Science & Technology Review
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Lawrence Livermore National Laboratory

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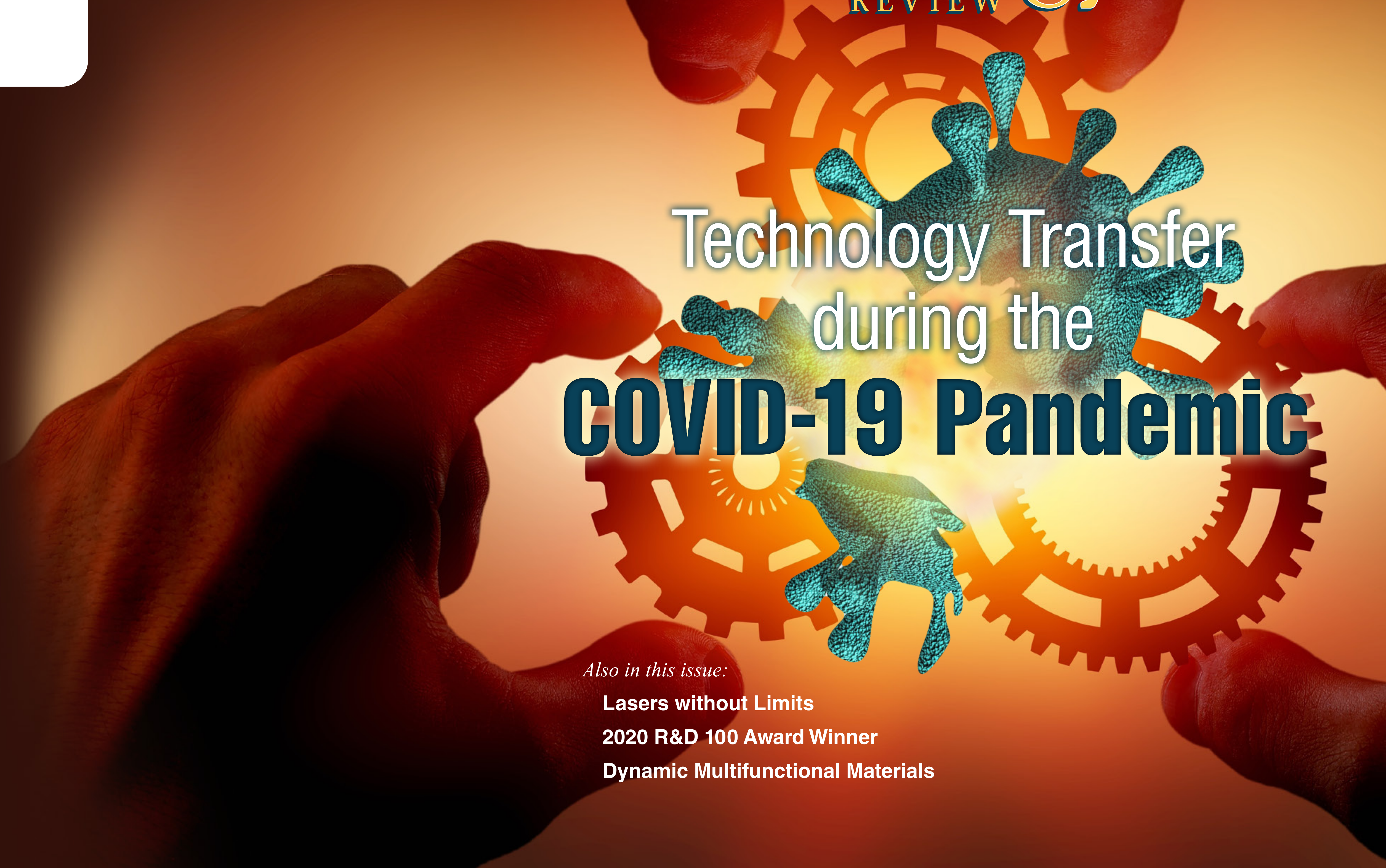
July 2021



Technology Transfer during the COVID-19 Pandemic

Also in this issue:

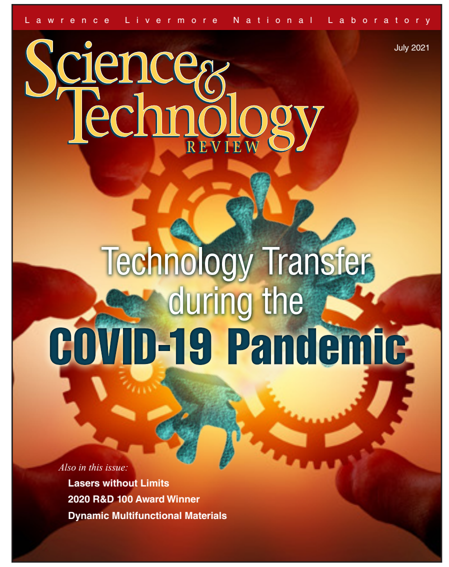
Lasers without Limits

2020 R&D 100 Award Winner

Dynamic Multifunctional Materials

About the Cover

In the early weeks of the COVID-19 pandemic, Lawrence Livermore researchers mobilized to address emerging challenges and develop capabilities for detecting the SARS-CoV-2 virus and fighting COVID-19, the diseased caused by the virus. As described in the article beginning on p. 4, the Laboratory's Innovation and Partnerships Office provided technology transfer expertise to deploy existing, in-development, and new technologies to help detect SARS-CoV-2 and treat COVID-19.



Cover design: Mary J. Gines

About *S&TR*

At Lawrence Livermore National Laboratory, we focus on science and technology research to ensure 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 eight 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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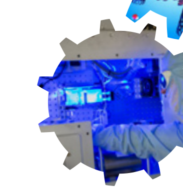


Departments

Deep Learning Improves Disease Diagnosis

Livermore computer scientists and colleagues at IBM Research Almaden in San Jose, California have developed new deep-learning models to accurately diagnose diseases from x-ray images with less labeled data. The team's paper, "Self-Training with Improved Regularization for Sample-Efficient Chest X-Ray Classification," won the Best Paper Award for Computer-Aided Diagnosis at the 2021 SPIE Medical Imaging Conference.

The machine-learning technique, which includes novel regularization and self-training strategies, addresses some well-known challenges in the adoption of artificial intelligence for disease diagnosis. The team applied their learning approach to benchmark data sets of chest x-rays containing both labeled and unlabeled data to diagnose five different heart conditions: cardiomegaly, edema, consolidation, atelectasis, and pleural effusion. Using a framework that applies strategies including data augmentation, confidence tampering, and self-training, the researchers saw an 85 percent reduction in the amount of labeled data required to achieve the same performance as the existing state-of-the-art in neural networks trained on the entire labeled data set.

Livermore computer scientist Jay Thiagarajan explains, "We're trying to address a fundamental problem. Data comes from different hospitals, it's difficult to label, and experts don't have the time to annotate it all. It's often posed as a multi-label classification problem, where we are looking at the presence of multiple diseases in one shot. We can't wait to have enough data for every combination of disease conditions, so we built a new technique that tries to compensate for this lack of data using regularization strategies that can make deep-learning models much more efficient, even with limited data. We've demonstrated that accurate models can be created with limited labeled data and perform as well or even better than neural networks trained on much larger labeled data sets."

Contact: Jay Thiagarajan (925) 424-2255 (jayaramanthi1@llnl.gov).

Missing Physics in Explosive Hotspots Uncovered

Scientists at the Lawrence Livermore National Laboratory Energetic Materials Center and Purdue University used the Laboratory's Quartz supercomputer to run large-scale, all-atom simulations to study the longtime relaxation properties of the kinetic and potential energy in hotspots and uncover missing physics in TATB (1,3,5-triamino-2,4,6-trinitrobenzene) hotspots and other explosives critical to managing the nation's nuclear stockpile. Their research is featured in the March 11, 2021, issue of the *Journal of Physical Chemistry Letters*.

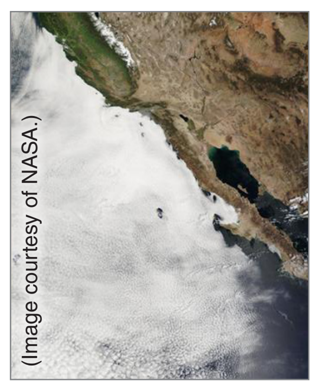
Livermore computational chemist Matthew Kroonblawd explains that "continuum-level multiphysics models used to assess safety and performance are highly empirical, making it difficult to transfer explosives models to different application conditions. The lack of transferable models is especially true for insensitive high explosives such as TATB. It is still not possible to build an explosives model from first principles, indicating that key physics aspects are missing."

The work highlights a neglected physical aspect of the early stages of explosive hotspot formation, localized regions of elevated temperature and potential energy that accelerate chemistry. A better understanding of how hotspots form and evolve provides a route to systematically improve models used to assess stockpile performance and safety. Identifying the cause behind differences in hotspot reaction rates will inform more general explosives models and improve their predictive accuracy and transferability.

Contact: Matthew Kroonblawd (925) 422-2221 (kroonblawd1@llnl.gov).

Reduction in Marine Clouds Amplify Warming

Low-level clouds, such as the marine stratocumulus clouds responsible for gloomy San Francisco summers, are widespread over global oceans and cool the planet by shading the surface from sunlight. A new analysis of satellite cloud observations, however, indicates that global warming causes these clouds to decrease, and that, overall, their cooling effect will be modestly reduced as the concentration of carbon dioxide (CO_2) in the atmosphere increases. The work, led by researchers at Lawrence Livermore National Laboratory in collaboration with colleagues from Scripps Institution of Oceanography and the NASA Langley Research Center, appears in the May 13, 2021, issue of *Nature Climate Change*.



(Image courtesy of NASA.)

The new study estimated how marine low clouds respond to natural variations in large-scale meteorological conditions, used global climate model simulations to determine how these meteorological conditions will change as atmospheric CO_2 increases, and then calculated how the clouds will respond to this modified meteorological environment.

To test their method, the researchers turned to a highly unusual and extreme sea-surface warming event, or "marine heat wave," observed in the northeast Pacific Ocean in 2015. Former Lawrence Livermore climate scientist and lead author of the study, Tim Myers says, "We showed that we could accurately predict the cloud changes detected by satellites during the marine heat wave, so we are confident we can predict how the clouds will respond to global warming."

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Commentary by Anup Singh

How Can We Help?

LAST month's issue of *Science & Technology Review* profiled Lawrence Livermore National Laboratory's dynamic approach to tackling the COVID-19 pandemic. By collaborating across the 17 Department of Energy (DOE) national laboratories and its external research partners, we deployed our bioengineering, biology, and biocomputational expertise to improve the detection and diagnosis of the SARS-CoV-2 virus that causes COVID-19 and help develop the vaccines and antivirals that could mitigate it. Decades of mission-critical work prepared the Laboratory for this response, and from the molecular to the national level, we have been at the vanguard in proposing workable solutions to the challenges posed by this terrible pandemic. But it is not enough to research and develop technological solutions and call it a day. An essential component of the Laboratory's mission fulfillment is ensuring that our scientific and engineering solutions make their way out into world and where they can serve millions.

In this issue of *Science & Technology Review*, the feature article on p. 4, explores the Laboratory's efforts to do just that during the pandemic. Over the last year and a half, our Innovation and Partnerships Office (IPO) worked to identify and transfer Livermore technology and engineering expertise to the marketplace to tackle COVID-19 and help make a difference. The IPO's agility, creativity, and know-how are a testament to the importance of "tech transfer" as part of Lawrence Livermore's mission fulfillment. Extant Livermore technology, built by bioengineers to detect various pathogens and developed and commercialized over the last two decades, provided critical tools to quickly detect the SARS-CoV-2 virus. This article also examines how a diverse team of Lawrence Livermore engineers and bioscientists joined together within days of COVID-19 shelter-in-place orders to develop, from scratch, a medical ventilator using parts outside the medical supply chain to avoid stressing manufacturers already producing medical devices at full capacity. A first for the scientists, engineers, and IPO team who transferred "engineering know-how" rather than technology to private sector partners.

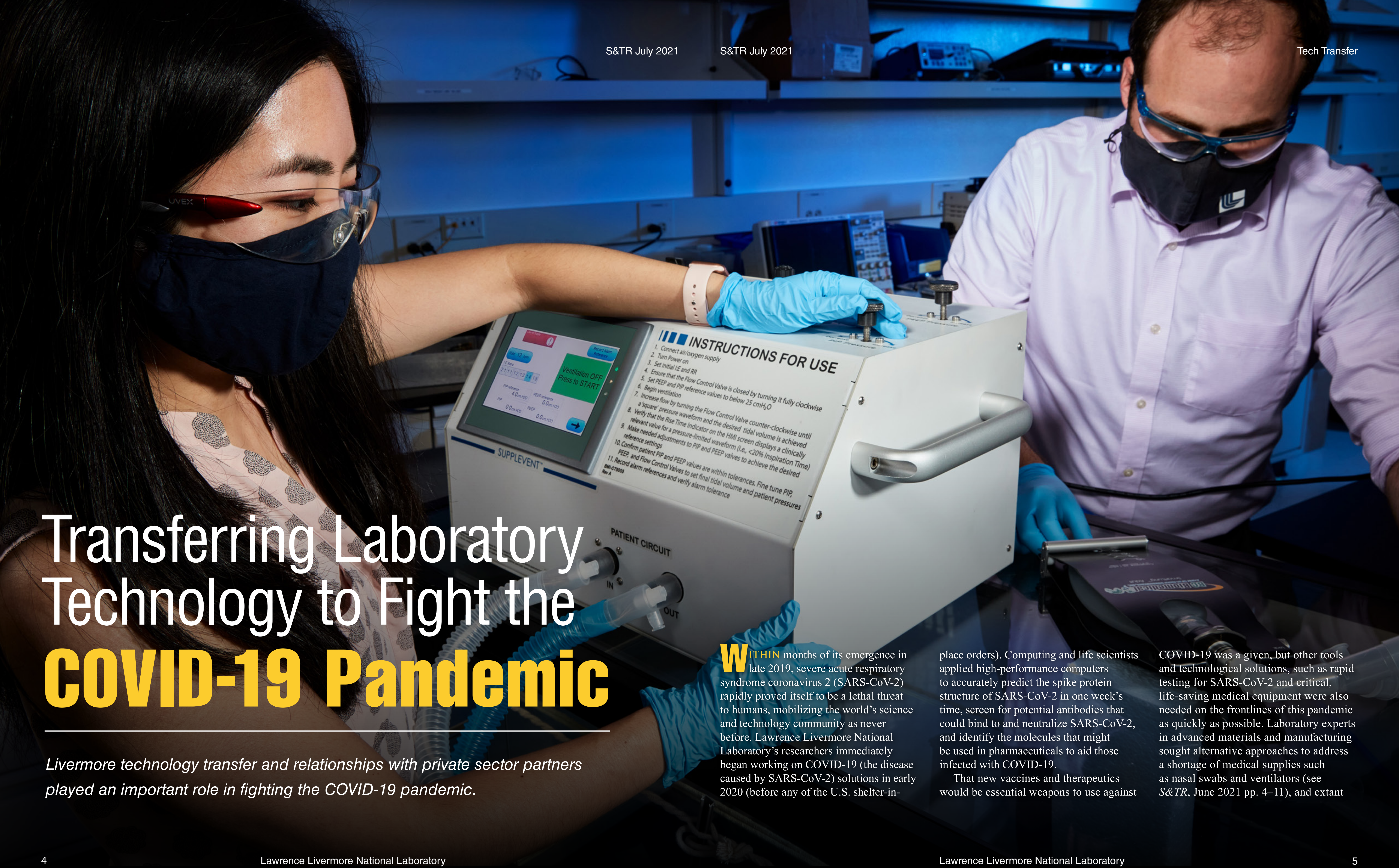
At the Laboratory, "How can we help?" was the first question on everyone's mind in March of 2020. Today, we continue to evaluate lessons learned during this pandemic and are preparing for the next. In doing so, we must keep long-term research in mind. The innovation base at Livermore continues to make translational impact in many other areas. The article on p. 12 highlights Versatile Cold Spray (VCS), an R&D 100 award-winning device that evenly deposits thermoelectric materials onto surfaces that could be used to capture energy and convert it into electricity. With further development, VCS promises to open up new pathways for the private sector to develop more cost efficient and reliable thermoelectric generation that could make energy use more sustainable.

The research highlight on p. 16 describes how a multidisciplinary Livermore team—materials scientists, computational scientists, engineers, biologists, and chemists—came together to create a breathable material constructed from carbon nanotubes and chemical-absorbing polymers to protect warfighters against biological agents and chemical weapons. With successful technology transfer, this incredible fabric could shield healthcare workers in critical care facilities or first responders.

As the home of the National Ignition Facility (NIF), the world's most energetic laser, and other high-energy-density research facilities, Livermore excels in advancing laser technology. We are now developing powerful high-repetition-rate lasers that will be able to explore matter further by executing tens of thousands of laser shot experiments in the time it takes to perform a single NIF laser shot. As described in the article beginning on p. 20, through the synchronization and integration of machine learning, materials development, and high-performance computer simulations and modeling, the Laboratory will be embarking on a new era of discovery that will totally change how we think about and study photon science—and, in doing so, uncover new engineering capabilities that will meet the challenges facing the nation.

By bringing photon science, additive manufacturing, and high-performance computing together, we aspire to forge new avenues of science and engineering that will not only benefit other laboratories in the United States, but around the world. As we look toward the future, we must remain agile, and we must prepare for the challenges that the nation will face–whatever they may be.

■ Anup Singh is associate director for Engineering.



Transferring Laboratory Technology to Fight the COVID-19 Pandemic

Livermore technology transfer and relationships with private sector partners played an important role in fighting the COVID-19 pandemic.

WITHIN months of its emergence in late 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) rapidly proved itself to be a lethal threat to humans, mobilizing the world's science and technology community as never before. Lawrence Livermore National Laboratory's researchers immediately began working on COVID-19 (the disease caused by SARS-CoV-2) solutions in early 2020 (before any of the U.S. shelter-in-place orders). Computing and life scientists applied high-performance computers to accurately predict the spike protein structure of SARS-CoV-2 in one week's time, screen for potential antibodies that could bind to and neutralize SARS-CoV-2, and identify the molecules that might be used in pharmaceuticals to aid those infected with COVID-19.

That new vaccines and therapeutics would be essential weapons to use against COVID-19 was a given, but other tools and technological solutions, such as rapid testing for SARS-CoV-2 and critical, life-saving medical equipment were also needed on the frontlines of this pandemic as quickly as possible. Laboratory experts in advanced materials and manufacturing sought alternative approaches to address a shortage of medical supplies such as nasal swabs and ventilators (see *S&TR*, June 2021 pp. 4–11), and extant

Livermore technologies previously developed to detect pathogens in clinical and biowarfare settings were swiftly adapted to spot SARS-CoV-2. During the pandemic, Livermore's Innovation and Partnerships Office (IPO) launched efforts to contribute to the fight against COVID-19 by accelerating the process of transferring Livermore technologies with COVID-fighting potential to its private sector partners. "Oftentimes, a technology with a great payback has a long, tortured story behind it," says Senior Science Advisor Dave Rakestraw, who coordinated Livermore's COVID-19 research response. "It can take decades for a technology to become the foundation of a successful company." To expedite the tech-transfer process during COVID, IPO deployed three key strategies: communicating and coordinating with existing commercial partners and the biomedical community, accelerating its licensing processes, and providing temporary royalty-free licenses for existing technologies with anti-COVID potential.

Strong Diagnostics

Past Laboratory success stories of licensed diagnostic technologies became contemporary success stories against COVID-19 early in the pandemic. Two companies, Bio-Rad Laboratories, Inc.and Cepheid, Inc. developed diagnostic tests for the SARS-CoV-2 virus using technologies that they had licensed from Livermore years ago. Both technologies provided the foundation for products used for years to identify other pathogens. "The Laboratory has a strong competency in diagnostics, so it's no surprise that we had technologies in our portfolio to apply against COVID-19 right away," says IPO Director Rich Rankin.

Polymerase chain reaction (PCR) is a well-established technology that biologists use to amplify small amounts of DNA into millions and billions of copies. Invented in 1983, PCR tests provided an innovative tool in medical diagnosis and biological research. Then, in the early 2000s, Livermore bioscientists refined the PCR technique to produce an even more sensitive test originally designed to detect tiny amounts of biowarfare pathogens in the battlefield. The successful droplet digital PCR test (ddPCR) simultaneously partitioned a sample into thousands of nanoliter volume droplets along with targeted PCR reagents. The ddPCR detects a variety of pathogen-expressed genes ranging from viruses such as human immunodeficiency virus, to bacteria including Salmonella and Listeria, and parasitic infections that cause diseases such as Malaria, as well as the presence of somatic or germline mutations. Its comprehensive detection capabilities elevated ddPCR to an essential, dynamic tool for diagnosing diseases in patients generally, as well as for genetic research.

Two companies, including one founded by a Livermore team led by Bill Colston in 2008, QuantaLife, Inc., commercialized the technology. QuantaLife was acquired in 2011 by Bio-Rad, which went on to develop ddPCR™ systems for a range of medical and research applications including cancer detection, pre-natal testing, stem cell treatment, food science, and microbial drug resistance. The technology won an R&D 100 Award in 2012. More than 5,100 research projects utilized ddPCR during the pandemic, including a study of COVID-19 residue on surfaces, which determined that hand-contact was the main transmission pathway to contamination in a laboratory setting.

In May 2020, Bio-Rad released a SARS-CoV-2 ddPCR test kit granted emergency use authorization (EUA) by the U.S. Food and Drug Administration (FDA). The SARS-CoV-2 ddPCR test runs on Bio-Rad's QX200 and QXDx ddPCR systems. "The test's high degree of sensitivity and ability to analyze difficult samples such as blood and saliva makes it more effective than other PCR tests for identifying the early stages of infection and detecting minimal residual disease in people recovering from COVID-19," says Yash Vaishnav, a Livermore business development executive (BDE). "It has been shown that ddPCR has a threshold for detecting SARS-CoV-2 lower than that of traditional PCR and an ability to detect the virus in saliva better than any other test. When the patient's sample might have a low viral load, ddPCR still has a better chance of correctly identifying a positive patient." The ddPCR COVID-19 test won the Federal Laboratory Consortium's (FLC's) 2021 awards in the "Impact" and "COVID-19 Response" categories and was one of two national FLC awards won by the Laboratory for its contributions to combatting the COVID-19 pandemic.

Early in the pandemic, an ad hoc Livermore team assembled this mechanical ventilator (left) in five weeks using available parts from outside of the ventilator supply chains to meet demand for COVID-19 patients.

Bio-Rad Laboratory Inc.'s Droplet Digital™ PCR (ddPCR™) System (left) incorporates technology originally licensed from Livermore. Bio-Rad developed an FDA-approved SARS-CoV-2 test early in 2020 enabling its ddPCR™ system to detect COVID-19 in clinical and environmental samples.

In the 1990s, Livermore scientist Allen Northrup and his team developed a microfluidic chip designed to accelerate PCR tests. Traditional PCR machines take hours to perform a thermal cycle—the heating of the sample—to reach a result. The Livermore microelectromechanical systems (MEMS) chip is much smaller than the conventional PCR apparatus and integrates the steps required to perform a test onto one chip. Heating the sample to the right temperature increases the genetic material's rate of replication. In the MEMS chip, tiny heaters and reaction chambers create a rapid heat–cool cycle that reduces the time to produce a result compared to conventional PCR tests.

Licensed in the early 1990s, "the Livermore technology used in this system is the foundation for some of the most popular methods for detecting COVID today," says Rakestraw. "It was originally developed at Livermore to detect biowarfare agents before using molecular diagnostics became common. When it was first created, this invention had no commercial market, but Livermore had developed a groundbreaking technology to address an important national security problem. It took more than 15 years for that technology to become clinically successful, but in today's world, this technology has made a difference by speeding up the time it takes to let someone know if they have tested positive for COVID-19."

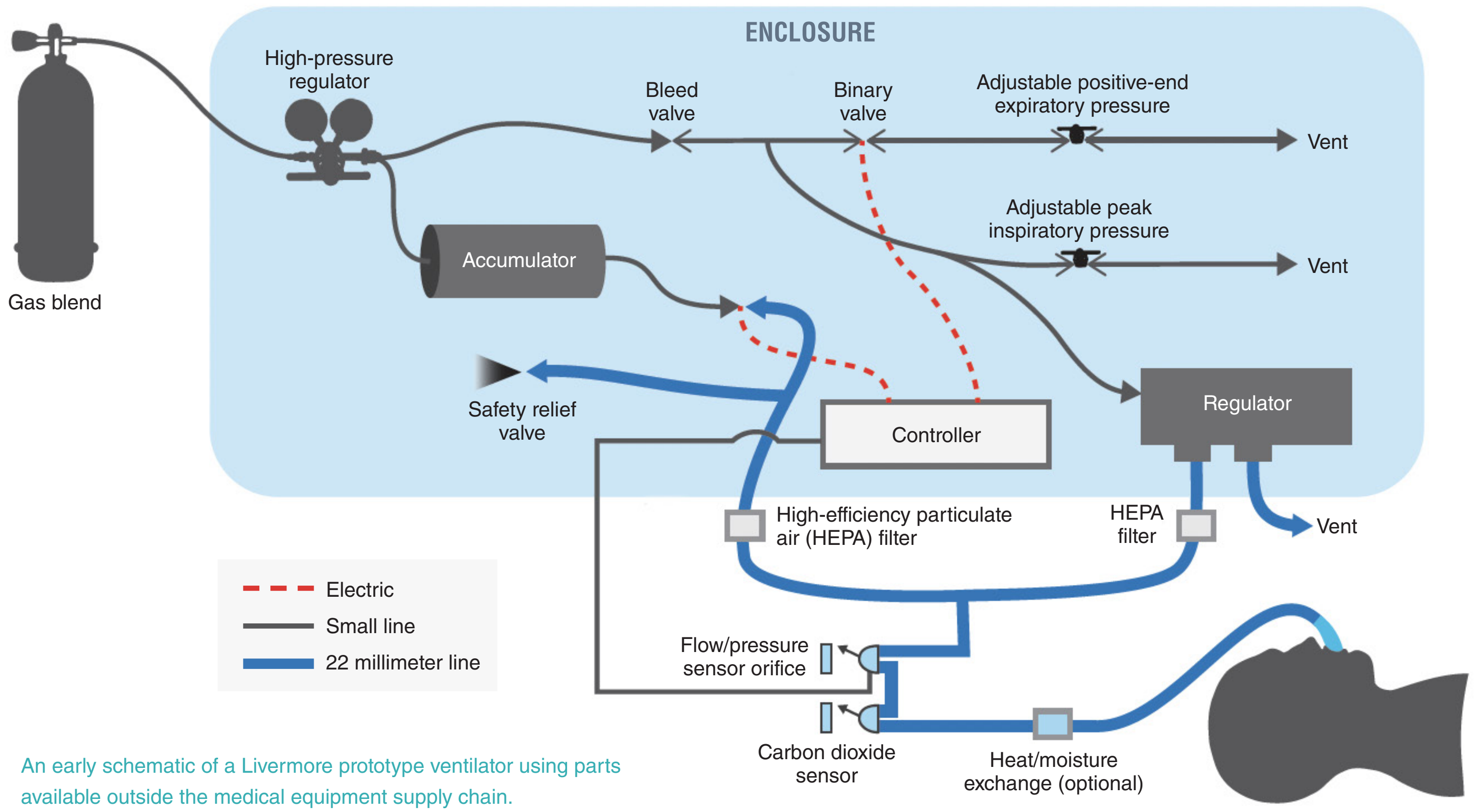
Cepheid is a molecular diagnostics company (acquired by Danahan Corporation) that develops molecular diagnostic testing systems for organisms and genetic-based diseases. In March 2020, it received an EUA from the U.S. FDA for its Xpert® Xpress SARS-CoV-2, a rapid molecular diagnostic test for qualitatively screening SARS-CoV-2. The test was designed to operate on any of Cepheid's automated GeneXpert® Systems, with a detection time of approximately 36 minutes. More than 23,000 of these systems are in use worldwide.

The Laboratory is now working on expanding the success of ddPCR and the MEMS chip with its Lawrence Livermore Microbial Detection Array (LLMDA) technology, which can detect more than 12,000 microbes and is used in clinical settings to assess co-infection with other diseases to help plan patient treatment. "Using its royalties, the Laboratory has funded adding a COVID test to our virus diagnostic system, which will provide medical professionals and emergency responders with a point-of-care tool for rapid detection," says Rankin. The LLMDA royalties from licensed Livermore inventions are also funding a study for detecting SARS-CoV-2 in wastewater samples to provide early warning of local outbreaks.

New Know-How Transfer

Working from home during the initial lockdown in March 2020, Jack Kotovsky, the leader of the Micro- and

Cepheid's GeneXpert® System uses Livermore-licensed technology that tests for pathogens using microelectromechanical (MEMS) chips to heat and amplify samples containing a pathogen. The company quickly developed and added an FDA-approved test for SARS-CoV-2 in early 2020 as the pandemic expanded. Shown above are the cartridge used by this test and the GeneXpert®II.



An early schematic of a Livermore prototype ventilator using parts available outside the medical equipment supply chain.

Nano Technology Section of the Materials Engineering Division, wondered how he and his colleagues could contribute to finding solutions for the COVID-19 pandemic. Estimates in the early days of the crisis anticipated that hospitals could be short hundreds of thousands of ventilators for critically ill patients. Kotovsky and his colleagues recruited an interdisciplinary team, sometimes meeting virtually and sometimes in person while masked in a laboratory, to design a ventilator that could be assembled from off-the-shelf parts outside the standard medical supply chain to resolve a potential shortage of life-saving ventilators. "We wanted to design something that we could send to clinicians within five weeks," says Kotovsky. "This process was new territory for us. Instead of inventing an entirely new technology, we were creating a piece of medical equipment that already exists, but from parts on-hand that could be assembled rapidly."

The team of 20 scientists and engineers from the Laboratory's Computing, Engineering, and Physical and Life Sciences directorates consulted medical doctors and ventilator manufacturers around the country to determine what features a rugged, easy-to-manufacture ventilator would need. The team also tried (and rejected) other approaches such as repurposing CPAP (continuous positive airway pressure) machines used to treat sleep apnea by circulating air into a sleeper's breathing passages. Instead, they looked for a source of low-pressure air regulators separate from any existing medical supply chains, to avoid stressing that manufacturing sector. The compressed schedule meant that any technology they developed had to make its way to frontline use faster than the usual technology transfer process. "It was clear that we needed to make the commercialization process happen in parallel with technology development, and that our anticipated partnership had to have manufacturability in mind," says Kotovsky. Just two weeks into the process, the design team and IPO began talking to potential manufacturing partners.

Genaro Mempin, the BDE who oversaw the ventilator's technology transfer process, says that the Laboratory released a federal business opportunity (FBO) notice to canvas the private sector for companies willing to work with the Laboratory on the ventilator and found Equilibar, a company that manufactures the type of regulator the team needed for the ventilator. BioMedInnovations, LLC (BMI), the partner company of Equilibar, which also manufactures precision air and fluid flow devices for medical applications, indicated their willingness to take on the entire process of prototyping the ventilator from the Laboratory's design, obtaining FDA EUA approval, and manufacturing the product. "Normally, we transfer intellectual property (IP) through licensing patents," he says. "In this case, the IP came in the form of the researchers' know-how, which is difficult to transfer without a patent."

IPO set up a cooperative research and development agreement (CRADA) with BMI to transfer the engineering know-how and allow the Laboratory and BMI to continue to collaboratively develop and test a prototype. CRADAs normally require months to negotiate and approve, but with the cooperation of the Laboratory's Office of General Counsel and the National Nuclear Security Administration's Livermore Field Office, this particular CRADA was approved in record time: less than two weeks.

BMI called on a partner company, Industrial Hard Carbon, LLC, which manufactures parts for NASCAR racing teams, and two of their partner companies, Roush Yates Manufacturing Solutions and Joe Gibbs Racing, to build ventilator components—with racing temporarily halted, they had available space on their production lines. BMI's ventilator product, marketed under the name SuppleVent™, received an FDA EUA in early June 2020. In April 2021, the FLC gave Lawrence Livermore and BMI a national Excellence in Technology Transfer award for designing and delivering the ventilator in just three months.

Kotovsky and his colleagues continue to explore alternative methods to ventilate patient lungs, including a simpler version of the extra-corporeal membrane oxygenation (ECMO) machine, which is used to pump and oxygenate a patient's blood outside the body during surgery. They are also examining the use of perfluorocarbon to diffuse oxygen into the bodies of patients with low blood oxygen. "In the next national emergency, I want to make sure those agencies think of Livermore first. We're a brain bank, we're used to teaming across disciplines, we're well-equipped, and we're motivated to respond. This is how we fulfill our mission," says Kotovsky.

Friendly Tech License

"When COVID-19 came along, we evaluated every technology we had that had any possible use against it," says Deputy Director of IPO Elsie Quaite-Randall, who oversaw the royalty-free license offering. "We developed a special nonexclusive, royalty-free, time-limited license that would allow anyone outside the Laboratory to use Livermore technologies to combat the COVID pandemic. It's designed to be as flexible as possible." The license is valid for a 12-month period as long as licensees use it to develop technologies against COVID-19. Two types of licenses are available, one for patents and one for software.

The license applies to about 30 Laboratory technologies, which are listed on the IPO website (ipo.llnl.gov) and cover data analysis and visualization, diagnostics, epidemiology, machine learning, protective equipment, and vaccines. For example, Cardioid, an optimized code that merges electrophysiology, fiber-generation, cardiac mechanics, torso-electrocardiograms, and cardiac meshing, simulates the electrical current running through cardiac tissue that triggers cells to contract like cascading dominoes, stimulating the heart to beat. Cardiotoxicity is a major concern in drug development. Cardioid software could be used as part of a machine learning–based simulation engine to predict and evaluate the effects of potential anti-COVID drugs on the heart.

A Diamond in the Rough

Facilitating the transfer of technologies developed at the Laboratory to the private sector requires specialists who develop partnerships aimed at commercialization. Business development executives (BDEs) in the Laboratory's Innovation and Partnerships Office (IPO) evaluate the features of newly reported Livermore inventions for commercial potential and determine whether the Laboratory should file patents, or copyrights in the case of software. "Livermore technology is considered 'early stage,'" Elsie Quaite-Randall, deputy director of IPO, explains. "Often, the researchers themselves don't know how their discoveries might be applied commercially. That's the job of a technology transfer office like Livermore's IPO. We're looking at a diamond in the rough." With patent or copyright protection in place, BDEs network with their industry contacts to zero in on each technology's commercial potential. In many cases, BDEs help secure additional funding for testing and improvements to cross the gap from early-stage invention to marketable technology. (See *S&TR*, May 2021, pp. 16–19.)

Once the technology is refined, BDEs offer licensing and partnership opportunities to industry partners with the expertise and resources to further develop and deliver Livermore's inventions to the marketplace. Licensees have the right to sell products or software based on a Livermore technology for uses defined in their licensing agreements in exchange for Laboratory licensing fees and/or royalties paid. Other partnerships, such as cooperative research and development agreements (CRADA) support specific capabilities of an invention. Livermore "tech transfer" ensures that Livermore inventions and software find their way into the world and meet the Department of Energy's goal of transitioning national laboratory innovations to society, and the pool of royalty funds then supports further Laboratory research and development.

The Biological Aerosol Mass Spectrometry (BAMS) system analyzes individual aerosol particles in real time to identify the potential presence and concentration of harmful biological particles in air samples. BAMS was designed for use in office buildings or at ports of entry such as airports or train stations to monitor for potential epidemic diseases or the release of biowarfare agents and could be adapted to rapidly detect aerosolized droplets of COVID-19.

Livermore scientists and other members of the ATOM (Accelerating Therapeutics for Opportunities in Medicine) Consortium created the ATOM Modeling Pipeline (AMPL), an open-source, modular, software pipeline for building and sharing models. AMPL generates machine-learning models that can predict safety and pharmacokinetic parameters and could speed safer, more effective anti-COVID drug development.

Other patents available under the license program include diagnostic technologies used in portable systems to rapidly detect pathogens. Another example is a new breathable smart material to guard against chemical and biological agents that could be used to protect health workers from exposure to SARS-CoV-2 and other viruses that spread before detection (see article on p. 16).

IPO publicizes these licenses through its website, and the Lab Partnering Service (LPS), which is managed by the Department of Energy's (DOE's) Office of Technology Transitions. The LPS website (covid19.labpartnering.org) offers COVID-relevant technologies available from all of DOE's national laboratories including Livermore, as well as relevant

Starting with the Livermore ventilator design, BioMedInnovations, Inc. developed its mechanical ventilator and released it as a commercial product under the name SuppleVent™. The prototype was finished, licensed, and FDA-approved three months after the Laboratory began the design project. (Photo by Garry McLeod.)

national laboratory facilities available to research partners. DOE's COVID-19 Technical Assistance Program helps small companies and businesses quickly connect with national laboratory expertise and provides U.S.-based entities performing COVID-19 research and development (R&D) with short-term help to overcome technical hurdles.

Before 1980, any technology development funded by the federal government was owned by it. That year, the Bayh-Dole Act passed shifting ownership of federally funded inventions, with the condition that the government develop a technology transfer process for those with commercial potential. "This act gave federal laboratories a technology transfer mission," says Quaite-Randall. "We have to figure out how to get these technologies to U.S. companies—it's really an economic development mission." Thanks to decades of R&D funding, DOE national laboratories are treasure troves offering technology to the private sector to apply against COVID-19, to spur economic growth, and to implement effective solutions during national emergencies.

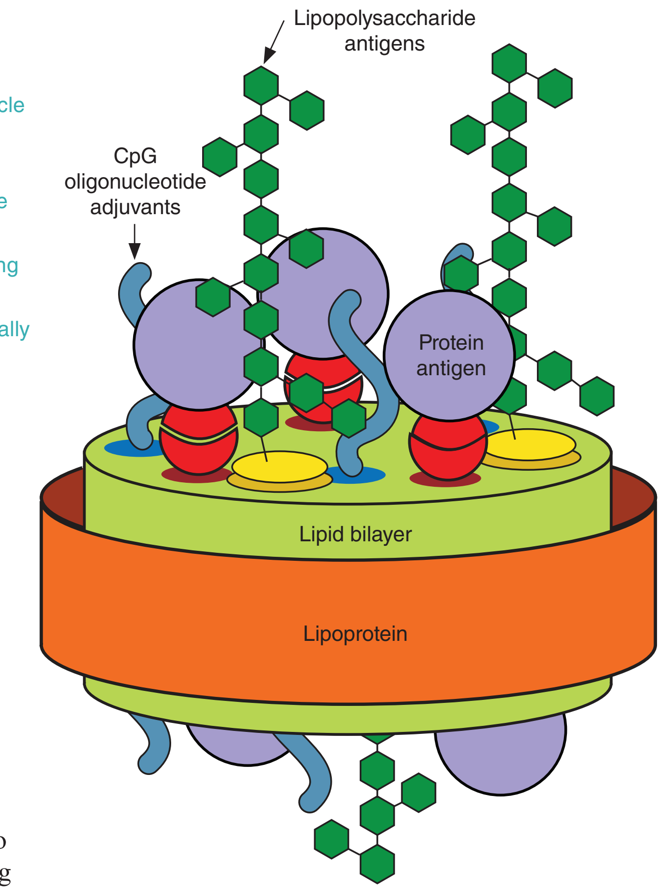
Tomorrow's Tech Today

Lawrence Livermore's tech transfer efforts made important contributions in the fight against COVID-19 over the last year and a half, but realizing that evolving microorganisms pose an ongoing threat, the Laboratory expects to expand its work in this area to meet current needs and prepare for future threats. In 2006, funded by the Laboratory Directed Research and Development Program, researchers developed nanolipoprotein particles (NLPs) that were originally intended to isolate proteins that thwarted conventional isolation means. NLPs also turned out to be useful for other applications including vaccinations. A Laboratory team led by Nick Fischer, Amy Rasley, and Matt Colemen is currently working with ConserV Bioscience Limited to use NLPs to develop a broad-spectrum (universal) coronavirus vaccine.

In partnership with the ATOM Consortium, the Laboratory is also using high-performance computing (HPC) to design new therapeutics against emerging diseases. The effort was begun in 2013 under a Lawrence Livermore Director's Research Initiative to apply HPC simulation and modeling to new drug discovery before this approach was widely accepted by the pharmaceutical industry. Today, the biomedical community recognizes that computing will play a significant role in fine-tuning pharmaceutical development. "We are on the cutting edge, and in 15 years, projects like these will make valuable impacts similar to the diagnostic technologies the Laboratory developed decades ago," says Rakestraw.

"The pandemic has demonstrated that we can move quickly during a national emergency," says Rankin. "Many discussions are taking place as the nation prepares for future pandemics—a tremendous amount of momentum is built into these areas."

—Allan Chen



The structure of a nanolipoprotein particle with representative cargos (protein antigens, lipopolysaccharide antigens, and Cytosine-phosphorothioate-guanine (CpG) oligonucleotide adjuvants). Nanolipoproteins, developed with funding from the Laboratory Directed Research and Development Program, were originally intended to help isolate proteins that were difficult to purify by other means, but have shown to be excellent delivery mechanisms for vaccines. The Laboratory has teamed with ConserV Bioscience to develop a broad-spectrum vaccine against coronaviruses.

Key Words: ATOM (Accelerating Therapeutics for Opportunities in Medicine) Consortium, BioMedInnovations, LLC, Bio-Rad Laboratories Inc.,Cardioid, ConserV Bioscience Limited, cooperative research and development agreement (CRADA),COVID-19, COVID-19 Technical Assistance Program (CTAP), Department of Energy Office of Technology Transitions, emergency use authorization (EUA), Equilibar, federal business opportunity (FBO), Federal Laboratory Consortium (FLC), Food and Drug Administration, intellectual property (IP), Lab Partnering Service (LPS), Lawrence Livermore Microbial Detection Array (LLMDA), nanolipoprotein particles (NLPs), microelectromechanical systems (MEMS) chip, National Nuclear Security Administration, polymerase chain reaction (PCR), QuantaLife, Inc., SARS-CoV-2, technology transfer.

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Versatile Cold Spray Harvests Waste Heat

ANY device that uses energy—from a refrigerator to a car to a turbine engine—loses heat to the surrounding environment. In the United States, up to 50 percent of the 23 quadrillion British Thermal Units (quads) of energy used by the industrial sector is lost to waste heat. To illustrate the significance of this energy loss, consider that 8 quads of energy would meet the nation's total energy needs for a month, based on Lawrence Livermore National Laboratory's 2019 energy use data. Finding a viable way to collect industry's waste heat would harness a significant, yet virtually untapped, energy resource.

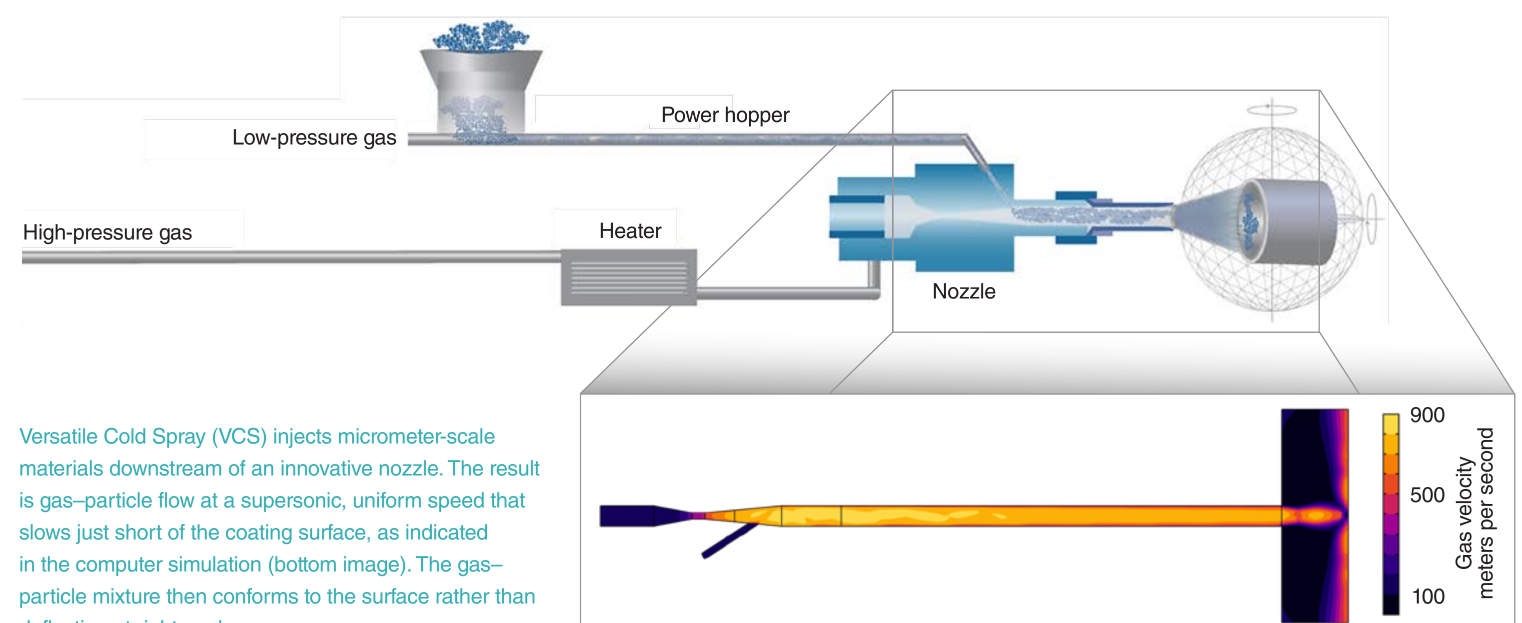
Thermoelectric materials may be the answer. The materials exhibit both high electrical conductivity and low thermal conductivity. Therefore, they generate electricity in response to changes in temperature. Coating heat-emitting surfaces, such as cooling fins and transfer pipes in industrial settings, with thermoelectric materials would create a means to capture heat otherwise lost to the surrounding air and then convert it into electricity. Ordinary manufacturing parts and components would become mini-generators making beneficial use of once-wasted heat. This resourceful concept falls short, for now, because techniques used to apply inherently brittle thermoelectric materials to the shapes and types of surfaces found in a typical manufacturing setting destroy the materials' unique heat harvesting qualities.

Versatile Cold Spray (VCS), an additive-manufacturing technology developed through a partnership between Lawrence Livermore and TTEC, LLC., solves the problem of maintaining thermoelectric function in materials applied in place, opening the door to capturing waste heat in industrial settings. "VCS stands apart from other additive manufacturing techniques by preserving the crystal structure and functional properties of brittle materials such as thermoelectrics," says Livermore physicist Harry Radousky, the project's lead investigator. "This feature, combined with VCS's portability and capability to achieve greater than 99 percent coating density, regardless of the surface type or shape coated, means that we can transform heat-emitting parts into working thermoelectric generators."

For this significant step forward in additive-manufacturing innovation, VCS received a 2020 R&D 100 Award. *R&D World* selects 100 new technologies worldwide for its annual award from nominees in categories including software, batteries, analytical instruments, security devices, and robotics, among others. "We are honored to win this award in partnership with Lawrence Livermore," says Richard Thuss, TTEC president. "We are even more gratified to have developed an easy-to-use device that can make beneficial use of the country's industrial waste heat and maximize our nation's energy resources."

Competitive Coating

VCS builds on conventional cold spray, a technique used to apply malleable materials such as steel, copper, and chrome, by spraying micrometer-scale material particles traveling at supersonic velocities onto a surface. "Cold," in the case of cold spray, is relative, referring to the fact that the gas is delivered at a temperature below the material's melting point. However, conventional cold spray cannot create functionality. The older technique only repairs materials, with the exception of adding corrosion- or abrasion-resistance to surfaces.



Versatile Cold Spray (VCS) injects micrometer-scale materials downstream of an innovative nozzle. The result is gas–particle flow at a supersonic, uniform speed that slows just short of the coating surface, as indicated in the computer simulation (bottom image). The gas–particle mixture then conforms to the surface rather than deflecting at right angles.

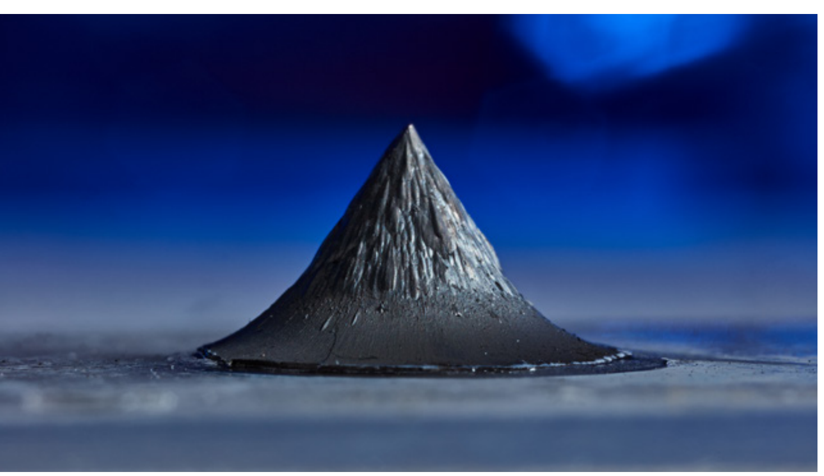
The particles in brittle, functional materials such as semiconductors, including thermoelectrics, and permanent magnets tend to shatter or deflect on impact rather than build a high-density deposit when applied using conventional cold-spray technology. Other additive-manufacturing technologies such as plasma spray, direct metal writing, and laser powder bed fusion (LPBF) either require extensive post-processing to recover functional properties of coating materials or they destroy the crystal structure altogether.

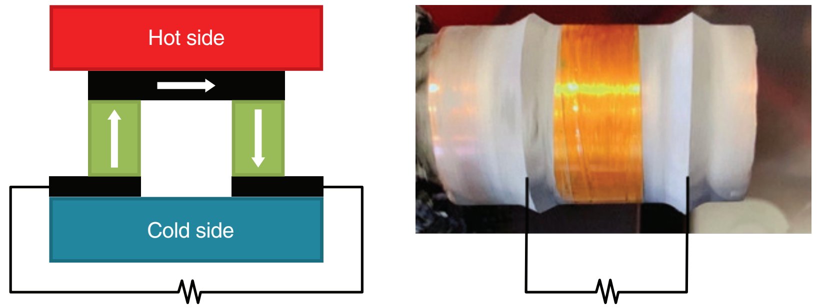
Using a patented nozzle design and tailored material feedstock, VCS delivers coating material particles at lower impact velocities compared to typical cold spray. Localized pressure gradients created directly above the coated surface enhance efficiency and prevent particle dispersal by the high-pressure gas. This enables deposited materials—both ductile and brittle—to embed and interlock on the surface, preserving the tailored microstructure driving their unique functional properties.

Controlling the size of the material particles in the coating feedstock further improves particle consolidation from becoming damaged or shattering. Additional coating layers build the concentration of the material on the surface to achieve greater than 99 percent coating density—a high mark for any additive manufacturing technology. The Livermore–TTEC team successfully tested VCS to deposit uniform coatings on metals, ceramics, glass, and some foam materials and in a range of shapes including the inside and outside of pipes.

Deployed as a lightweight spray unit and controller, VCS can coat components already installed in manufacturing facilities,

VCS can deposit dense layers of brittle thermoelectric materials, such as the bismuth telluride layers shown below, that would shatter on impact and lose function if applied with conventional cold-spray technology. (Photo by Garry McLeod.)





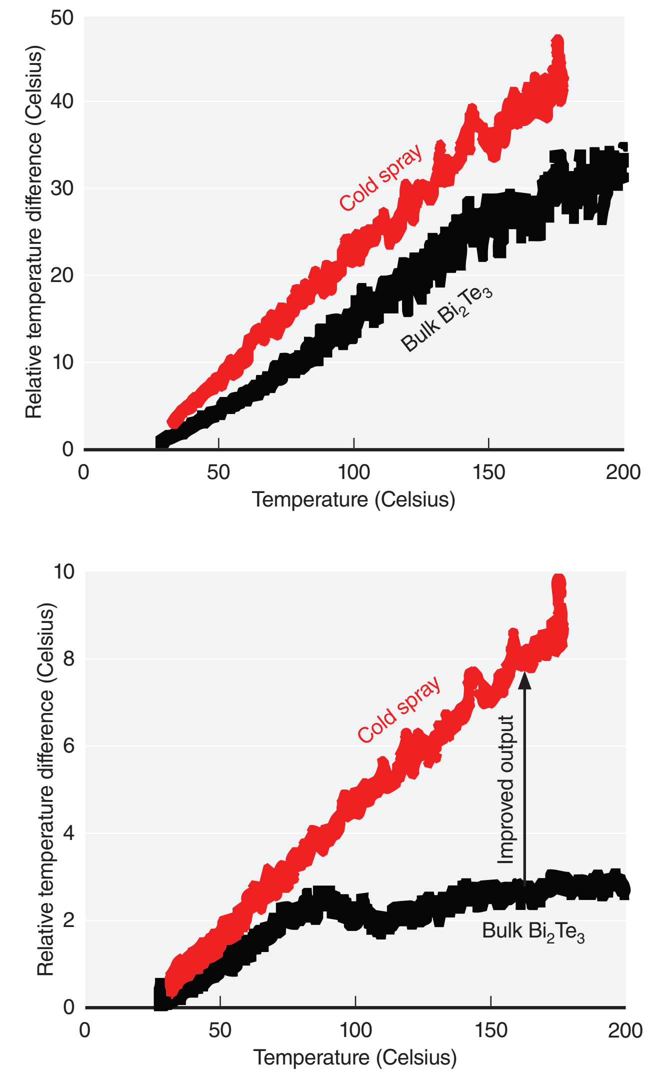
Thermoelectric materials harvest waste heat and convert it to an electric current (left). Coating a transfer pipe or other heat-emitting component with p- and n-type thermoelectric electrodes creates a thermoelectric generator (right). Thermoelectric coatings—p-type and n-type bismuth telluride—have been applied in this example. VCS is capable of uniformly coating any shape component in place, such as the copper pipe pictured, and achieving >99% density.

unlike larger or fixed-in-place tools such as LPBF. The spray unit could be mounted on a robotic arm as well for greater coating efficiency. The streamlined design, low energy demands, and operation using primarily nitrogen, instead of expensive helium used in other cold-spray techniques, keep operating costs low.

Harvesting Waste Heat

To test the possibilities for reusing industrial waste heat as an energy resource, the Livermore–TTEC team created a prototype thermoelectric generator. They used VCS to coat the outer surface of a copper pipe with bismuth telluride, a thermoelectric material, creating parallel p- and n-type electrodes. In spraying the material, VCS achieved close to full density and was nearly free of pores on the pipe's surface. The team measured output current and then compared the results to that of a prototype in which bulk bismuth telluride was simply adhered to a pipe using conductive epoxy. The output current for the VCS-coated pipe increased dramatically at high temperatures, indicating VCS's ability to maintain the functional thermoelectric qualities of the coating material. In addition, VCS's ability to coat without using binders ensures excellent mechanical and thermal contact between the coated surface and thermoelectric material and sufficient electrical contact at the electrodes.

The Livermore–TTEC team has also demonstrated VCS's effectiveness in depositing other functional materials, such as magnets for motors or generators and insulation that serves as a protective layer for energy harvesting and energy storage devices. By adding different materials in sequence, VCS can create complex devices combining semiconductor, magnetic, thermal, and electrical isolation functions. This capability will dramatically simplify the

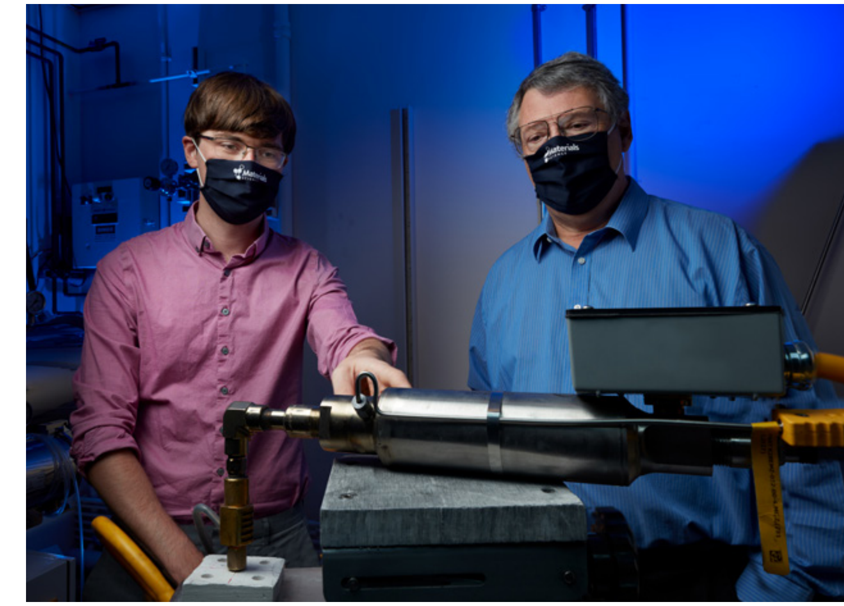


Comparing the performance of the thermoelectric generator created using VCS (red data points) and bulk material (bismuth-telluride Bi_2Te_3) adhered to a pipe (black data points), the materials maintain a similar temperature gradient between hot and cold sides (top graph). The VCS-applied material, however, outperforms the bulk application at higher temperatures (bottom graph) due to a combination of enhanced Seebeck coefficient—the thermoelectric response to temperature differences across a material—and improved thermal contact with the hot pipe.

manufacturing of entire thermoelectric generators by reducing the process to a single technique rather than a series of separate steps.

More Collaboration, More Versatility

Livermore physicist Alex Baker led a collaboration with TTEC to install TTEC's VCS system in a glove box at the Laboratory



Using a laboratory prototype of the portable, easy-to-operate VCS unit, Livermore physicists Alex Baker (left) and Harry Radousky study the technology's effectiveness at depositing different materials on a variety of substrates. (Photo by Garry McLeod.)

and apply advanced diagnostics to further understand all the process can offer. "The next step for VCS will be controlled-atmosphere deposition of air-sensitive materials, which our team needs to study more closely here at the Laboratory," says Baker.

Since winning the R&D 100 Award, the Livermore–TTEC team has discussed possibilities to expand the use of VCS with thermoelectric generator manufacturers and integrated systems. "The use of VCS for energy harvesting devices, magnetic materials, and electrical and thermal insulators provides an unmatched level of versatility," says Baker. A next step will be developing prototypes that can only be fabricated using VCS, creating a strong business model for the technology. Adds Radousky, "We're excited to see what new ideas come along now that we can run experiments onsite at Livermore. We're open to collaborations, keen to test a wide range of materials, and ready to demonstrate that VCS really lives up to the 'versatile' in its name."

—Suzanne Storar

Keywords: additive manufacturing, bismuth telluride, cold spray, magnets, R&D 100 Award, thermoelectric generator, thermoelectric material, waste heat recovery.

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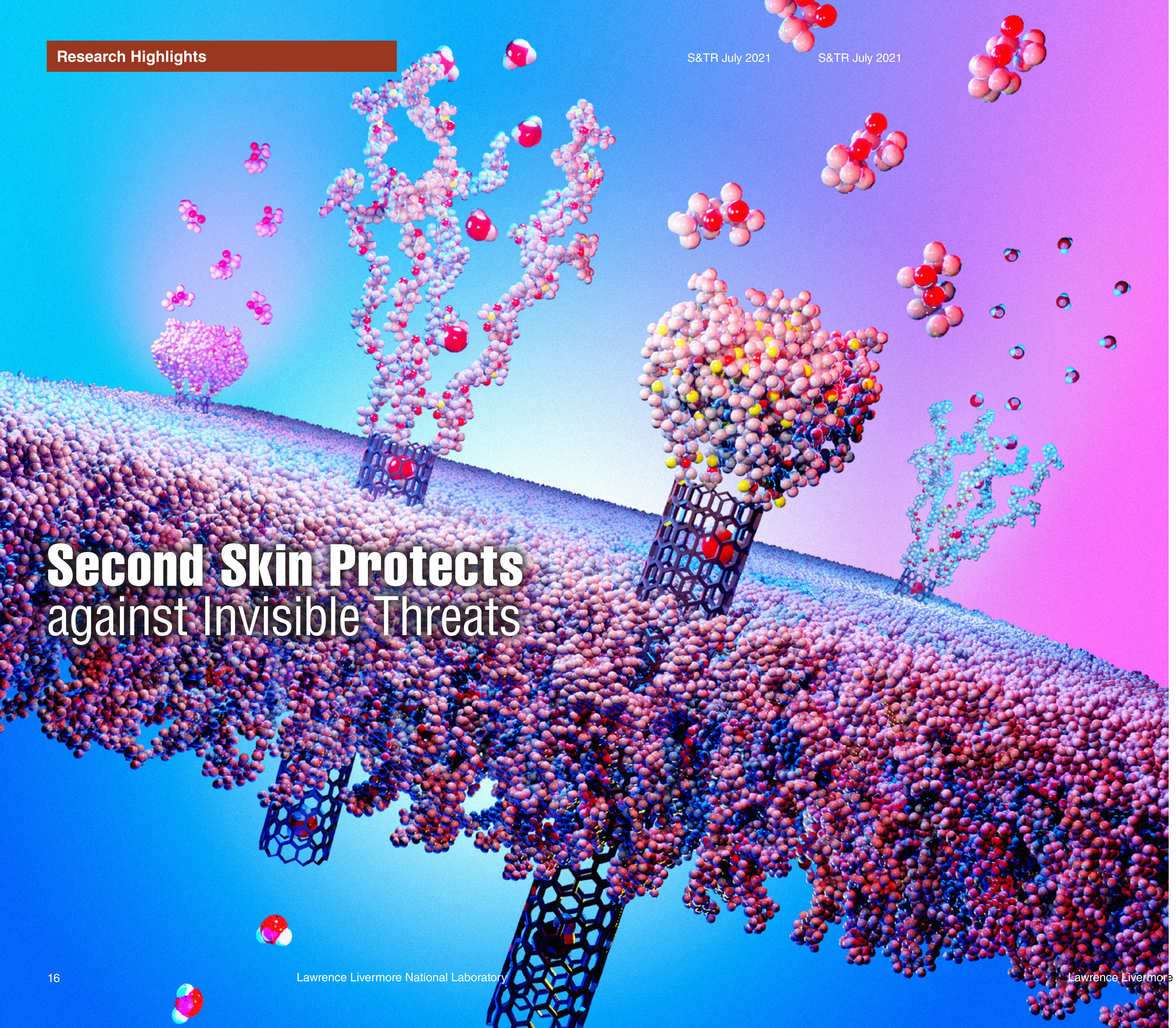


Second Skin Protects against Invisible Threats

FIRST responders, medical personnel, and soldiers on the frontlines of conflicts and emergencies prepare to encounter conventional weapons, but often they are not adequately equipped to face invisible threats from chemical and biological agents while executing their jobs. Sarin and chlorine gas have been used recently in the Syrian conflict, and the COVID pandemic has shown that protection against viruses is an urgent need. To help protect frontline workers against chemical and biological weapons, the Defense Threat Reduction Agency (DTRA) has been funding a Laboratory team and its collaborators to develop "smart" materials for uniforms that can shield against these threats. As the Laboratory continues work on the second phase of this project, called the Dynamic Multifunctional Materials for a Second Skin "D[MS]^2" program, researchers are building on the successes of the first phase of their work to make the material elastic and resistant to biological, blister, and nerve agents. The "second skin" material is made up of two layers. The first layer, consisting of carbon nanotubes (CNTs) embedded in a polymer matrix, blocks biological agents, and the second threat-responsive polymer layer blocks nerve and blister agents.

Most importantly, this innovative two-layer material can breathe and is comfortable to wear even over long use. Traditional military uniforms designed to block chemical weapons are passive systems based on impermeable barriers or adsorptive laminates, but they are heavy and stiflingly hot. They hinder the body's ability to cool itself. Wearers risk heat stress, especially if they are performing strenuous work in hot environments potentially contaminated with nerve, blister, or biological agents. So far, first responders and military personnel have had to sacrifice comfort for protection from biological and chemical hazards; however, the new second skin materials are porous and rapidly wick water vapor (sweat) away from the skin while still protecting against threats.

Building the Base Layer

Lawrence Livermore researchers built the base layer out of trillions of CNT pores, which are so small that bacteria and even viruses cannot pass through them. The base layer consists of a membrane of vertically aligned CNTs with a diameter less than 5 nanometers, which is 5,000 times thinner than a human hair. The CNTs are vertically "grown" in a tightly packed forest,

This rendering shows the carbon nanotubes (CNTs) embedded in a polymer matrix and functionalized with responsive polymers. In a safe environment, the membrane "breathes," and the water vapor (below) can flow easily through the CNTs and past the responsive polymer chains at their ends. If an environmental threat exists, the polymer chains collapse, preventing chemical agents from entering the pores. (Image by Ryan Chen.)

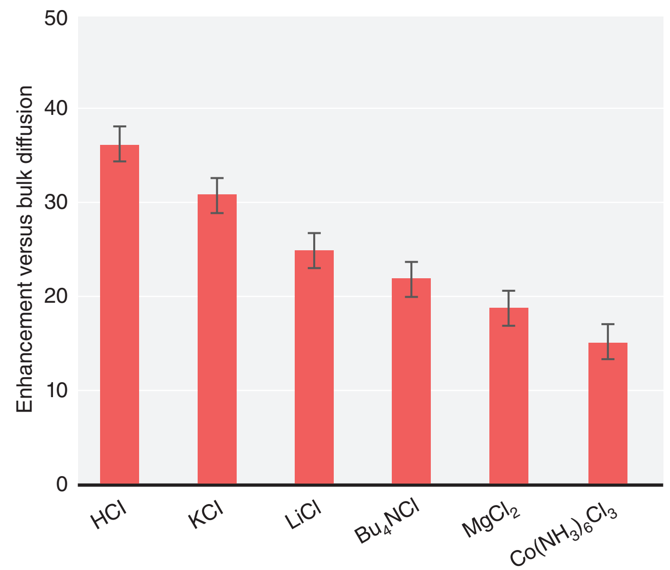
Lawrence Livermore National Laboratory

and the gaps between the nanotubes are filled with a polymer to prevent leakage. Water molecules can easily pass through the CNTs at a rate greater than other commercially available breathable materials and more than an order of magnitude faster than predicted by gas diffusion theories. (See *S&TR*, December 2016, pp. 20–23.)

"When testing our dynamically responsive membranes, there were some unexpected results. Because of the intrinsic smoothness of the pore walls, CNTs have exceptionally fast gas and liquid flow. Counterintuitively, the flow per pore gets even faster as the tubes get smaller, and we found that the overall membrane breathability increases even as the diameter of the CNTs decreases," said Francesco Fornasiero, Livermore's leader of the multi-institutional team of researchers. "In other tests, we found that small ions such as potassium, chloride, and sodium, which are exuded in perspiration, also permeated through CNTs much faster than expected."

Threat-Responsive Polymer Layer

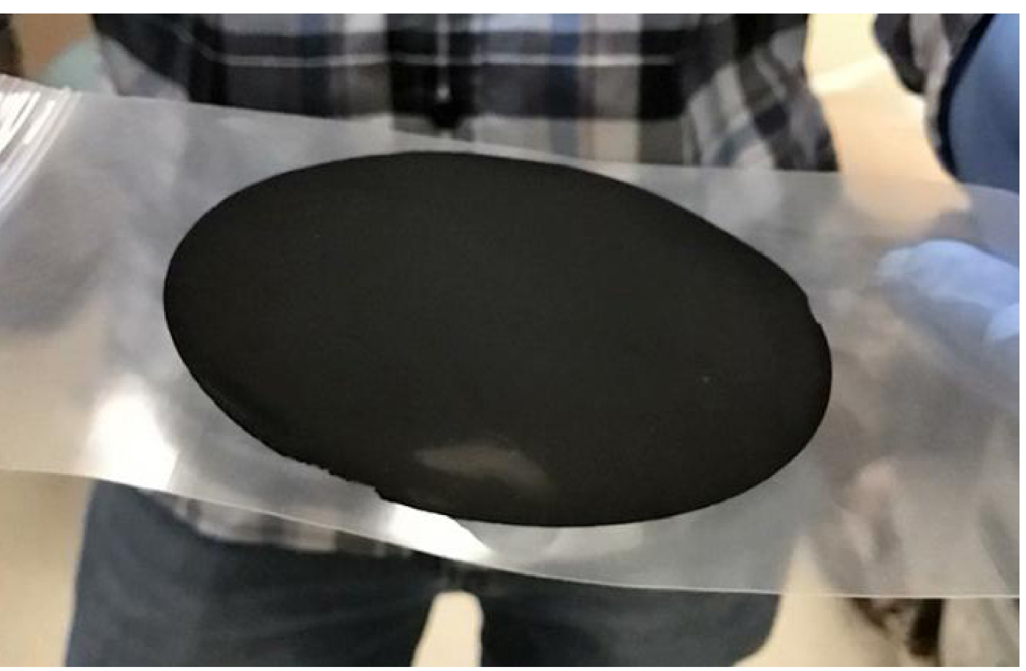
Unlike biological agents, chemical agents are too small to be blocked by CNTs, so the team developed a second "smart" layer that can protect against nerve agents only when protection is needed. They are also working on expanding that protection to address blister agents. This ultrathin, threat-responsive polymer layer is grown on the surface of the base membrane with polymer chains extending outward from the CNT composite surface. If a nerve agent comes into contact, these chains immediately collapse, temporarily blocking the pores, but this effect can be reversed by treating the material with a base, effectively decontaminating the suit, and possibly allowing its reuse.



Salt diffusion rates inside CNTs are more than one order of magnitude faster than in bulk aqueous solutions.

One of the most remarkable features of the material is that the protective response is localized, blocking permeation of the threat only in the contaminated area, while other parts of the uniform remain breathable. Another important feature is that the material automatically provides protection even if the wearer is unaware that a threat is present.

After developing the Phase I materials, DTRA asked if Livermore could make the membrane more comfortable to wear. By eliminating pockets of air between the uniform and the wearer's skin, stretchable materials reduce a large fraction of the uniform's thermal resistance or temperature difference between the material's two sides. To accomplish this, the team changed how the material is fabricated, and work continues to demonstrate that this elastic second skin maintains the same level of breathability and protection of the Phase I membranes.



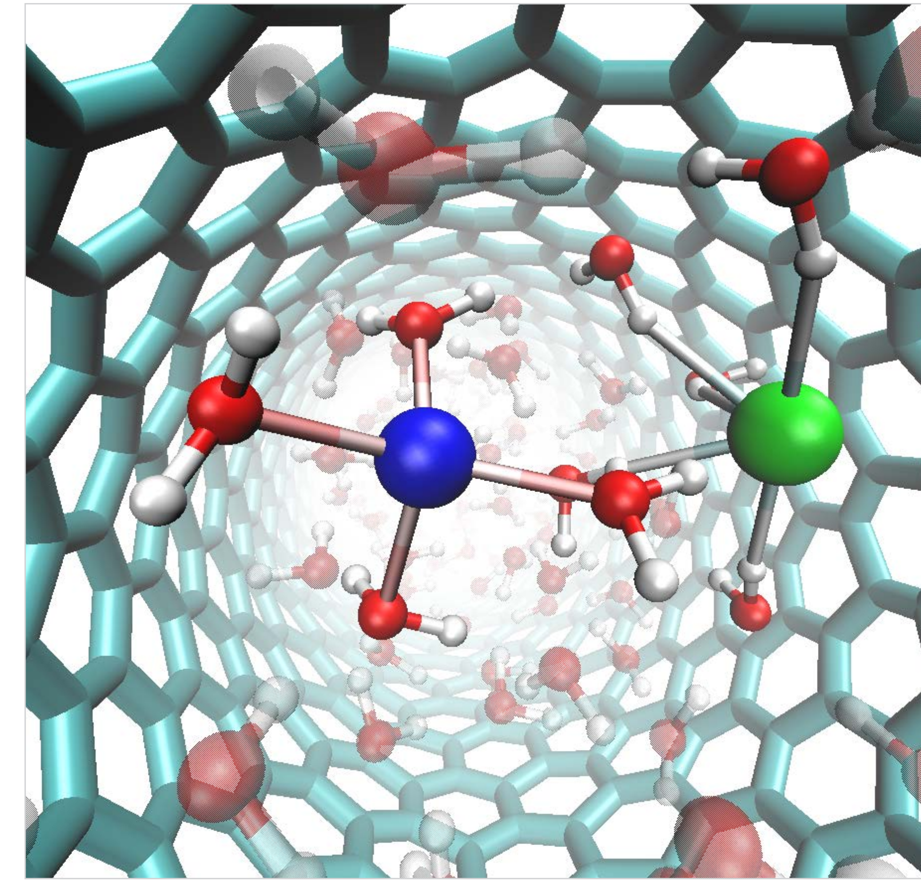
This membrane, also known as "second skin" for its protective properties, is made of vertically aligned, single-walled CNTs embedded in a polymer matrix, and could provide the protective layer of a first-responder uniform.

While addressing Phase II goals, the team is looking ahead to Phase III, which involves scaling up the process for material production and improved manufacturability. The current process will need to be streamlined before the material can be produced in large volumes, and the team is exploring options for continuous, scalable fabrication techniques. Collaborators at the U.S. Army Combat Capabilities Development Command Soldier Center and Edgewood Chemical Biological Center will help with the suit design and material properties evaluation, including their protection level.

Need for Similar Materials in Other Applications

As the team members continue working on the material for first responder and soldier uniforms, they have also conducted some preliminary tests for other applications that need the unique transport properties of CNTs. A first, obvious application is for breathable and comfortable medical scrubs for doctors and nurses, who regularly deal with biological threats, as well as sheets and hospital gowns for patients.

In another medical application, CNT membranes could enable significantly shorter treatment time for hemodialysis patients, thereby greatly improving their quality of life. CNT membranes are expected to allow small molecules like salt, urea, and other waste products in the bloodstream to pass through much more rapidly than conventional dialysis membranes, while retaining the larger and valuable components such as proteins and red blood cells. CNTs could also be used to separate macromolecules—proteins, DNA, and polysaccharides, for example from smaller components used during their synthesis, modifications, or labeling that need to be removed from the final product. Other potential applications include recovery of pharmaceuticals used during synthesis, water purification, desalination of dilute solutions, and wastewater treatment. For example, in one recent experiment, the team used CNTs to remove dilute dyes from concentrated salt solutions. This process could allow the dye industry to reclaim and potentially reuse dye, converting a waste stream into useful feedstock. Furthermore, membranes with CNT pores provided superior filtration and separation when compared to other state-of-the-art products with similar pore sizes.



Small ions permeate through the inner volume of nanometer-wide CNTs in this artistic rendering of single-walled CNTs (above). The ions permeate at rates that surpass diffusion in bulk water by an order of magnitude. (Image by Tuan Anh Pham.)

The Laboratory has been building expertise in novel uses of the unique transport properties of CNTs over many years. The second skin team has drawn on a diverse skill set found across the Laboratory, from materials science and nanotechnology to physics, polymer science, and computational modeling. Ongoing work with collaborators at Massachusetts Institute of Technology, Rutgers University, and Chasm Advanced Materials continues to help push the boundaries of this technology area.

—*Karen Rath*

Key Words: biological agent, breathability, carbon nanotube (CNT), chemical agent, first responder, ion permeation, membrane, nerve agent, polymer matrix, second skin, soldier, uniform.

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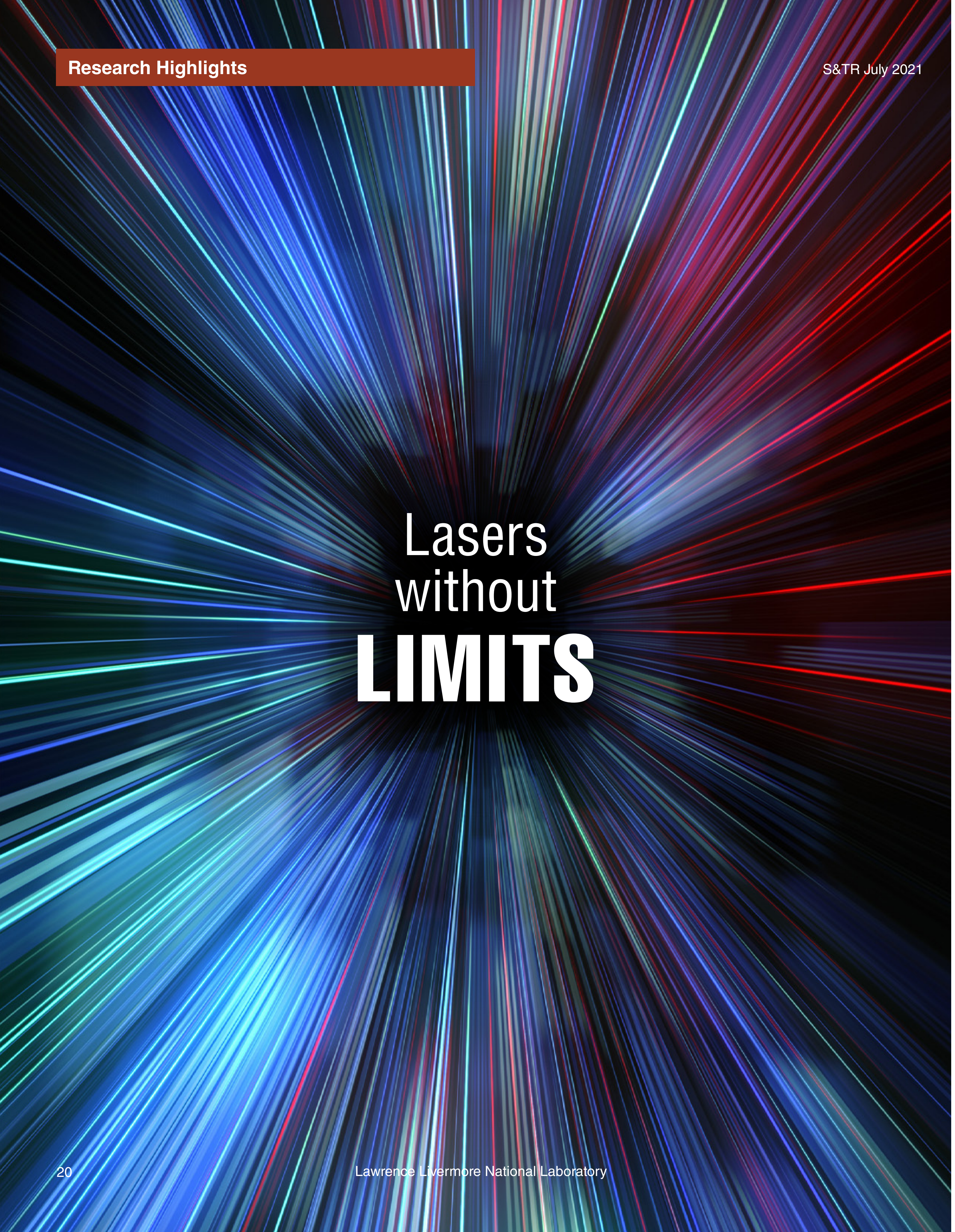


Lasers without LIMITS

SINCE opening in 2009, the National Ignition Facility (NIF) has helped scientists produce dizzying amounts of cutting-edge research and brought the Department of Energy (DOE) closer to producing a self-sustaining nuclear fusion reaction. With precision diagnostics, targets, and a carefully managed maintenance schedule, NIF fires its 192 beamlines at close to full capacity, gathering data from approximately 400 experimental shots per year. What would happen if scientists could shoot NIF more powerfully, more often?

Livermore scientists and engineers are anticipating the next generation of laser technology: very-high-average power short-pulse lasers. Designed, developed, and constructed by Lawrence Livermore, the High-Repetition-Rate Advanced Petawatt Laser System (HAPLS) at the Extreme Light Infrastructure (ELI) Beamlines facility in Dolní Břežany, Czech Republic fires up to 10 hertz (Hz) or 10 times per second. “While not yet the scale or energy of the NIF’s Advanced Radiographic Capability (ARC), HAPLS can perform about 40,000 experiments in the time it takes ARC to perform one, which means you can potentially get 40,000 times more data,” says Tammy Ma, the Advanced Photon Technologies (APT) program element leader for high-intensity laser high-energy-density (HED) science at Lawrence Livermore. High-repetition-rate short-pulse facilities such as HAPLS are the next frontier in laser technology, and Livermore has the expert know-how to take them to the next level.

Photon Science Paradigm Shift

Underground nuclear testing was once the backbone of Lawrence Livermore’s stockpile stewardship mission. When the Comprehensive Nuclear-Test-Ban Treaty took effect in 1996, focus shifted toward evaluating the reactions that take place inside nuclear weapons using detailed computer simulations and powerful laser systems. NIF was a genuine game-changer for the scientists and engineers performing this work, as it allowed for the controlled study of materials at high-energy-density conditions similar to those inside nuclear weapons.

At NIF and other mid-scale laser facilities around the United States, how often the laser can shoot limits the number of experiments that can be performed. In a March 2020 article for *Scientific American*, Ma wrote that a good day in the lab 15 years ago might produce no more than eight data points. With a high repetition-rate extremely high-power laser in the DOE complex, in a single second, scientists would be able to produce large amounts of valuable data and perform more experiments. These experiments will increase the phase space of high-energy-density plasmas that can be explored and accelerate advancements in HED science. “The entire culture of photon science will have to be altered. The paradigm completely changes,” says Ma.

Around 20 years ago, science conducted with Livermore’s Nova petawatt or quadrillion watt laser set the stage for short-pulse laser experimentation around the world. In the intervening years, U.S. leadership in short-pulse, high-power laser capability slipped away, while Europe and Asia honed their expertise, deploying 80 to 90 percent of new high-intensity laser systems. With its APT program within NIF, Livermore continues to innovate and lead in the development of next-generation laser architectures with the potential to push petawatt-scale lasers beyond 10 Hz and even up to the kilohertz (kHz) rate (1,000 shots per second). “It’s important to think big. Enabling the next generation of HED science at 10s, 100s, and 1,000s of Hz repetition rates requires major advances in high-energy laser technology, and this really forms the core of APT’s mission,” says Tom Spinka, APT’s program element leader for laser development.

Livermore delivered the High-Repetition-Rate Advanced Petawatt Laser System (HAPLS) to the Extreme Light Infrastructure Beamlines facility in the Czech Republic in 2017, representing the Laboratory’s expertise in high-repetition-rate petawatt laser construction.

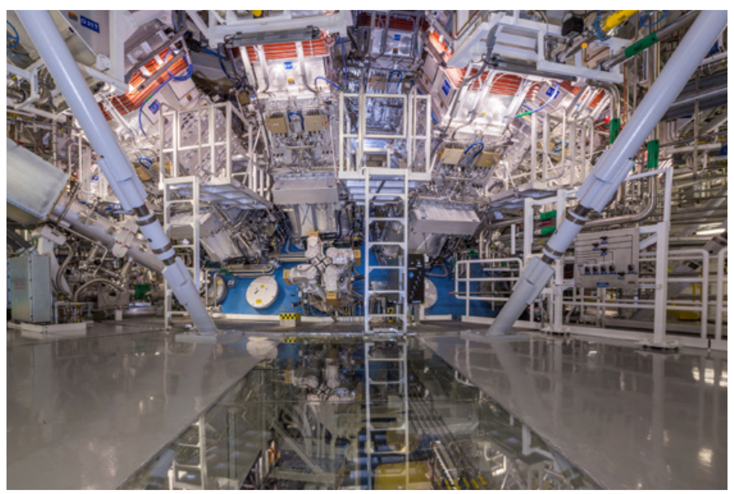
A Series of Feedback Loops

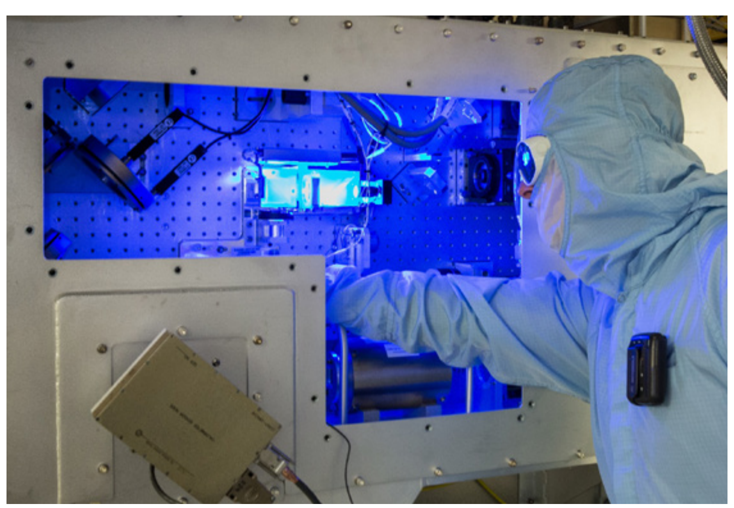
Making high-repetition-rate lasers a reality requires the simultaneous advancement of multiple experimental subsystems or competencies that exist at the Laboratory—one of the few places in the world where all the pieces of this puzzle come together. For example, now that high-power lasers can shoot at the Hz level, diagnostics must be able to collect data at that tempo, and the experimental facility must accommodate increased levels of debris, radiation, and electromagnetic pulses. Ma and her team have envisioned a fully integrated HED experiment infrastructure that capitalizes on high-repetition-rate lasers and a series of feedback loops to simultaneously accelerate both empirical discovery and computer model development. These loops would include a laser control loop, an experiment performance loop, and a modeling and simulation loop intricately integrated to provide intelligent experimentation. "These high-repetition-rate lasers are not going to unlock their full potential unless you have all the subsystems working in sync," says Ma. While many facilities focus on increasing the rate at which they can fire laser shots, the Livermore high-repetition-rate team is investigating how those shots will be most profitably distributed. Brian Spears, director of Livermore's Cognitive Simulation Initiative, describes the selection of the next experiment as a central challenge. "Once you can take data on the hertz time scale, the real question becomes, 'How do I avoid firing blindly? How do I choose the smartest experiment to execute when I only have 100 milliseconds to think about it?' The integrated loops give us the framework for answering these questions."

The laser control loop would monitor laser performance via machine learning (ML) trained with data from experiments and modeling, including the input–output of each amplifier and compressor, beam profile at places with high risk of optical damage, energy measurements, and control points for spectral shaping and seed energy variation. Using the predictions from ML, the laser control loop can reduce the impact of environmental perturbations on the output of the laser by adjusting various laser parameters to compensate. "Higher repetition rates actually benefit this type of prediction because the environmental conditions are less likely to change between shots. But we're also dealing with variables that affect laser operation. Being able to train an algorithm to compensate for all of them will be a challenge," says Tom Galvin, an APT staff scientist working on the laser control loop of the infrastructure. "This project removes bottlenecks in data processing and optimizes pulse parameters."

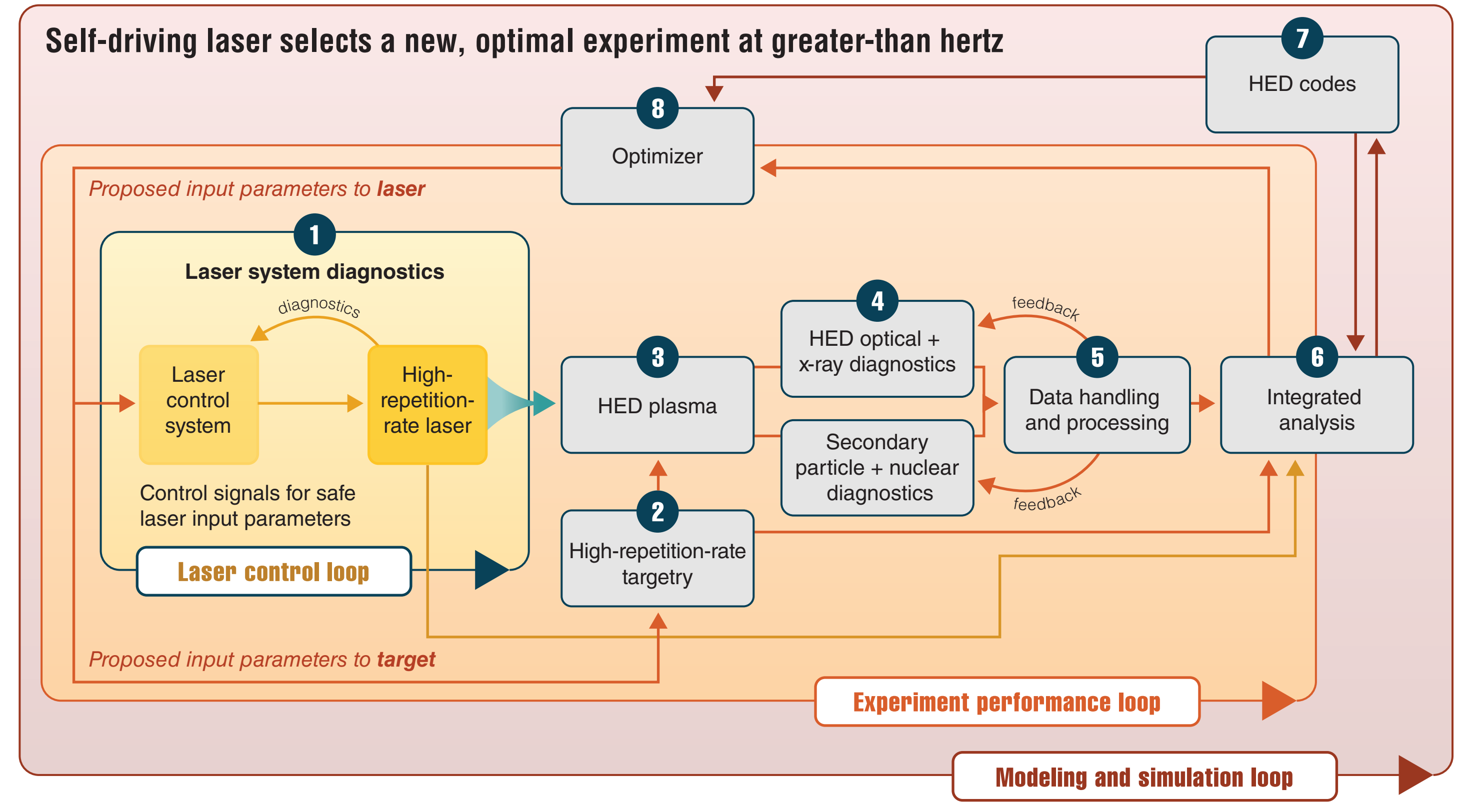
The experimental performance loop will select targets at delivery speeds that will match the repetition rate of the laser with a closed feedback loop, allowing the system to navigate optimized target production, such as bright photon sources. New advances in additive manufacturing could mass produce complex targets "on-demand" to deliver targets designed to optimize outcomes. Derek Marsical, an HED scientist in APT, is working on the experimental performance loop and has been converting existing film-based diagnostic detector media to electronic media. "In general, passive media have worked well due to the extreme radiation and electromagnetic pulses generated and compatibility with typical shot rates. In less than one year, many of the workhorse diagnostics have been updated so they can accommodate the current generation of high shot rate lasers, and more are on the way," says Marsical.

In the past, experimental design and analysis relied on time-consuming, human-operator dependent processes that were subject to individual bias, intuition, and error. "To truly have a high-repetition-rate diagnostic that can be integrated into a fully self-driving system, the system must be able to distill the data into quantities of interest on a time scale shorter than the experimental rate. Machine learning is ideal for this task and a neural network can be taught to accurately deduce these quantities by training on large sets of experimental and simulated data," says Marsical. The modeling and simulation loop will use real-time, high-performance computing models coupled with contemporary artificial intelligence techniques with streaming experimental data to create an automated system that continuously adapts and optimizes a laser-plasma experiment. These capabilities developed at Livermore will also be mapped to other Office of Science laser facilities.





The Advanced Radiographic Capability (ARC) at the National Ignition Facility (NIF) is a "laser within a laser," using four petawatt-class beams to utilize short-pulse techniques within NIF. Although the new short-pulse, high-intensity lasers coming online today are not yet the scale or energy of ARC, they are capable of firing at hertz rates or greater.



Lawrence Livermore's core competencies provide the ideal environment for encouraging the development of a next-generation, short-pulse, high-power, high-repetition-rate laser system. Laser diagnostics help to preserve and improve the laser itself (1), new targets are built using advanced manufacturing techniques (2), high-energy-density (HED) plasmas are generated at the rate the laser fires (3), the shots produce experimental data recorded on a suite of diagnostics (4), that then feed into data handling and analysis (5 and 6). With the analysis provided from each experiment, researchers and engineers can improve codes and create models and simulations (7 and 8) in real time that can provide increased physics understanding and guide the next experiment.

tools to assimilate observations from high-repetition-rate diagnostics to analyze multi-modal data in real-time, compare simulated predictions, and utilize inverse modeling where synthetic diagnostics enable the reconstruction of the full state of plasma from incomplete and noisy observations. This capability could give scientists access to experimentally constrained estimates of fundamentally unobservable quantities, like the internal electron distribution from a laser-accelerated particle beam experiment.

With a high-repetition-rate, short-pulse, high-power laser, experiments can happen more often and more efficiently with tremendous flexibility in experimental design and execution. It offers a substantial number of potential scientific milestones in optics, advanced manufacturing, machine learning, and plasma physics. "Developing these systems requires that experimenters, modelers, and computer scientists learn each other's languages. This more tightly integrated approach to problems will not only result in accelerated progress, but a wider and deeper understanding of the physics," says Marsical.

"When we finally bring all the subsystems together, we'll figure out our limitations," says Ma. "Our current rate of learning is really only limited by how fast we can conduct and assess our experiments." To target this challenge, a set of several projects funded by the Laboratory Directed Research and Development program and the Office of Science over the next few years will support the development of novel repetition-rate compatible diagnostics, accelerated cognitive simulations to advance high-energy-density physics, and the coupling of machine-learning

–Ben Kennedy and Genevieve Sexton

Key Words: advanced manufacturing, Advanced Photon Technologies (APT), artificial intelligence, Extreme Light Infrastructure (ELI) Beamlines facility, high-energy-density (HED) science, High-repetition-rate laser, High-Repetition-Rate Advanced Petawatt Laser System (HAPLS), machine learning, National Ignition Facility (NIF), photon science, short-pulse lasers.

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Patents and Awards

In this section, we list recent patents issued to and 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. For the full text of a patent, enter the seven- or eight-digit number in the search box at the U.S. Patent and Trademark Office's website (uspto.gov).

Patents

System and Method for Rapid, High Throughput, High Pressure Synthesis of Materials from a Liquid Precursor
Mike Armstrong, Sorin Bastea
U.S. Patent 10,882,017 B2
January 5, 2021

Angled Slit Design for Computed Tomographic Imaging of Electron Beams
John Elmer, Alan Teruya
U.S. Patent 10,888,284 B2
January 12, 2021

System and Method for Grain Refinement and General Control of Grain Morphology in Laser Additive Manufacturing
Tien Roehling, Gabe Guss, Saad Khairallah, Manyalibo Joseph Matthews, Sheldon Wu
U.S. Patent 10,888,956 B2
January 12, 2021

Polarization, Densification, and Exfoliation of Porous Materials by High-Energy Ion Beams
Sergei Kucheyev, Swanee Shin
U.S. Patent 10,896,804 B2
January 19, 2021

Method and Apparatus for Ensuring a Uniform Temperature Profile in Ribbon Fiber Lasers and Amplifiers
Derek Drachenberg, Jay Dawson, Michael Messerly, Paul Pax
U.S. Patent 10,897,116 B2
January 19, 2021

Expandable Implant and Implant System
Thomas Wilson, Ward Small, IV, William Benett, Jason Ortega, Duncan Maitland, Jonathan Hartman
U.S. Patent 10,898,199
January 26, 2021

Heat Treatment to Anneal Residual Stresses During Additive Manufacturing
James Demuth, Andrew Bayramian, Bassem El-Dasher, Joseph Farmer, Kevin Kramer, Alexander Rubenchik
U.S. Patent 10,898,954 B2
January 26, 2021

MEMS Metal-Quartz Gyroscope
Sangtae Park, Satinderpall Pannu
U.S. Patent 10,900,783 B2
January 26, 2021

Planarization of Optical Substrates
Christopher Stolz, James Folta, Paul Mirkarimi, Regina Soufli, Christopher Walton, Justin Wolfe, Carmen Menoni, Dinesh Patel
U.S. Patent 10,901,121 B2
January 26, 2021

Arbitratry Pulse Shaping with Picosecond Resolution over Multiple-Nanosecond Records
John Heebner, Bedros Afeyan
U.S. Patent 10,901,295 B2
January 26, 2021

Cryogenic Pressurized Storage with Hump-Reinforced Vacuum Jacket
Salvador Aceves, Francisco Espinosa-Loza, Guillaume Petitpas, Vernon Switzer, Elias Rigoberto Ledesma-Orozco, Victor Alfonso Alcantar-Camarena
U.S. Patent 10,928,006 B2
February 23, 2021

Additive Manufacturing System and Method Having Toolpath Analysis
Michael King, Ryan Fellini
U.S. Patent 10,928,805 B2
February 23, 2021

Awards

The "Getting to Neutral" Carbon Emissions Team received a **DOE Secretary Achievement Award** for its groundbreaking study that identified a robust suite of technologies to help California reach the goal of becoming carbon neutral by 2045.

For the third consecutive year, Lawrence Livermore National Laboratory was awarded **Glassdoor's Employees' Choice Award**, recognizing the Best Places to Work in 2021. The Employees' Choice Award, now in its 13th year, is based solely on the input of employees, who elect to provide anonymous feedback by completing a company review about their job, work environment, and employer.

Charles and **Debbie Ball** each received the **Office of the Secretary of Defense (OSD) Medal for Exceptional Public Service** while on assignment with OSD. The citation noted that Charles Ball made substantial contributions to U.S. national security by leading Department of Defense (DOD) reforms to the mission of countering weapons of mass destruction. Debbie Ball's citation recognized her performance during a critical time in which the DOD published the 2018 Nuclear Posture Review and began an enormous effort to obtain congressional support to modernize the nation's nuclear deterrent. The medal is presented by the U.S. Secretary of Defense to non-career federal employees, private citizens, and foreign nationals.

Abstract

Transferring Laboratory Technology to Fight the COVID-19 Pandemic

Lawrence Livermore technologies have provided solutions to detect the SARS-CoV-2 virus that causes COVID-19 and develop medical equipment for treating patients. Some technologies already in use in the medical marketplace were quickly adapted to fight COVID-19. The Laboratory's private sector partnerships are essential to transferring such technologies to the commercial market. As the disease spread, the Laboratory's technology transfer processes were accelerated to meet the challenge of combatting the pandemic. Existing medical diagnostic technologies marketed by Bio-Rad Laboratories, Inc., and Cepheid, LLC, and licensed from Livermore proved useful in detecting the SARS-CoV-2 virus in clinical and research settings. A Laboratory effort to develop a ventilator using parts outside the existing medical ventilator supply chain worked in parallel with the technology transfer process to move know-how into an actual product. The Laboratory made pandemic-relevant technologies available through a time-limited, royalty-free, nonexclusive license to entities conducting research and development against SARS-CoV-2.

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Planetary Research: Past and Future

Livermore leverages its expertise in astrophysics, nuclear science, cosmochemistry, and high-performance computing to explain the solar system's formation and prepare for the challenges of life on other planets.

Also in this issue...

- *Laboratory teams have maximized employee safety while continuing mission-critical work during the COVID-19 pandemic.*
- *Livermore's Energetic Materials Center celebrates three decades of providing technical expertise to support the nuclear security enterprise.*
- *Disruptive research investment expands research pathways and encourages risk tolerance among Livermore's innovators.*

Coming Next Issue