yersinia pestis*, *Yersinia pseudotuberculosis*.

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L-Gel Decontaminates Better Than Bleach

Scientists have developed a material that is safe for people and the environment but deadly to the agents of biological and chemical warfare.

THE recent cases of anthrax spores deliberately spread through the mail reminded all Americans, and especially managers of federal and state agencies responsible for public health and safety, about potential terrorism with chemical and biological weapons. The anthrax cases have also underscored the need for safer and more efficient methods to decontaminate offices and homes of deadly biological agents.

During the late 1990s, scientists at the Department of Energy national laboratories foresaw the need for a safe, reliable, and easily deployable decontaminating agent that could be used for civilian defense against biological and chemical terrorism. DOE managers agreed with the scientists and asked them to use their expertise in chemistry, biology, and environmental protection to develop new decontamination products and procedures.

Lawrence Livermore responded to this request with a team formed from the Environmental Protection Department and three directorates—Chemistry and Materials Science; Nonproliferation, Arms Control, and International Security; and Biology and Biotechnology Research. The team of diverse experts developed a compound called L-Gel (the L is for Livermore), which combines a mild, commercially available oxidizer with a silica gelling agent to create a substance that coats walls, ceilings, and other materials like a paint, effectively decontaminating the coated surface.

The material is nontoxic, noncorrosive, easy to manufacture, easily deployable, and relatively inexpensive (about $1 to cover a square meter). Tests at Livermore's laboratories and field trials at both federal and foreign facilities have shown that L-Gel has been extremely effective at decontaminating all classes of chemical warfare agents as well as surrogates for biological warfare agents.

Livermore technology transfer specialists are currently engaged in negotiations with several companies to license the manufacturing and marketing of L-Gel. If negotiations proceed apace, government agencies could have the material by the end of the fiscal year (September 30) to respond to any terrorist incident involving chemical or biological agents.

Different Needs for Civilians

According to L-Gel development leader Ellen Raber, a geochemist and head of Livermore's Environmental Protection Department, several decontaminating agents are effective against either chemical or biological warfare agents. However, these materials, which are mainly strong chemicals, were developed by the military for battlefield use, and they pose environmental and health risks when used in civilian settings. At the minimum, they can damage everyday materials such as furniture and office equipment.

Other methods that have been used in civilian settings have serious drawbacks. For example, solutions of laundry bleach work well as decontaminants but are very corrosive. Incineration and irradiation have obvious practical limitations in office settings or face public resistance. Chlorine dioxide gas, used late last year to decontaminate the Hart Office

Building that houses members of the U.S. Senate, is a laborious process and poses a safety risk to workers. It also requires the gassed building to be neutralized before people can reenter.

The Livermore team focused on finding an effective decontaminating agent and application system that is safe to use, does not damage commonly used materials and surfaces, is friendly to the environment, and is effective against both chemical and biological warfare agents. "We wanted something that was less corrosive than bleach, that is easy to apply, and that does not leave workers with a huge cleanup job," Raber says.

Raber points out that speed of decontamination, which is all-important in military applications, is less important in civilian applications, where decontamination times of one to several hours may be adequate. More important in a civilian scenario are ease of application, minimal training required for use, moderate expense, and environmentally acceptable byproducts.

The team also recognizes that the new product needs to be effective in three potential settings of a terrorist incident against civilians: an outdoor location such as a stadium, a semienclosed place such as a subway station, and an enclosed space such as an office building. Using the decontaminating material on interior surfaces can have quite different requirements from those appropriate for outdoor use, where natural attenuation from environmental conditions (for example, ultraviolet radiation from sunlight) might well be adequate for effective decontamination.

Start with the Oxidizer

The development effort began with Livermore scientists Ray McGuire and Don Shepley evaluating several acidic oxidizer solutions that could degrade chemicals into nontoxic, environmentally acceptable components. (Oxidizing solutions do not completely destroy chemical agents but rather break key chemical bonds to render the toxic compound inactive.) The oxidizers considered could be deployed in liquid spray systems or incorporated into compatible gels for clinging to surfaces such as ceilings and walls.

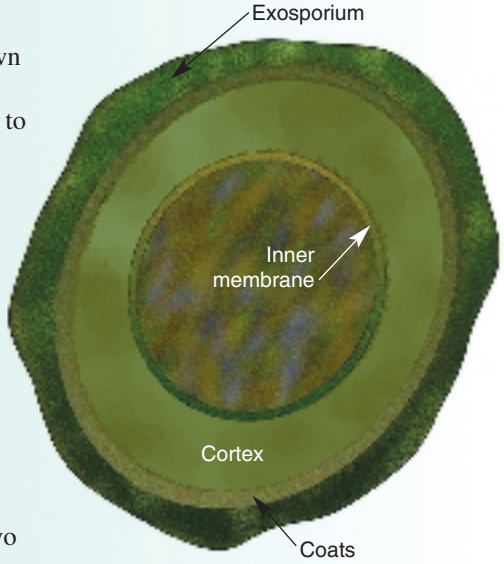
McGuire chose an acidic rather than a basic oxidizer solution, primarily to aid the decontamination of VX, a potent nerve agent. Acidic oxidizer solutions are also known to be effective at decontaminating certain biological warfare agents, including bacterial spores, which are extremely difficult to kill because of their hard, multilayered coats. The coat allows a spore to remain in a dormant state for many years until, under the right environmental conditions, it transforms into a live organism.

"Anthrax is the most difficult biological agent to kill because of its resistant outer coat," says Raber. An oxidizer in acidic solution breaks down the proteins that are found in anthrax coats. Once the oxidizer gets through to the nucleus, its molecules destroy strands of the anthrax DNA or RNA.

The goal was to find the most effective oxidizer at the lowest effective concentration. The oxidizers that were evaluated included potassium permanganate, peroxydisulfate, peroxymonosulfate, hydrogen peroxide, and sodium hypochlorite. The oxidants were evaluated in laboratory tests on chemical warfare surrogates for such agents as VX, sarin (used in the Tokyo subway terrorist incident), and sulfur mustard (used during World War I).

Livermore bioscientist Paula Krauter evaluated the same group of oxidizers on surrogate biological agents and toxins that would likely be used in terrorist attacks. *Bacillus subtilis* was used for spore-forming agents such as anthrax, *Pantoea hericola* was the surrogate for plague, and ovalbumin was the surrogate protein for botulinum toxin.

The initial laboratory tests showed that potassium peroxymonosulfate was more than 99 percent effective at oxidizing both chemical and biological warfare surrogates that were placed on common materials such as carpet, wood, and stainless steel. The results led to the selection of Oxone, a commercial product manufactured by DuPont, which contains potassium peroxymonosulfate—its active ingredient—in a water solution. Previous research at U.S. military laboratories had demonstrated the effectiveness of Oxone in decomposing both VX and mustard-type agents, but the compound had not been previously tested on biological agents.



The cross section of a bacterial spore, such as anthrax, shows its hard, multilayered coats, which both make the spore difficult to kill and allow it to remain dormant for many years.

Gel Adds Staying Power

The team recognized that spraying water-based solutions of Oxone would not be effective in all cases. Consequently, McGuire and Mark Hoffman investigated carrier materials that would thicken the oxidizer so it would better cling to walls, ceilings, and other surfaces to increase contact time with the biological or chemical agent.

Hoffman chose colloidal amorphous silica as the carrier material for several reasons. First, unlike crystalline silica, which is toxic, colloidal amorphous silica is safe to use and is found in many household paint formulations. Also, silicon dioxide colloidal particles are commercially available, don't require manufacturing in a special facility, and, because they are chemically inert, are compatible with oxidant solutions. When mixed with the oxidizer, the gel can be applied with simple delivery systems, such as paint sprayers. After application, it thickens and tends not to sag or flow down walls or drip from ceilings. Finally, silica gel materials can be easily vacuumed up after they have dried.

Livermore chemists have extensive experience with colloidal silica gel. From the late 1960s to the late 1980s, the chemists developed a series of extrudable high explosives based on the gelling of energetic liquids. Although this research did not advance to the explosives production stage, the development effort provided useful experience for working with silica-gel materials. It was a logical step to adapt this work to the gelling of aqueous oxidizers for candidate decontaminants, says Hoffman. "Our research with high explosives gave us a good feel for working with silica gels."

Hoffman selected Cab-O-Sil EH-5 fumed silica as the gelling agent. The final formulation was named L-Gel 115, which is a formulation of aqueous Oxone solution gelled with 15 percent EH-5 silica gel. The viscosity can be varied, depending on the application. Under development is a second formulation, called L-Gel 200, which contains 10 percent t-butanol cosolvent to promote penetration on surfaces with heavily coated paint or varnish.

The biocidal effect of peroxymonosulfate, the oxidizer in L-Gel, is seen on this nutrient agar plate of *Bacillus subtilis* spores (surrogates for anthrax). Three spots of silica gel were added to the plate. Two of the spots contained peroxymonosulfate and one (at right) did not. The peroxymonosulfate-containing gel inhibited spore germination in the zone surrounding the gel, even leaching into the agar.

Field Tests Prove Effectiveness

The final L-Gel 115 formulation was subjected to a series of tests at Livermore facilities using surrogates of potential terrorist chemical and biological agents. The tests involved placing surrogate chemical and biological agents on various common materials—varnished wood, painted steel, glass, fiberglass, and carpet—adding L-Gel to the surface, allowing the gel to dry for 30 minutes to several hours, and then determining the percentage of surrogate that had been decontaminated. L-Gel proved greater than 99 percent effective on all surfaces and for all agents.

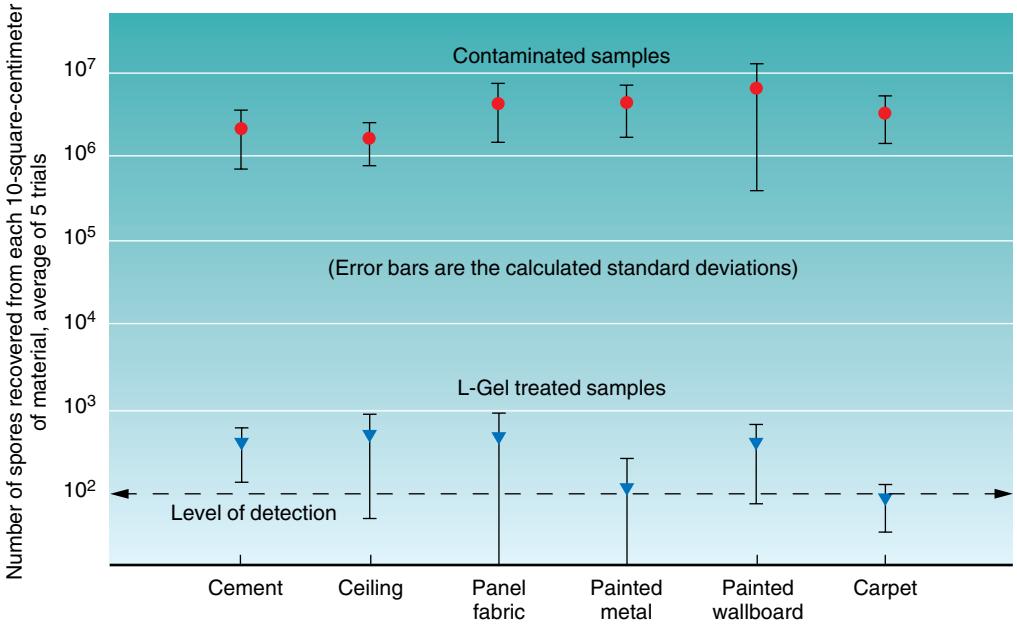
The Livermore biological researchers also tested L-Gel on safe strains of the deadly biological agents *Bacillus anthracis* (anthrax) and *Yersinia pestis* (plague). These strains—Sterne and Strain D27, respectively—could be safely used in experiments because they are nonvirulent, that is, they do not contain the genes that create the lethal toxins present in the real organisms. (See the article beginning on p. 4 about research on sources and pathways of virulence in organisms.) The researchers used the agar plate resistance test, a standard technique to measure the efficacy of antibiotics. In this test, about one million cells (or spores, in the case of *B. anthracis*) were combined with liquid agar, then poured onto a petri dish containing nutrients for cell growth. The strains were also tested against dilutions of L-Gel, which proved more than 99.9 percent effective in killing the cells and spores.

L-Gel also was tested against surrogate spore-forming bacteria in two field exercises. In December 1999, researchers Krauter and Tina Carlsen participated in biological warfare field tests that were conducted by the Soldier Biological and Chemical Command at the U.S. Army Dugway Proving Ground, Utah. The tests compared the ability of several decontamination materials to inactivate surrogate organisms placed on six 40-square-centimeter panels of acoustic ceiling tile, tightly woven carpet, fabric-covered office partition, painted wallboard, concrete slab, and painted metal. Each panel was contaminated with about 10 billion spores per square meter.

After L-Gel was applied, the panels were swabbed about 24 hours later. The number of live spores on most test panels was reduced by an average of 99.988 percent.

In October 2000, Krauter and Hoffman participated in a biological warfare agent room-decontamination exercise that was conducted again at the Dugway Proving Ground. The tests used full-scale, mock offices constructed in an abandoned building. Flooring was divided into quarters consisting of carpet, vinyl tile, varnished oak, and painted concrete. Walls consisted of stucco, wood paneling, plasterboard, and carpet, and the ceiling was constructed of suspended ceiling tile. The room was contaminated with 4 grams of spores. After application of L-Gel, about 400 samples were collected from multiple locations in the

Researcher Paula Krauter applies L-Gel to "contaminated" panels of different materials to test the gel's effectiveness.



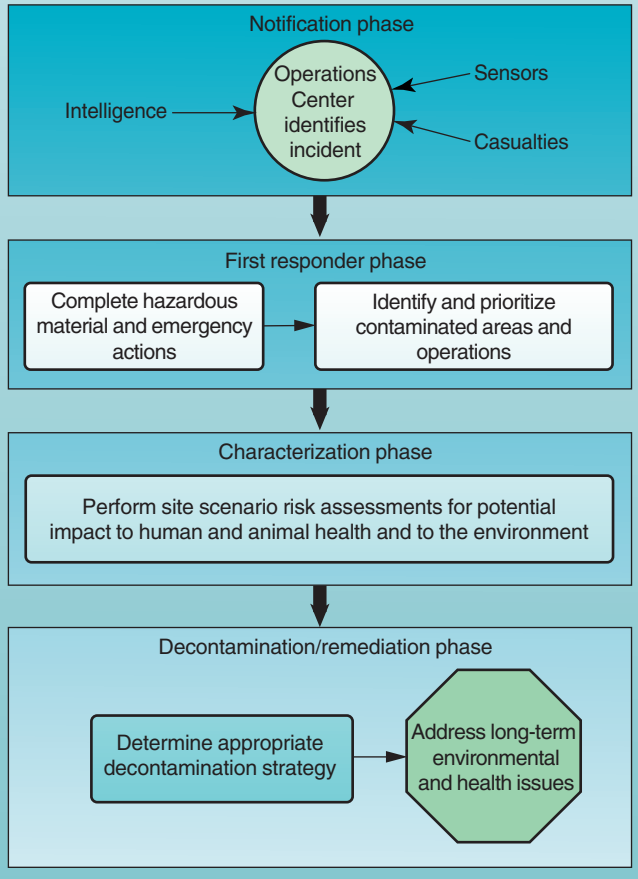
L-Gel was tested against surrogate spore-forming bacteria at the Soldier Biological and Chemical Command at the U.S. Army Dugway Proving Ground, Utah. In one test, surrogate organisms were placed on six 40-square-centimeter panels of acoustic ceiling tile, tightly woven carpet, fabric-covered office partition, painted wallboard, concrete slab, and painted metal. L-Gel reduced the number of live spores on most test panels by an average of 99.988 percent.

How Clean Is Clean Enough?

When a terrorist attack on civilians potentially involves biological or chemical warfare agents, decision makers will need to make fast and informed choices about how to respond. A team of Livermore researchers from the Safety, Security, and Environmental Protection Directorate has developed a process that guides users to make the best emergency response decisions involving notification, identification, characterization, decontamination, and cleanup.

In 1998, at the request of DOE's Office of Nonproliferation and National Security, the team developed a biological agent decontamination plan in the form of a flowchart. It was then used in a recommendation from the Environmental Protection Agency to the National Security Council, the President's principal forum for considering national security and foreign policy issues. In 2001, the Livermore team added chemical warfare agents to the plan, now termed the Chemical and Biological Agent Decision Process.

The process helps users to determine what actions need to be taken at the outset; if an actual or potential impact to health, property, or the environment exists; whether or not decontamination is needed; what steps should be taken and when; and how to verify that cleanup and remediation are complete so that the area can be designated as safe to reenter or reuse.



Under the process, each of four phases (notification, first responder, characterization, and decontamination/remediation) progresses to the next phase as soon as all its issues have been addressed. The format includes numerous yes/no decision points and links to more detailed information on specific topics. The decision process takes into account different environments, such as an outdoor site, and considers individuals in the general population who may be at higher risk for illness and injury.

According Ellen Raber, head of Livermore's Environmental Protection Department, the biological agent decontamination plan addresses a need by several federal agencies for an up-to-date summary of information necessary to evaluate acceptable decontamination levels and procedures. The goal of the plan is to help minimize the number of deaths and illnesses, damage to the natural and built environment, and the extent of economic damage (for example, crop or livestock damage) resulting from a biological terrorism incident.

In developing the plan, Livermore experts did a thorough literature search and consulted with colleagues at the U.S. Army, the U.S. Environmental Protection Agency, and federal health agencies, including the U.S. Public Health Service. The team noted that responding to a civilian event involves different priorities than those for a military setting. For example, during a battle, quick decontamination is critical so soldiers can continue their mission. In a domestic urban scenario, however, considerations of public health and environmental issues are usually more important than immediate decontamination. Also, the decontamination process may need to be staged, with cleanup of gross contamination—for example, of puddles of toxic materials—followed by more localized decontamination, such as cleaning up materials in cracks.

The flowchart is structured so that cleanup criteria are dependent upon the decontamination site. Much stricter criteria are necessary for indoor settings such as offices or homes than for outdoor scenarios where wind, sunlight, temperature, and rain may effectively decontaminate biological agents, toxins, and chemical warfare agents.

Raber says the decision process must include answering the question, "How clean is clean enough?" In this respect, it is more difficult to establish target cleanup levels for biological agents than for chemical agents, in large part because of public acceptance and perception issues. She notes that the public may demand zero living organisms after decontamination, but achieving such a level may not be practical or necessary. In the case of anthrax, for instance, it takes about 6,000 inhaled anthrax spores to cause respiratory anthrax. Furthermore, some biological agents such as anthrax are already indigenous to many farming communities and exist without incident. "Zero concentration of a biological agent and zero risk, in many cases, are clearly not a necessity," she says.

Raber also points out that it is possible to do a poor job of decontamination and to make it look good by doing a poor job of sampling and analysis. "In the end, decontamination must be defensible to regulatory agencies and to the public."

room. L-Gel reduced the number of spores by about five orders of magnitude and, in these experiments, did not damage office surfaces, with the exception of bleaching some rust on ceiling supports.

L-Gel was also independently tested on real chemical warfare agents at four locations from October 1998 to October 2000. The tests were conducted at the Military Institute of Protection, Brno, Czech Republic; Edgewood Chemical and Biological Forensic Analytical Center, Maryland; the Defense Evaluation and Research Agency, United Kingdom; and the Soldier Biological and Chemical Command at Dugway. Field tests showed that L-Gel was a more effective decontaminant of real VX, GD (nerve agent), and sulfur mustard than the current military standard, calcium hypochlorite, on such materials as acrylic-painted metal, polyurethane-coated oak flooring, and indoor–outdoor carpet.

Two of the field trials also demonstrated that the L-Gel 200 formulation has improved penetration and thus promotes solution and oxidation in thickened chemical agents. L-Gel 200 was tested on real chemical warfare agents such as thickened distilled mustard and thickened soman (persistent nerve agent) as part of the Restoration of Operations series of experiments at Dugway Proving Ground. The agents were applied on steel test panels, Air Force air–ground equipment paint, and Navy shipboard coating.

Meets Safety Standards

With L-Gel's excellent performance demonstrated in both laboratory and field trials, it was time to partner with one or more commercial firms that could manufacture the material quickly and efficiently. Fortunately, says Raber, "L-Gel is simple to manufacture. It's comparable to mixing paint." L-Gel is relatively noncorrosive (its pH is about 4, similar to that of vinegar or lemon juice), and Environmental Protection Agency testing shows its residual materials to be nonhazardous. It also meets the Department of Transportation's nonhazardous and noncorrosive requirements and is stable during shipping.

L-Gel is premixed and then shipped and stored as a semisolid resembling Jello at room temperature. If unopened, its shelf life is expected to exceed a year. It is reliquefied to the consistency of house paint by vigorous shaking by hand or a power stirrer. It can be applied with any type of commercially available spray device, whether airless or compressed-air units, with any stainless-steel atomizing nozzle.

Although L-Gel clings to walls and ceilings, it does not harm most painted surfaces or carpets. Decontamination takes about 30 minutes. When dry (in about 1 to 6 hours), the gel residue, unreacted oxidizer, and decontaminated chemical or biological agents can simply be vacuumed up and discarded as nonhazardous waste. For outdoor use, no cleanup is required.

Raber says L-Gel compares favorably to other decontamination methods that have been used recently to kill anthrax spores. The tried-and-true method is a bleach solution. However, bleach is extremely corrosive to metal surfaces and must be used with care by cleaning crews.

A foam developed at Sandia National Laboratories in New Mexico has also been effective for decontaminating chemical and biological agents. This material is sprayed on surfaces like a firefighting foam. Most of the foam dissipates, and the residual material is then washed off. It has been used to clean offices of Congress and at ABC News. Raber suggests that L-Gel and the Sandia foam could work in tandem, with L-Gel sprayed on walls and ceilings and the Sandia foam applied to large pieces of equipment and floors.

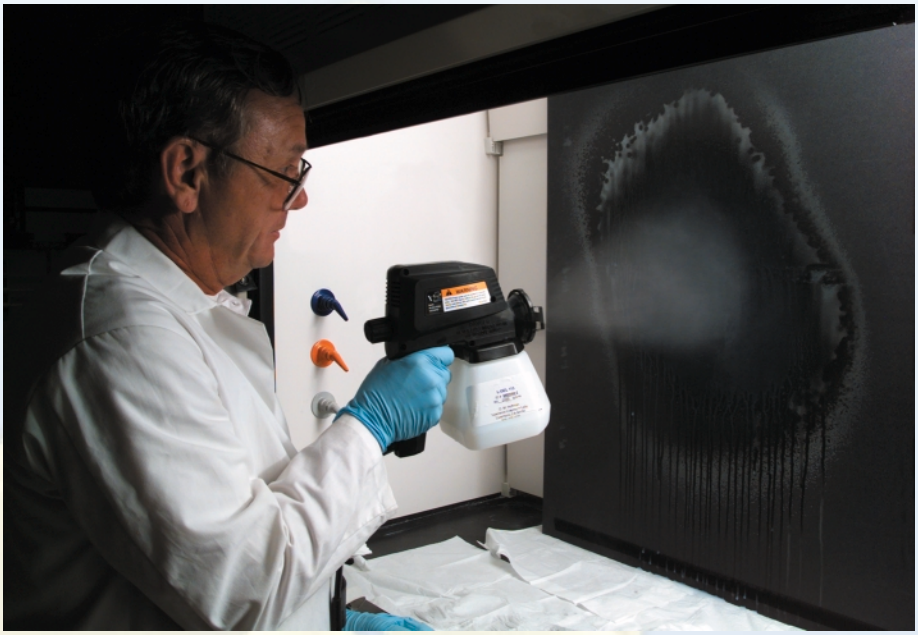
Chlorine dioxide, used to decontaminate U.S. Senate offices, is a gas that kills bacteria but also is

A second test at the Dugway Proving Ground in Utah tested L-Gel in a mock office setting.

L-Gel is shipped premixed as a semisolid. It is reliquefied to a house-paint consistency by vigorously shaking it by hand or using a power stirrer.

hazardous to human health and thus must be applied by trained personnel. Afterward, its vapors must be sucked out of rooms and then filtered through an ascorbic acid bath to decompose it. Raber notes that gases and aerosols have clear advantages for decontaminating ventilation systems and hidden spores, and research needs to continue to find an environmentally safe gas or aerosol that is effective for these applications.

Irradiation, popular in Europe, kills bacteria and spores and is effective in decontaminating mail, food, and other objects. However, the method requires large machines, which are essentially small accelerators, and is not currently viable for large-scale room decontamination.



Livermore chemist Mark Hoffman uses a household paint sprayer to apply L-Gel to a test panel.

In the News

News about L-Gel has spread rapidly, and Raber has been interviewed by several newspapers, television stations, and National Public Radio. She has also received a large number of inquiries from emergency response groups across the country interested in additional information and samples.

The developmental work for L-Gel 115 is complete, and Raber's team has begun to develop a new formulation to decontaminate ventilation systems. "Right now, we don't have an easy way to decontaminate air ducts," she says. The team is working on an encapsulation method to aerosolize L-Gel (make it into tiny droplets) so that it could be blown into ventilation systems.

In the meantime, licensing of L-Gel manufacture is well under way, and Raber is hopeful that major organizations will soon have an important yet nontoxic new weapon to counter any biological or chemical attack.

—Arnie Heller

Key Words: anthrax, biological warfare, Chemical and Biological Agent Decision Process, chemical warfare, decontamination, L-Gel, peroxymonosulfate.

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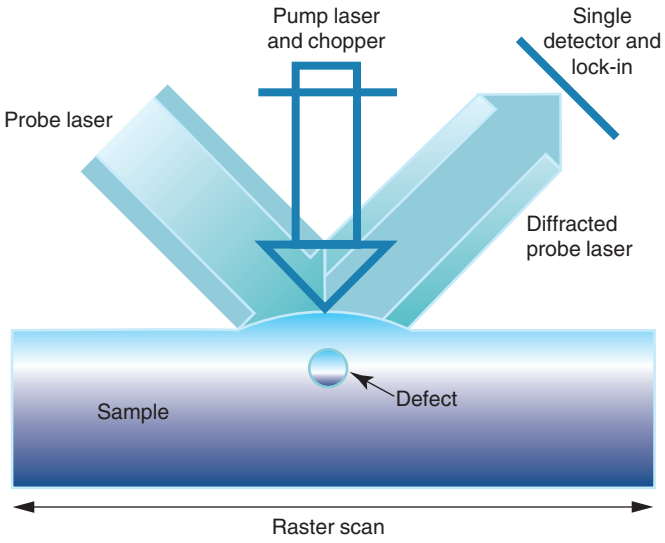
Faster Inspection of Laser Coatings

LASERS have been a Lawrence Livermore specialty almost since the first laser flashed in 1960. Dealing with the challenges that arise as these lasers get bigger and more powerful is, of necessity, a specialty too.

The process of creating an intense laser beam requires that the beam traverse many pieces of optical glass. Oftentimes, the glass requires highly reflective mirror coatings so that the laser's energy is not lost as it passes through. But during the coating process, miniscule defects—called nodules—inevitably occur. As lasers get larger, they require larger pieces of glass, and more defects occur. On a laser mirror a half-meter across, there may be as many as a million defects. While more than 99.99 percent of defects have no influence on optical performance, a few of the defects will limit the laser fluence (a measure of the energy passing through) that the mirror will survive; finding those few among a million is like trying to find the proverbial needle in a haystack.

In the mid-1990s, Livermore began to explore the best means for locating coating defects. Optical microscopy and atomic force microscopy can reveal nodules but cannot distinguish the thermal defects in thin films that arise during the coating process. Engineer Chris Stolz and others at Livermore began working with scientists at Eastern Michigan University who were experts in photothermal microscopy, an imaging technique that can locate and characterize both nodules and thermal defects in laser mirror coatings.



Defects absorb light from the pump laser and cause a surface bump to form. The probe laser detects the bump, and the photodetector records changes in the probe's optical diffraction caused by the deformation. The resulting signal indicates the amount of optical thermal absorption at the specified wavelength.

Finding the Needle

In photothermal microscopy, a pump laser set at a specific wavelength heats a surface. Surface and subsurface defects that absorb the light at that wavelength cause a bump to form on the surface, as shown in the figure below. A second laser beam, known as the probe laser, detects the change in the surface, and a photodetector records changes in the probe's optical diffraction caused by the bump, or deformation. The pump beam is "chopped," or interrupted periodically. The photodetector locks into the chopping frequency, and the resulting photothermal signal is an indicator of how much heat at the specified wavelength was absorbed.

The benefit of photothermal microscopy was made clear in its earliest tests, which examined a 9-millimeter by 9-millimeter area of coating. One defect, which had the highest photothermal signal, was not visible optically. Later, during laser damage testing, the defects with the highest photothermal signal proved to have the lowest damage threshold. (The damage threshold is the laser energy level that the material is designed to endure but beyond which damage will likely occur.) A high-energy laser needs glass with the highest possible damage threshold.

Studying various kinds of defects in glass coatings allowed the researchers to zero in on the few that reduce the damage threshold. Photothermal microscopy images also validated the use of laser conditioning—treatment of defects with a laser—as a way to reduce the absorption of defect fluences, as shown in the top figure on p. 18.

From Scanning to Imaging

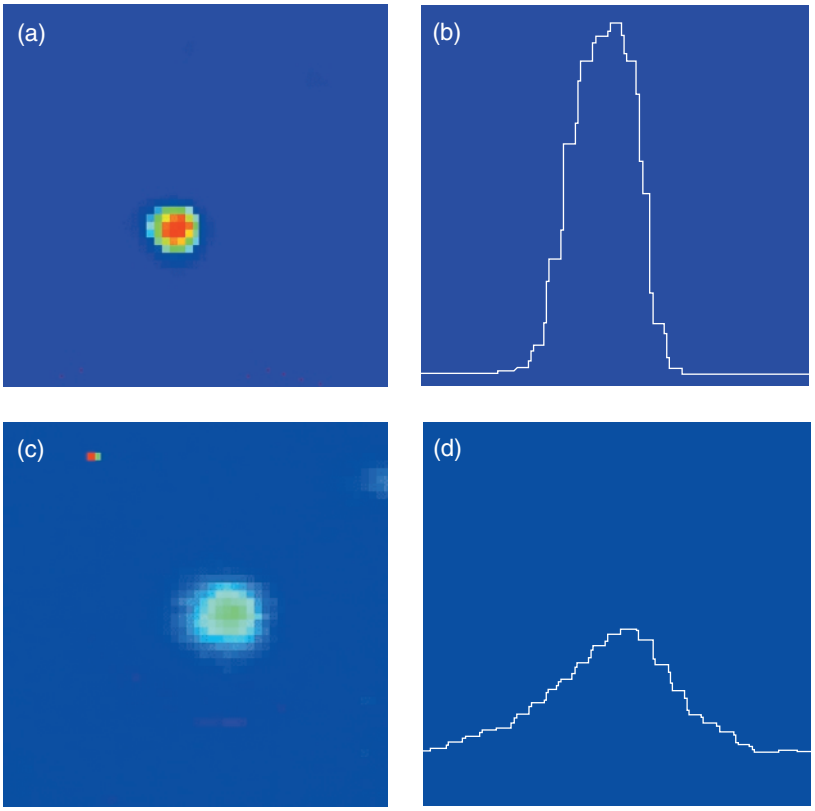
The photothermal microscopy system worked well but, because it used a raster-scanning technique, was extremely slow. The results of raster scanning are what you see when the graphics on a Web site or other computer graphics gradually improve line by line or pixel by pixel. In photothermal

microscopy, the pump and probe beams are raster-scanned while the detector collects data a single pixel at a time. Together, they generate a photothermal microscopic map of a given inspection area at a rate of 1 second per pixel. That speed is impractical for inspecting large surfaces of coatings.

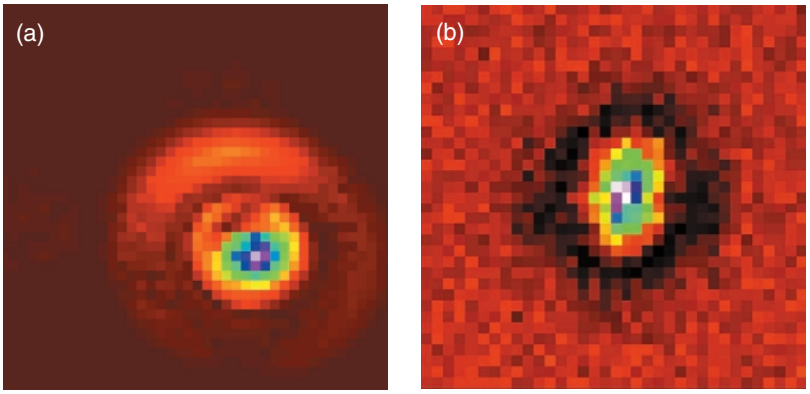
Recently, engineers Diane Chinn and Stolz, working with others at Livermore and Wayne State University, modified the scanning technology to create photothermal imaging microscopy, which is 10,000 times faster than the raster-scanning method. Using the imaging mode, photothermal microscopy can inspect a 1-square-centimeter area in just 2 seconds.

For photothermal imaging, Chinn and the others expanded the pump and probe beams to about 5 millimeters. They used a 1,024- by 1,024-pixel charge-coupled-device camera to detect the diffracted pump beam. In scanning mode, the detector was locked in electronically to the chopping frequency of the pump beam, but in the imaging mode, the collected images are phase-delayed relative to the pump beam to achieve optical lock-in.

The bottom figure at right compares images of a glass sample with an antireflective coating using both the raster-scanning and imaging modes. Aluminum dots were sputtered onto the glass substrate before coating. The two images showing aluminum absorption are comparable, but the time it took to produce them is not. The raster-scanned image took 35 minutes to obtain, while the one generated through the imaging mode took just 40 seconds.



(a) A photothermal microscopy image and (b) the diffraction signal of a nodule defect before laser conditioning. (c) The same defect after laser conditioning. (d) Its diffraction signal has been reduced by a factor of 125, which in turn reduces the likelihood that this defect would cause damage at the National Ignition Facility's fluence.



(a) A map of a sputtered aluminum dot under an antireflective coating using photothermal microscopy in the raster-scanning mode. It took 35 minutes to obtain this image. (b) The same dot imaged using photothermal microscopy in the imaging mode. Producing this image took just 40 seconds.

Applied to NIF

The team's proof-of-principle work was funded by Laboratory Directed Research and Development. Now, with project funding, the team is beginning to apply the process to optics for the National Ignition Facility (NIF).

When NIF comes on line in the next few years, it will be the largest, most energetic laser in the world as well as the largest optical instrument ever built. NIF will require lots of optical glass—7,500 large optics (as large as a meter along the diagonal) and more than 30,000 small optics. The

primary task of these optics will be to separate and steer 192 laser beams through a 250-meter-long building and to amplify the laser energy before that energy is focused onto a fusion target the size of a dime.

Electron beam deposition lays down multilayer coatings of hafnia and silica on NIF optics. With the raster-scanning technique, imaging a 1-centimeter-square area of NIF optical coating at 10-micrometer resolution would take a full 278 hours. Inspecting the acres of coatings on NIF optics would have taken decades at that rate. The faster photothermal microscopy imaging technique, however, is a viable method for inspecting NIF's coatings.

One of a Kind

"We have proved that this new system can produce the fast, high-quality images we need to inspect NIF coatings," says Chinn. "And it is a capability that doesn't exist anywhere else in the world." Photothermal imaging microscopy will have other uses as well. Chinn sees it helping microtechnology engineers to assess computer chip lithographic techniques. It may also be useful for studying hard coatings and thermal barriers in the automotive and aerospace industries.

"If this system works in-house as we hope it will," continues Chinn, "we plan to move the technology into the coating vendors' shops for their use. This is a much faster method for identifying problem areas than anything else out there."

—Katie Walter

Key Words: laser glass, multilayer hafnia–silica coatings, National Ignition Facility (NIF), photothermal microscopy.

For further information, contact Diane Chinn (925) 423-5134 (chinn3@llnl.gov).

From Kilobytes to Petabytes in 50 Years

"The day when the scientist, no matter how devoted, can make significant progress alone and without material help is past."
—E. O. Lawrence, founder of Lawrence Livermore National Laboratory, on accepting the 1939 Nobel Prize for Physics

THE history of Lawrence Livermore National Laboratory is inexorably tied to the evolution of supercomputers—the largest, fastest, most powerful computers in the world. Even before the Laboratory's gates opened for the first time in September 1952, founders E. O. Lawrence and Edward Teller recognized that computers were needed to better calculate the thermonuclear explosions for the nuclear weapons the "Rad Lab" in Livermore was destined to design.

Designing nuclear weapons and predicting their behavior has always been a difficult technical and scientific challenge. In a thermonuclear explosion, matter is accelerated to millions of kilometers per hour while experiencing densities and temperatures found only in stars. In addition, weapon designers needed to identify and understand the important physical properties of matter under these exotic conditions. With little experimental data available, Livermore's designers turned to computers to simulate and visualize the processes and the physics of nuclear weapons.

To fulfill its critical national defense mission, the Laboratory constantly sought out the most advanced computers with the most capability. In the 1990s, with the cessation of underground nuclear testing, advanced supercomputers figured prominently in plans for stockpile stewardship, helping scientists predict the behavior of the aging nuclear stockpile to better assess its safety, reliability, and security.

Mag Tape and Punch Cards

Livermore's first supercomputer, the Remington-Rand Univac-1, had 5,600 vacuum tubes and was over 2 meters wide and 4 meters long. Between April 1953 and February 1957, the Univac executed as many calculations as 440 human "calculators" could perform in 100 years if they worked 40 hours a week, 52 weeks a year, and made no mistakes. Memory, however, was an issue.

The Univac's memory consisted of mercury tanks that could store 9 kilobytes of data—a tiny fraction of what today's pocket-sized handhelds can hold. The code that performed all its operations was stored on magnetic tapes that had to be loaded into the machine in parts. Calculations could involve as many as nine tapes, and the nine reel mechanisms were troublesome, accounting for much of the machine's 25 percent downtime. Clearly, machines with more memory were needed.

With the arrival of the IBM 701 in 1954, scientists expected that nuclear explosives computations would run much faster. The IBM, which was the first fully electronic computer, was 12 times faster than the Univac, had twice the memory, and primarily used punch cards for input and output. Scientists took advantage of the improved capabilities to increase resolution and add more detailed physics, so the computational runs continued to average 100 hours.

A series of IBM machines followed the 701. The IBM 704—twice as fast as the 701—even played a part in the early

space race between the U.S. and the Soviet Union. Soon after the launch of the Soviet Sputnik I satellite in October 1957, the Laboratory received an urgent request to help predict when the satellite would come back to Earth. Livermore's IBM 704s were the only computers in the U.S. able to perform the calculations. Joe Brady, a now-retired Laboratory scientist, recalls, "We used two 704s for 70 hours straight, only stopping to rush outside to see the satellite orbiting overhead." Laboratory computation workers accurately calculated the satellite's plunge into the atmosphere in early December, an extrapolation of 58 days from launch. The 704s eventually gave way to IBM 709s, which were faster still, thanks to special-purpose input/output channels to speed up processing, and batch processing—a new technique that permitted many individual tasks to be processed without a human operator's assistance.

In the late 1950s, Edward Teller proposed that the Laboratory commission a computer from commercial suppliers. In May 1960, Remington-Rand delivered the Livermore Advanced Research Computer (LARC) built to Livermore's specifications. At that time, there was an international moratorium on nuclear testing, and upgraded computing capabilities were urgently needed by weapon designers. With a high-speed magnetic core memory for storing about 240 kilobytes and 12 auxiliary memory drums for storing about 24 megabytes more, the LARC had such dense wiring that technicians had to use special tools similar to surgical instruments to probe its insides. Next came the "Stretch," an IBM machine with about 780 kilobytes of memory that could perform 100 billion calculations in a day.

As the 1960s progressed, the computer market changed. Most manufacturers abandoned the highly specialized large-computer market of the national laboratories to concentrate on the computer needs of the rapidly growing business and financial markets. In 1963, the Laboratory turned to Control Data Company (CDC), which furnished all of Livermore's supercomputers for the next 15 years, including the CDC 6600 in 1964 and the CDC 7600—10,000 times faster than the original Univac-1—in 1969. The Laboratory received serial number 1 of each of the machines and, by using them, helped CDC ready their computers for the wider commercial market.

The Univac was the first computer to store information on magnetic tape. Running a program was a hands-on operation, with a physicist or programmer toggling console switches to execute the problem. Although highly accurate, the Univac was cantankerous, breaking down two or three times a day. Early workers regarded it as an "oversized toaster."

Entering a Parallel Universe

About this time, computers began exploiting computational parallelism. The CDC STAR-100s in 1976, followed by the Cray 1s, introduced vector architectures. Cray came out with the first closely coupled processor systems with its two-processor Cray X-MPs. The final Cray machine, installed at the National Energy Research Scientific Computing Center (now located at Lawrence Berkeley National Laboratory), had 16 central processing units (CPUs) and about 2 megabytes of memory.

In the early 1990s, massively parallel machines—that is, employing scalar architectures—such as the Meiko and the BBN (by Bolt, Beranek, and Newman) began to arrive at the Laboratory. As Mike McCoy, a deputy associate director for Livermore's Computation Directorate, explains, "About this time, we began looking at not just sheer capability, which has been the motivator at the Lab since day one, but price performance as well. Up to and including the Crays, we would depend on a single vendor to supply the capability we needed.

Part of getting the price performance we needed involved moving away from specialized processors for parallel machines to commodity processor systems." The Meiko and the BBN were the first supercomputers of this type. Instead of using a few, enormous, one-of-a-kind processors, the Meiko and the BBN used many mid-sized workstation processors (the BBN, for instance, had 128 such processors). "We learned how to build software for parallel systems on these computers," notes McCoy. "These systems were what made us able to transition to the massively parallel ASCI [Advanced Simulation and Computing program, formerly called Accelerated Strategic Computing Initiative] systems."

In 1995, the Department of Energy and its defense laboratories—Livermore, Los Alamos, and Sandia—were directed to undertake the activities necessary to ensure continued stockpile performance in the absence of underground nuclear testing. DOE's ASCI program is a key component to meeting this challenge. The ASCI program is developing a series of ever more powerful, massively parallel supercomputers that employ thousands of processors working in unison to simulate the performance of weapons in an aging nuclear stockpile. The second ASCI supercomputer—the Blue Pacific, built by IBM—was received at Livermore in September 1996. It was installed, powered up, and running calculations within two weeks. IBM's ASCI White, which was delivered to the Laboratory in three stages during the summer of 2000, is currently the world's most powerful computer. Performing 12 trillion operations per second (teraops), it is 30 billion times faster than the Laboratory's very first computer, the Univac-1.

In late 1999, Livermore researchers achieved a major milestone with the first-ever three-dimensional simulation of a nuclear weapon's primary (the first stage of a hydrogen bomb) using the ASCI Blue Pacific. The simulation ran a total of 492 hours on 1,000 processors and used 640,000 megabytes of memory in producing 6 million megabytes of data contained in 50,000 graphics files. A second major milestone, a three-dimensional simulation of a nuclear weapon secondary, was completed on ASCI White in spring of 2001. Late in 2001, Livermore and Los Alamos met a third milestone on this system, coupling the primary and secondary.

Forward to the Future

With all that has occurred in the last 50 years, it's nearly impossible to predict what the far future will hold. "To meet ASCI's requirements, more powerful processors with more memory are needed to create a proxy of the world around us, from the microscale to the macroscale," says Dona Crawford, associate director of Computation. "At the same time, we are creating terabytes—soon to be petabytes—of data." Two trends, Crawford notes, need to continue into the near future. First, the Laboratory must acquire faster processors with more memory for simulation and modeling. Second, new ways must be created for storing, finding, visualizing, and extracting the data. "We need to merge high-end computing and high-end information technology," she concludes. "Scientific data management, in particular, is becoming more of an issue." (See the box on software development, p. 23.)

Within three years, the ASCI community plans to locate a 60-teraops machine with approximately 20,000 processors—the Purple machine—at Livermore in the soon-to-be-built Terascale Simulation Facility. Groundbreaking for this facility will occur in spring of this year. Beyond Purple lies a world of tantalizing prospects, including BlueGene/L (L stands for

The ASCI White, with power to perform 12 trillion operations per second, was delivered to the Laboratory during the summer of 2000.

Software Development

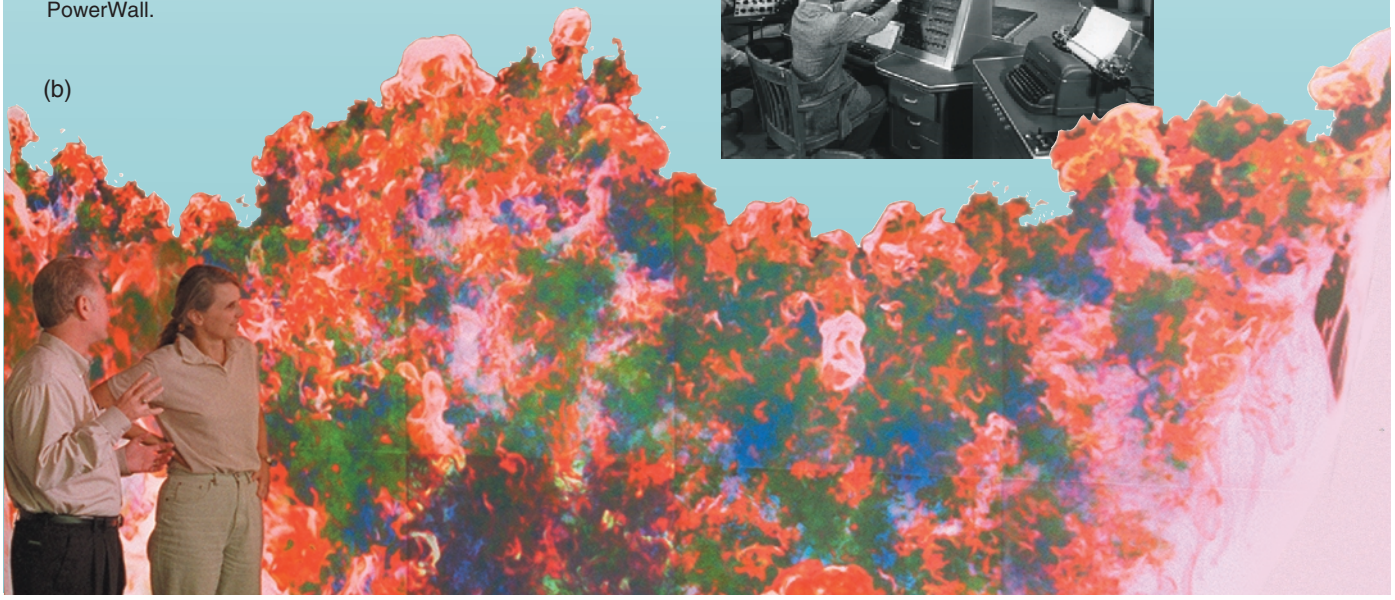
The supercomputers Livermore acquired were often the first of their kind—sometimes even prototypes of the final version—and had little support software. As a result, Livermore's scientists took the lead in developing software for operating the system (such as assemblers, loaders, and input/output routines) as well as for simulating and modeling physical phenomena. Because Laboratory users pushed the machines to their limits, Livermore's programmers had to find—or often invent—the most efficient programming and computing techniques. For instance, when certain aspects of the FORTRAN computer language turned out to be awkward or limiting for scientific applications, software developers created an enhanced version called LRLTRAN (Lawrence Radiation Laboratory FORTRAN). It took nearly two decades for many of the advanced features in LRLTRAN to be incorporated into standard FORTRAN. In addition, Livermore developed the time-sharing concept—in which a central processing unit (CPU) alternates between working on several jobs at once rather than one at a time—into its first practical use for supercomputers. The Laboratory also led the way in computational physics (the numerical simulation of physical phenomena) on supercomputers. Computer codes often hundreds of thousands of lines long are used to model complex processes that are too difficult or impossible to calculate exactly.

This expertise in codes continues today, with computer scientists writing or adapting codes for large parallel machines such as the Advanced Simulation and Computing (ASCI, for its former name, Accelerated Strategic Computing Initiative) systems. The sophisticated codes now under development promise a level of physical and numerical accuracy more like that of a scientific experiment than a traditional numerical simulation. In materials modeling, for instance, ASCI White will track 10 billion atoms simultaneously, beginning to predict what scientists will see when imaging materials through electron microscopes.

Interpreting, visualizing, and accessing the data are themselves challenges. From the early days of simple x–y plots to today's complex three-dimensional images, Livermore computer scientists have developed programs to help researchers access massive quantities of data in visual formats. This capability is particularly important for the future, given that ASCI-level supercomputers generate terabytes—soon to be petabytes—of raw data. As computers grow in speed, number-crunching capability, and memory, scientific researchers edge into data overload as they try to find meaningful ways to interpret data sets holding more information than the U.S. Library of Congress. Livermore's computer scientists are exploring techniques such as metadata, data-mining, and visualization to deal with the massive amounts of data.

(a) Results from Univac computations were spewed out as reams of numbers by a Remington-Rand typewriter modified to serve as an on-line printer. (b) Results from today's complex simulations are converted by powerful visualization software into three-dimensional detailed views, such as this one shown on the Livermore-developed PowerWall.

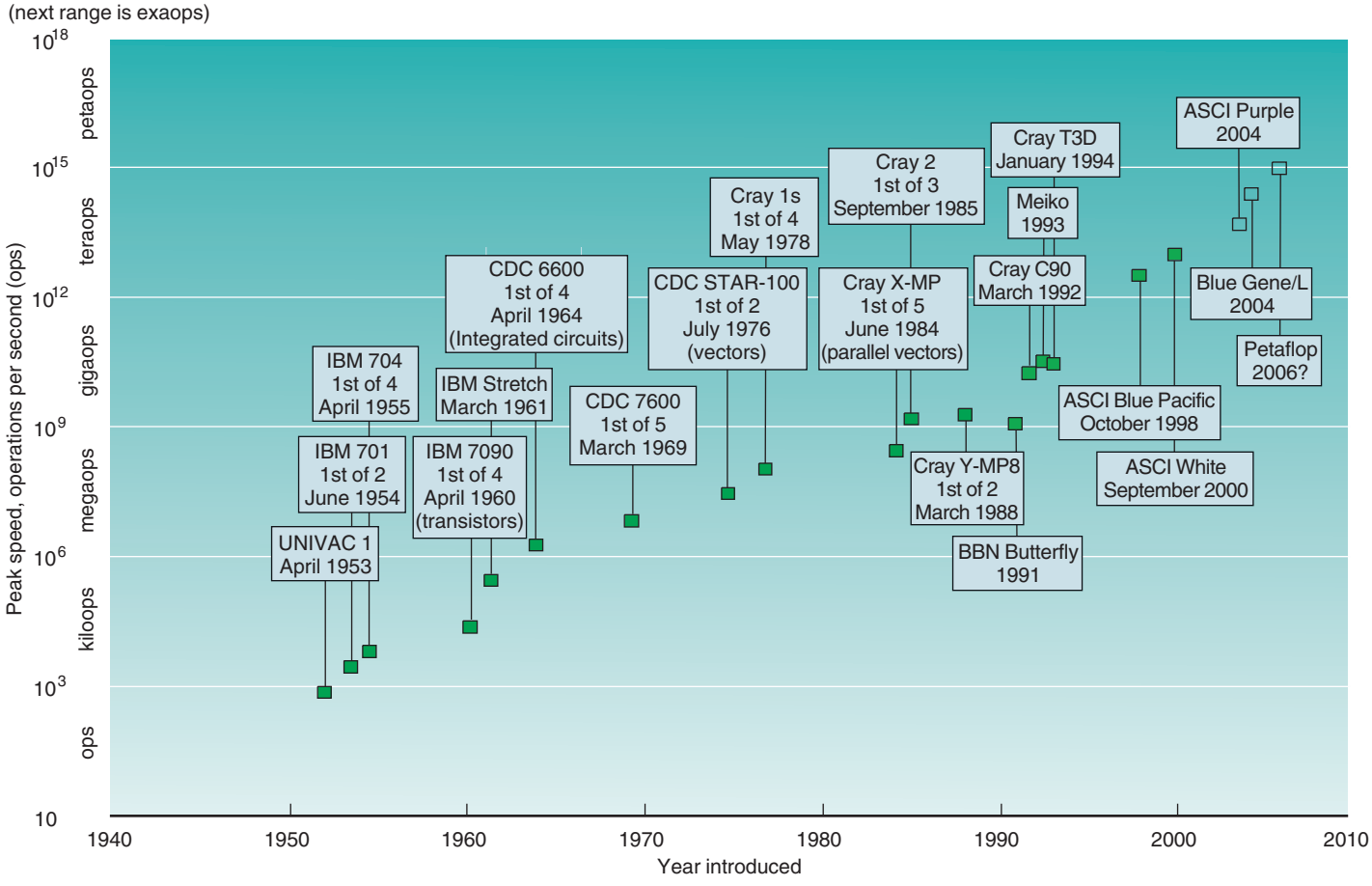
(b)



light), a machine 15 times faster than today's fastest supercomputers. "BlueGene/L would be a radical departure from previous machines," notes Mark Seager, program manager for ASCI Terascale Systems. BlueGene/L would use IBM's "system on a chip" based on commercial embedded-processor technology. Seager explains, "Embedded processors are optimized for low cost and low power and for usability in many configurations." McCoy notes that systems like BlueGene/L are the next big step in getting more performance at a lower price. "From ASCI Red to Purple, the systems use workstation processors targeted at the high-performance computing market. With BlueGene/L, we'd move from that curve to one using commodity PC processors. At the same time, we'd also move from using proprietary vendor software to open-source software such as the Linux operating system. These moves would result in considerably lower costs for the power we'd get—about $0.1 million per teraops for BlueGene/L, compare with White's $9 million per teraops or Purple's $3 million per teraops."

A rendering of the Terascale Simulation Facility, which will house ASCI Purple, a machine capable of performing 60 trillion operations per second.

BlueGene/L would have 65,000 nodes or cells, 360 teraops—larger than the total computing power of the top 500 supercomputers in the world today—and between 16 and 32 terabytes of memory. "The questions facing us for BlueGene/L are: Can we build it? Can we write software for it? Can we write scientific simulations for it? We believe the answers are 'yes' to all," says Seager. Six times more powerful than ASCI Purple, BlueGene/L would open new



Timeline of Livermore's key supercomputers and their peak computing power.

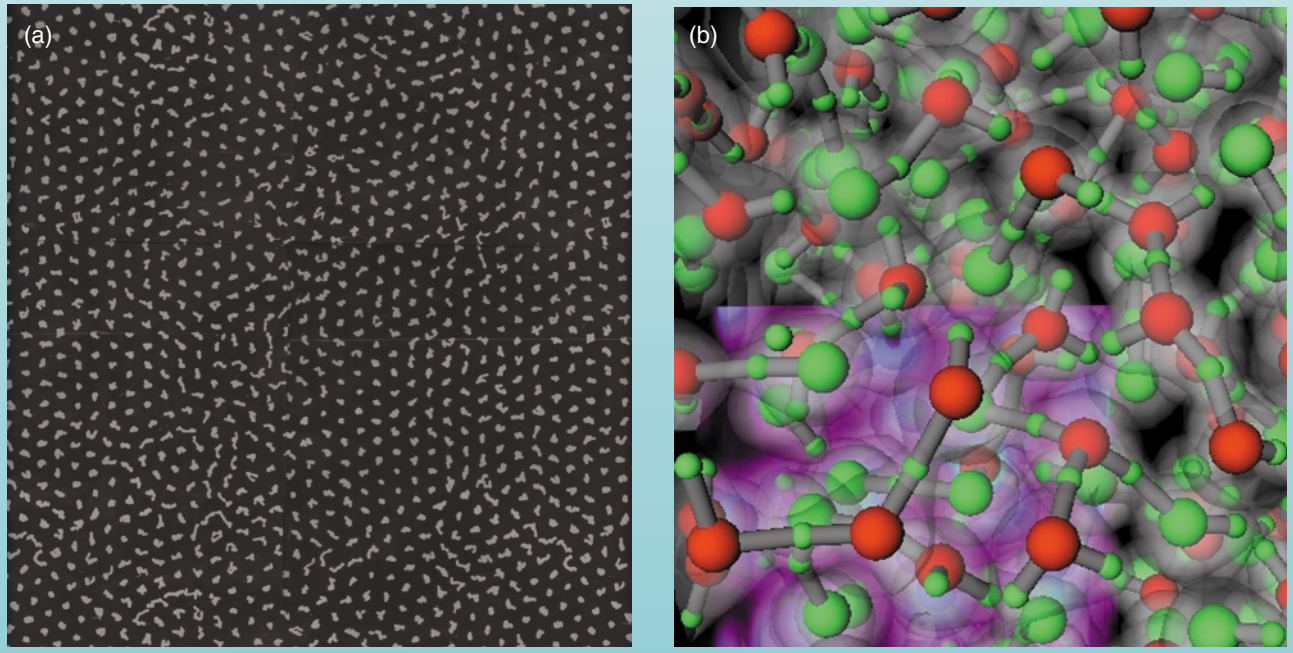
From Personal Computers to Clusters

While supercomputers were always an integral part of Livermore's nuclear weapons design and stockpile stewardship efforts, other areas of the Laboratory also benefited from the computer revolution, particularly as computer systems became smaller, more powerful, and less expensive. In the 1970s, small microprocessor systems such as the PDP-11 began to be used in research tasks—digitizing oscilloscope traces, for example, and controlling experiments in chemistry labs. Then the personal computer, or PC, arrived, followed by more powerful microcomputers and workstations.

By the mid-1990s, many researchers in nonweapons areas were taking advantage of the relatively inexpensive and powerful desktop computers in their offices, or they used terminals tied to scientific workstations. Although having many advantages, these machines did not always have the necessary computational power, particularly for running three-dimensional simulations, which require the enormous computational horsepower of the latest generation of supercomputers.

Finally, in 1996, Livermore programs and researchers outside the stockpile stewardship effort gained access to unclassified Accelerated Strategic Computing Initiative–level terascale supercomputers through the Multiprogrammatic and Institutional Computing Initiative (M&IC). (See *S&TR*, October 2001, pp. 4–12.)

The M&IC acquired increasingly more powerful clusters, or groups, of computers such as the Compaq TeraCluster2000. As the Laboratory begins to celebrate its 50th year, Livermore researchers are at the forefront of simulating a wide range of physical phenomena in the unclassified arena, including the fundamental properties of materials, complex environmental processes, biological systems, and the evolution of stars and galaxies. Mike McCoy, deputy associate director for Integrated Computing and Communications, says, "Livermore Computing has become an institutional resource much like the library, a place where researchers from any program can expect resources to support their research."



Particle tracking past and present contributes to a better understanding of the fundamental properties of materials. (a) In this example of Livermore physicist Berni Alder's pioneering computer simulation work, published in *Physics Review* in 1962, a simulation performed on the Livermore Advanced Research Computer supercomputer tracked 870 particles over time. (b) Recent work on the ASCI Blue Pacific includes this quantum-level simulation of a mixture of hydrogen fluoride and water molecules at high temperatures and pressures. The simulation tracked hundreds of atoms and thousands of electrons extremely accurately.

vistas in scientific simulation. "For instance," says Seager, "you begin to approach what you need to model complex biological systems. Having BlueGene/L would be like having an electron microscope when everyone else has optical microscopes, it's that much of a leap forward."

And after that? "Perhaps there will be computers that align DNA to do processing, or Josephson junction machines, or all-optical machines. Who knows what will happen in hardware, software, and information technology in the next 50 years," says Crawford. "Whatever innovation ends up driving the next era in computing will probably explode on the scene, much like the Internet did."

Fifty years ago, the birth of the electronic scientific computer ushered in a new era. Rather than having to accept crude approximations because the more exact equations were too difficult to solve, scientists could use the great speed and high accuracy of computers to simulate the phenomena they were trying to understand. Livermore researchers pushed the limits of each advanced machine, from using crude one-dimensional codes on the Univac and early IBM machines to complex three-dimensional codes on the current ASCI machines. Through ASCI and the coming generations of supercomputing machines, another era appears on the horizon, an era in which enormously fast and powerful supercomputers will allow computer simulation to come into its own as a predictive science along with theory and experiment.

—Ann Parker

Key Words: Advanced Simulation and Computing (ASCI), ASCI BlueGene/L, ASCI Purple, ASCI White, computation history, Cray, IBM, Livermore Advanced Research Computer (LARC), supercomputer, Univac.

For further information, see the following Web sites on computation, past and present:

Computation at LLNL:
www.llnl.gov/comp/

ASCI at LLNL:
www.llnl.gov/asci/

Oral History of Computation at LLNL:
www.nersc.gov/~deboni/Computer.history/

For further information about the Laboratory's 50th anniversary celebrations, see the following Web site:

www.llnl.gov/50th_anniv/

Lawrence Livermore National Laboratory

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

High Numerical Aperture Ring Field Projection System for Extreme Ultraviolet Lithography

Russell Hudyma

U.S. Patent 6,318,869 B1

November 20, 2001

An all-reflective optical system for a projection photolithography camera has a source of extreme ultraviolet radiation, a wafer, and a mask to be imaged on the wafer. The optical system includes a first concave mirror, a second mirror, a third convex mirror, a fourth concave mirror, a fifth convex mirror, and a sixth concave mirror. The system is configured so that 5 of the 6 mirrors receive a chief ray at an incidence angle of less than substantially 12 degrees, and each of the 6 mirrors receives a chief ray at an incidence angle of less than substantially 15 degrees. Four of the six reflecting surfaces have an aspheric departure of less than substantially 7 micrometers. Five of the 6 reflecting surfaces have an aspheric departure of less than substantially 14 micrometers. Each of the 6 reflecting surfaces has an aspheric departure of less than 16 micrometers.

Highly Damped Kinematic Coupling for Precision Instruments

Layton C. Hale, Steven A. Jensen

U.S. Patent 6,325,351 B1

December 4, 2001

A highly damped kinematic coupling for precision instruments. The kinematic coupling provides support while causing essentially no influence to its natural shape. Such influences would come, for example, from manufacturing tolerances, temperature changes, or ground motion. The coupling uses three ball–cone constraints, each combined with a released flexural degree of freedom. This arrangement enables a gain of higher load capacity and stiffness, but can also significantly reduce the friction level in proportion to the ball radius divided by the distance between the ball and the hinge axis. The blade flexures reduce somewhat the stiffness of the coupling and provide an ideal location to apply constrained-layer damping, which is accomplished by attaching a viscoelastic layer and a constraining layer on opposite sides of each of the blade flexures. The three identical ball–cone flexures provide a damped coupling mechanism to kinematically support the projection optics system of an extreme ultraviolet lithography system or other load-sensitive apparatus.

Method for Fabricating Composite Carbon Foam

Steven T. Mayer, Richard W. Pekala, James L. Kaschmitt

U.S. Patent 6,332,990 B1

December 25, 2001

Carbon aerogels used as a binder for granularized materials, including other forms of carbon and metal additives, are cast onto carbon- or meta-fiber substrates to form composite carbon thin-film sheets. The thin-film sheets are used in electrochemical energy storage applications, such as electrochemical double-layer capacitors (aerocapacitors), lithium-based battery insertion electrodes, fuel cell electrodes, and electrocapacitive deionization electrodes. The composite carbon foam may be formed by prior known processes, but with the solid particles being added during the liquid phase of the process, that is, before gelation. The other forms of carbon may include carbon microspheres, carbon powder, carbon aerogel powder or particles, or graphite carbons. Metal and/or carbon fibers may be added for increased conductivity. The choice of materials and fibers will depend on the electrolyte used and the relative trade-off of system resistivity and power to system energy.

Apparatus and Method for Collection and Concentration of Respirable Particles into a Small Fluid Volume

Jonathan N. Simon, Steve B. Brown

U.S. Patent 6,337,213 B1

January 8, 2002

An apparatus and method for the collection and concentration of respirable particles into a small fluid volume. The apparatus captures and concentrates (1 to 20 micrometers) respirable particles into a submilliliter volume of fluid. The method involves a two-step operation, collection and concentration. Collection of particles is done by a wetted surface with small vertical slits that act as capillary channels. Concentration is carried out by transferring the collected particles to a small-volume (submilliliter) container by centrifugal force, which forces the particles through the vertical slits to a nonwetted wall surface of a container. The particles are deflected to the bottom of the container and analyzed with a portable flow cytometer or a portable polymerase chain reaction DNA analysis system.

Method for Detection of Extremely Low Concentration

Brian D. Andresen, Fred S. Miller

U.S. Patent 6,338,824 B1

January 15, 2002

An ultratrace detector system for handheld gas chromatography that is highly sensitive, for example, to emissions generated during production of weapons, biological compounds, or drugs. The detector system is insensitive to water, air, helium, argon, oxygen, and carbon dioxide. The system is basically composed of a handheld capillary gas chromatograph, an insulated heated redox-chamber, a detection chamber, and a vapor trap. As an example of how it works, the detector system may use gas-phase redox reactions and spectral absorption of mercury vapor. The gas chromatograph initially separates compounds that percolate through a bed of heated mercuric oxide in a silica or other metal aerogel material acting as an insulator. Compounds easily oxidized by mercuric oxide liberate atomic mercury, which subsequently passes through a detection chamber that includes a detector cell, such as quartz. The chamber is illuminated with a 254-nanometer ultraviolet mercury discharge lamp that generates the exact mercury absorption band used to detect the liberated mercury atoms. Atomic mercury strongly absorbs 254-nanometer energy and is therefore a specific signal for reducing compounds eluting from the capillary gas chromatograph. Afterward, the atomic mercury is trapped, for example, in a silicon-aerogel trap.

Method for Forming a Barrier Layer

Timothy P. Weihs, Troy W. Barbee, Jr.

U.S. Patent 6,339,020 B1

January 15, 2002

Cubic or metastable cubic refractory metal carbides act as barrier layers to isolate, adhere to, and passivate copper in semiconductor fabrication. One or more barrier layers of the metal carbide is deposited in conjunction with copper metallizations to form a multilayer characterized by a cubic crystal structure with a strong texture. Suitable barrier-layer materials include refractory transition metal carbides such as vanadium carbide, niobium carbide, tantalum

carbide, chromium carbide, tungsten carbide, and molybdenum carbide.

Apparatus for Improving Performance of Electrical Insulating Structures

Michael J. Wilson, David A. Goerz
U.S. Patent 6,339,195 B1
January 15, 2002

This invention removes the electrical field from the internal volume of high-voltage structures, for example, bushings, connectors, capacitors, and cables. The electrical field is removed from inherently weak regions of the interconnect, such as between the center conductor and the solid dielectric, and placed in the primary insulation. This is accomplished by providing a conductive surface on the inside surface of the principal solid dielectric insulator surrounding the center conductor and connecting the center conductor to the conductive surface. The advantages of moving the electric fields from the weaker dielectric region to a stronger area are improved reliability, increased component life and operating levels, reduced noise and losses, and smaller, compact design. This electric field control approach is currently possible on many existing products at a modest cost. Several techniques are available to provide the level of electric field control needed. Choosing the optimum technique depends on material, size, and surface accessibility. The simplest deposition method uses a standard electroless plating technique, but other metallization techniques include vapor and energetic deposition, plasma spraying, conductive painting, and other controlled coating methods.

Method for Beam Steering Compensation in an Ultra-High Power Liquid Laser

Earl R. Ault
U.S. Patent 6,339,608 B1
January 15, 2002

Waste heat from the excitation process and absorption of laser radiation causes laser media to heat up and induces optical wavefront distortion, which in turn creates optical phase errors. This method uses a system to derive an error signal from the optical phase errors. The error signal is fed back to the power supplies for the semiconductor diodes that excite the lasing liquid. This results in the introduction of an electrically controllable wedge into the optical cavity to correct the optical phase errors.

Solar Cell Module Lamination Process

Paul G. Carey, Jesse B. Thompson, Randy C. Aceves
U.S. Patent 6,340,403 B1
January 22, 2002

Fluoropolymers are used to laminate solar cell modules and protect them from adverse environmental conditions, thus enabling more extended use of solar cells, particularly in space applications. A laminate of fluoropolymer material provides a hermetically sealed solar cell module structure that is flexible and very durable. The laminate is virtually chemically inert, highly transmissive in the visible spectrum, dimensionally stable at temperatures up to about 200°C, highly abrasion-resistant, and exhibits very little ultraviolet degradation.

Awards

Valerie Roberts, area integration manager of infrastructure for the National Ignition Facility (NIF), recently was named **Outstanding Woman in Construction**, an award cosponsored by Arizona State University and the Greater Phoenix Chapter of the National Association of Women in Construction.

Roberts is a 1987 graduate of the Del E. Webb School of Construction at Arizona State University. She received her M.S. in civil engineering from the University of New Mexico in 1991. Her experience in engineering and construction includes industrial as well as defense and large Department of Energy projects. For NIF, she has successfully managed the construction of the conventional facility and the design, fabrication, and installation of the laser beam-path infrastructure.

The Livermore Chamber of Commerce has honored **Karen Kiernan** with its **2001 Education Award**. The award is given to a business, individual, or organization that contributes to the "excellence of education" in Livermore.

Kiernan is the special projects manager for Public Affairs. She was recognized for a long history of promoting education activities from grade-school levels to community college. She was cited for her development, implementation, and management of the Tri-Valley Science and Engineering Fair, now in its sixth year.

Of the honor she received, Kiernan said, "I've always been a big believer in education–business partnerships, so it is especially rewarding when the community finds my work valuable. I also appreciate Laboratory management recognizing the importance of LLNL contributing to the community and supporting my endeavors."

Paul R. Dickinson, assistant director for program development in the University Relations Program, was elected **president** of **Keep California Beautiful**, a statewide nonprofit environmental education group that promotes individual responsibility for California's environment through community-based litter prevention and recycling programs. He has been a member of this group for about 7 years.

For 10 years, Dickinson had served as executive director of the Partnership for Environmental Technology Education, a nonprofit organization that he founded. With support from the Laboratory, he is now applying his experience in program development to expanding the influence of Keep California Beautiful.

Abstracts

Tracking Down Virulence in Plague

Bioscientists at Livermore and elsewhere across the Department of Energy complex are studying the plague bacterium (*Yersinia pestis*) as part of the National Nuclear Security Administration's Chemical and Biological National Security Program. At Livermore, work continues on the development of DNA signatures that can be used to quickly detect and identify plague outbreaks. In the Pathogen Pathway Project, *Y. pestis* is being used as a prototype for studying virulence and the interactions of a pathogen and its host. Another *Yersinia* bacterium (*Y. pseudotuberculosis*) has been sequenced for comparative purposes. Its DNA is very similar to that of *Y. pestis*, but it causes only mild intestinal discomfort. Suppression subtractive hybridization is being used to compare the DNA of the two *Yersinia* genomes. The response of thousands of *Y. pestis* genes is being determined with transcript profiling. A gene elimination, or knock-out, experiment to learn about specific genes is just getting under way. A mass spectrometry approach is being used to identify virulence proteins.

Contact:

Pat Fitch (925) 422-3276 (fitch2@llnl.gov).

L-Gel Decontaminates Better Than Bleach

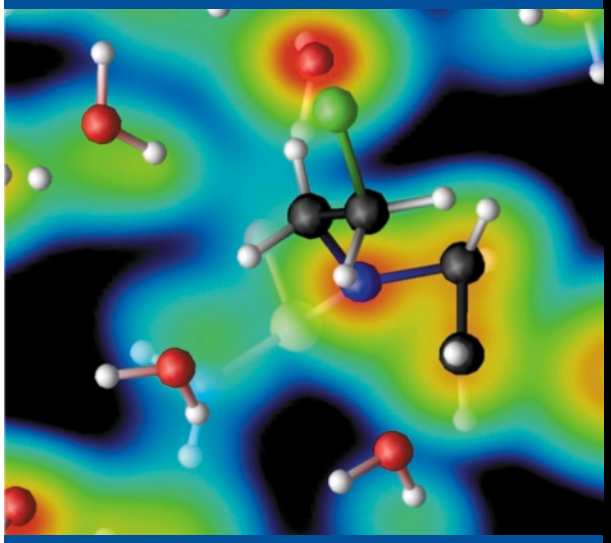
A team of Livermore researchers has developed a decontamination compound called L-Gel, which combines a mild, commercially available oxidizer with a silica gelling agent. The material is nontoxic, noncorrosive, easy to manufacture, easily deployable, and relatively inexpensive (about $1 for every square meter applied). L-Gel sticks to walls, ceilings, and other materials for effective decontamination. Tests in Livermore's laboratories and field trials at U.S. and foreign facilities show that L-Gel is extremely effective at decontaminating all classes of chemical warfare agents as well as surrogates for biological warfare agents. The material is premixed and then shipped and stored as a semisolid. If unopened, its shelf life is expected to exceed a year. It is reliquefied to a house-paint consistency by shaking or stirring and can be applied using any type of commercially available spray device.

Contact:

Ellen Raber (925) 422-3985 (raber1@llnl.gov).

U.S. Government Printing Office: 2002/783-051-70012

Simulating Atomic Behavior during Experiments



Using quantum molecular dynamics simulations, scientists can get an accurate picture of atomic-level interactions during an experiment.

Also in April

- ***The Forensic Science Center's analysis of the smallest bits of evidence helps solve crime locally, nationally, and internationally.***
- ***Compact and ultrapowerful, Livermore's solid-state heat-capacity laser makes possible a mobile tactical weapon of the future.***
- ***50th Anniversary Highlight—Since the Laboratory's beginnings, innovative engineering has allowed Livermore to excel at science and technology in the national interest.***

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