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BROOKHAVEN
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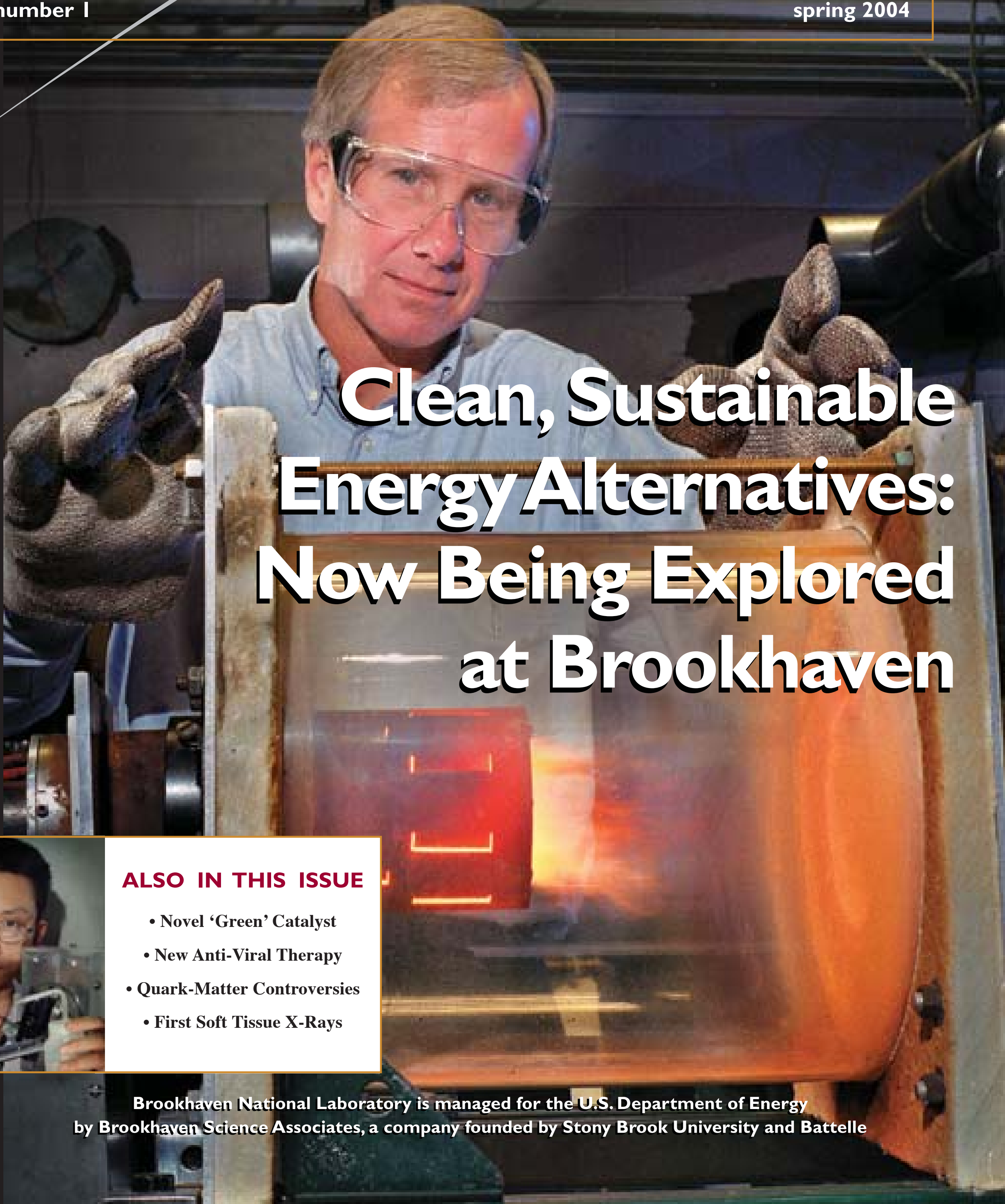

Clean, Sustainable Energy Alternatives: Now Being Explored at Brookhaven

ALSO IN THIS ISSUE

- Novel ‘Green’ Catalyst
- New Anti-Viral Therapy
- Quark-Matter Controversies
- First Soft Tissue X-Rays

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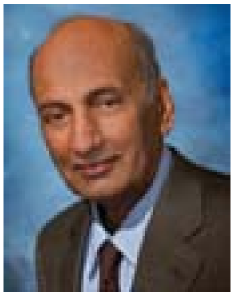
by Brookhaven Science Associates, a company founded by Stony Brook University and Battelle

Welcome to

discover BROOKHAVEN
a U.S. Department of Energy National Laboratory

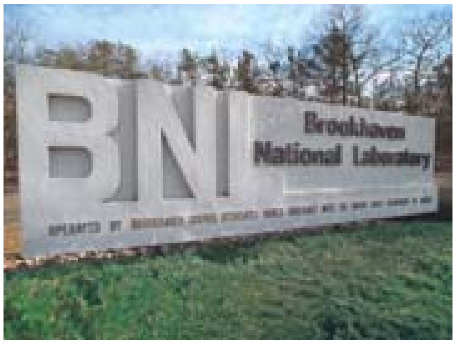
a magazine dedicated to exploring and explaining
the scientific research and discoveries made at
the U.S. Department of Energy's
Brookhaven National Laboratory.



BY PRAVEEN CHAUDHARI
BROOKHAVEN LABORATORY DIRECTOR
AND BROOKHAVEN SCIENCE ASSOCIATES PRESIDENT

Foreseeing Brookhaven's Scientific Future

ONE RESULT OF THE PRESENTATIONS made at the Quark Matter 2004 conference in January is that the Relativistic Heavy Ion Collider (RHIC) at Brookhaven has been making headlines recently, as the news media has been speculating whether or not RHIC has already made quark-gluon plasma (see page 14). Science reporters at the meeting have also been wagering on whether or not RHIC experiments have detected the presence of a hypothesized precursor of quark-gluon plasma, called color glass condensate.



While those scientific questions await definitive answers based on unquestionable data taken during the present and upcoming heavy-ion runs by RHIC's four experiments, another question — one that was first asked moments after RHIC received construction approval in 1990 — was answered last fall by the U.S. Department of Energy Spencer Abraham.

In June 2002, the Energy Secretary had informed us that Brookhaven's next big facility will be the Center for Functional Nanomaterials. But the question "What is Brookhaven's next big machine?" was just answered by DOE last November. In a news-making address to the National Press Club, Secretary Abraham told the nation that this national laboratory's next big machines are three: RHIC II, NSLS II, and eRHIC (see, respectively, pages 16, 21, and 17).

In support of Brookhaven's present and future operations, the President's budget for fiscal year 2005 contains about a $30 million increase for Brookhaven. This includes $20.5 million for the continued design and first year's construction of the Center for Functional Nanomaterials (see discover Brookhaven, winter 2002-03), plus a 5.5 percent increase in funding for RHIC, which will help us get the most physics out of the present machine.

More good news is that the National Science Foundation has budgeted, one year earlier than anticipated, the initial $30 million for the next big experiment at Brookhaven's Alternating Gradient Synchrotron (AGS) accelerator: the Rare Symmetry Violating Processes (RSVP) experiment. By looking into the universe's lack of symmetry between matter and anti-matter and into the possible existence of a universal fifth force, RSVP will build upon the AGS's Nobel prize-producing ability as a high-energy, high-intensity proton accelerator, as well as the 1963 discovery of charge parity (CP) symmetry violation at the AGS which led to the 1980 Nobel Prize in Physics.

In related news, Brookhaven Science Associates (BSA), which is the company founded in 1998 by Stony Brook University and Battelle Memorial Institute to manage and operate the Laboratory under contract with DOE, has been informed of the Energy Department's intent to extend its agreement with BSA through April 2008. As it was noted, DOE will exercise its option to extend the contract "consistent with applicable regulations in recognition of the laboratory's superior performance."

While past performance does not guarantee the future, I do believe, based on the promise of present and future research, facilities, and funding, that Brookhaven has solid scientific prospects before it.

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ON THE COVER: Pictured with a Brookhaven-developed alternative oil burner is Thomas Butcher. Within Brookhaven's Energy Sciences & Technology Department, he heads the divisions in which research and development are done on building heating and energy efficiency, geothermal and wind power systems, and advanced fuel production and storage (see cover story, page 10).

BROOKHAVEN
NATIONAL LABORATORY

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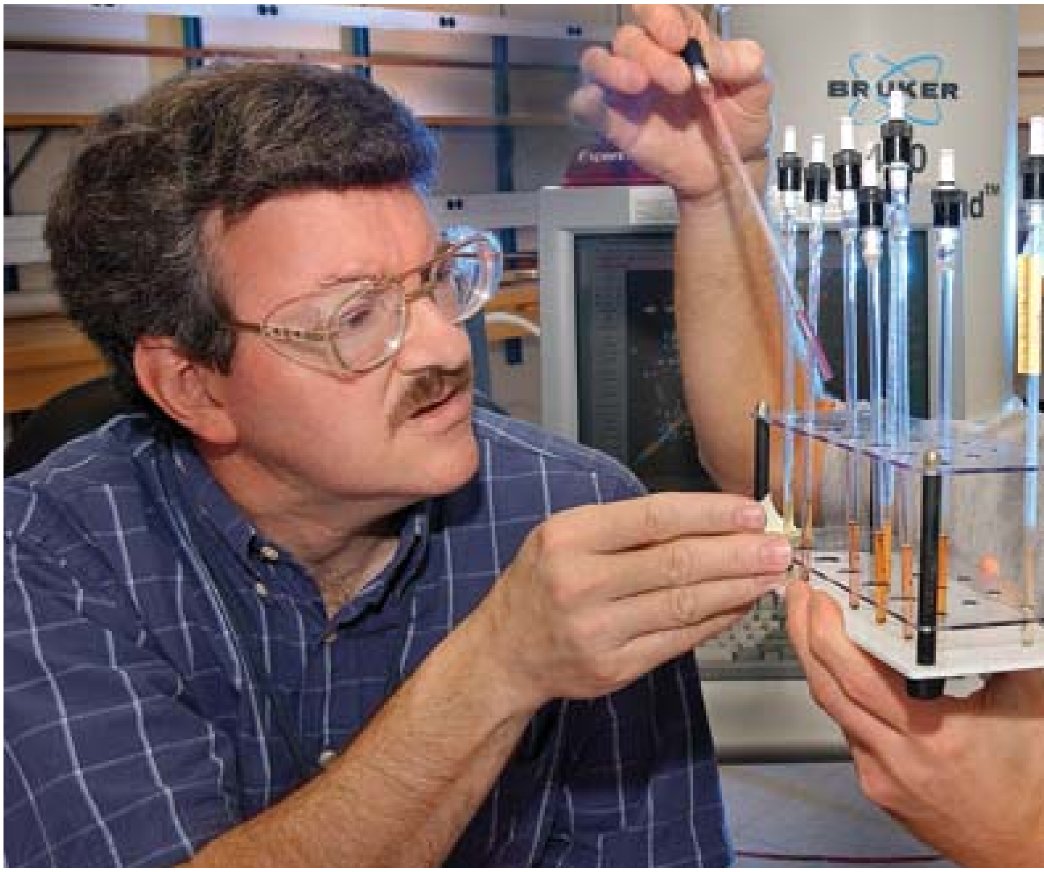
a passion for discovery

Brookhaven chemists
have developed
a new catalyst that
converts chemical reactants
into usable products
without producing waste.

BY LAURA MGRDICHIAN AND
KAREN MCNULTY WALSH

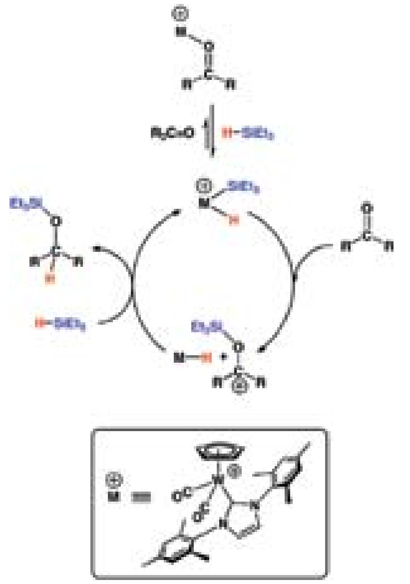


Brookhaven-developed Recyclable Catalyst May

AT INDUSTRIAL PLANTS, where the household products in our kitchens, garages, backyards, and bathrooms are made, generating waste continues to be an inevitable part of the creation process. Even the production of organic compounds, such as pharmaceuticals, results in unusable by-products that can be hazardous to the environment and costly to eliminate.

These waste chemicals are generated from reactions that produce plastics, herbicides, pesticides, paper, cleansers, rubber, and lubricants, to name a few. According to the U.S. Environmental Protection Agency, industrial manufacturing processes produce tens of millions of pounds of organic waste chemicals each year. Many of these substances have already been documented as contaminants to wildlife and natural resources.

At Brookhaven Lab, chemists Morris Bullock and Vladimir Dioumaev have joined in the movement of scientists looking for ways to address this problem. Using funding from the U.S. Department of Energy's Office of Science, they have developed a catalyst that converts chemical reactants into usable products without producing waste, allowing it to be used over and over again. The discovery may help reduce the amount of hazardous waste entering the environment, as well as the amount of money that businesses spend to treat and dispose of waste.



The proposed mechanism for the reaction in which the "green" catalyst is employed and, thereby, eliminates the production of waste.

The new "green" catalyst accomplishes two significant goals. First, it works by removing one stage of the reaction: the new catalyst eliminates the need to use solvents in the process by which many organic compounds are synthesized. The catalyst does this by dissolving into the reactants, thus eliminating the need for a separate solvent in which the reagents are mixed to set the reaction in motion.

"Avoiding the use of solvents is an important way to prevent waste in chemical processes," says Bullock.

Brookhaven chemists Morris Bullock (left) and Vladimir Dioumaev examine catalyst samples before analyzing them using nuclear magnetic resonance spectroscopy.

Help to Reduce Hazardous Industrial Waste

Second, the catalyst has the unique ability of being easily removed and recycled. This is so because, at the end of the reaction, the catalyst precipitates out of products as a solid material, allowing it to be separated from the products without using additional chemical solvents. Instead, "It separates itself," comments Dioumaev. "You can simply pour the products into another container and use the catalyst again."

TRIAL AND ERROR

The procedure may sound straightforward, but finding a catalyst that works correctly was a complicated task. "The concept is simple, but striking a balance between maintaining catalyst solubility throughout the reaction and precipitation at the end was a diabolical problem," explains Bullock.

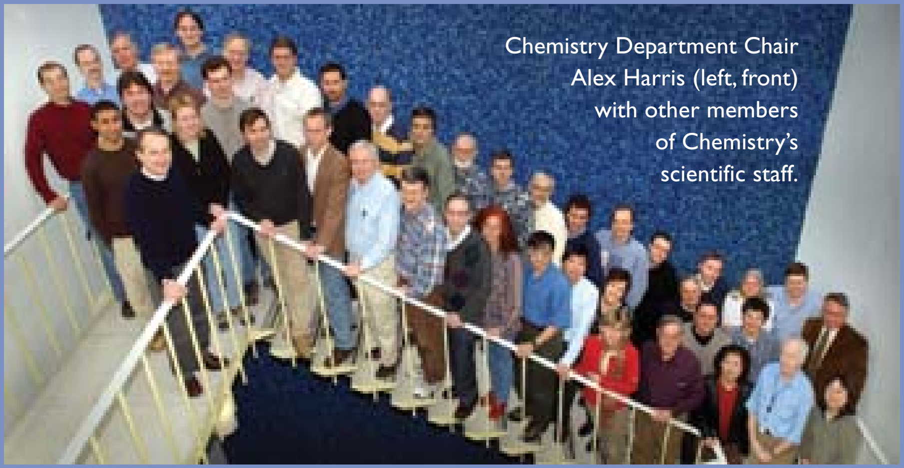
To work, the catalyst must stay dissolved long enough for the reactants to

BNL's Chemistry Department

The two Brookhaven chemists — Morris Bullock and Vladimir Dioumaev — who developed the recyclable catalyst (see story) are just two of the 67 scientists now working in Brookhaven's Chemistry Department. While some past and present Chemistry staff are members of the National Academy of Sciences or holders of the E.O. Lawrence Award or other honors, one Chemistry emeritus — Raymond Davis Jr. — earned the 2002 Nobel Prize in Physics, as well as a 2002 National Medal of Science, for pioneering contributions to astrophysics, in particular for the detection of solar neutrinos.

With an annual budget of $18 million provided predominantly by the U.S. Department of Energy's Office of Science, today's Chemistry Department has a new chairman — physical chemist Alex Harris. His goals for the Chemistry Department are to build additional cross-disciplinary collaborations, especially in materials science and condensed-matter science; continue the successful collaboration with the Laboratory's Medical Department in brain imaging and addiction research; develop additional nanoscience initiatives in anticipation of the opening of the Center for Functional Nanomaterials at Brookhaven; and broaden the Department's use of the National Synchrotron Light Source (see pages 18-21). Experimental and theoretical Chemistry Department research at Brookhaven is divided into five areas:

- CATALYSIS: the study of the structure and reactivity of compounds, such as transition-metal hydrides, that alter the rate of chemical reactions and, in the case of the newly developed recyclable catalyst, may be recovered essentially unaltered at a reaction's end. The goal is to help in the development of clean, efficient fuels, as well as other new and useful chemical substances.
- GAS-PHASE MOLECULAR DYNAMICS: the investigation of the mechanisms involved in the chemical reactions of gases. Included are reactions produced by molecular collisions, as well as by photodissociation, which is the use of photons to break apart compounds. The aim is to understand combustion, which is used to produce 80 percent of the world's energy.
- PHOTO- AND RADIATION-INDUCED REACTIONS: research into the efficient capture and storage of light energy. By studying transition-metal complexes and other systems in solution, the objective is to expand the understanding of electron-transfer reactions, excited states, solvent dynamics, and other chemical transformations. Furthering this understanding will help in the development of long-term storage methods for solar energy, which could then be used as a source of fuel.
- IMAGING & NEUROSCIENCE: collaborative studies involve the development of tracers and the use of medical scanning technology, such as positron emission tomography and magnetic resonance imaging. The purpose is to gain new knowledge of normal physiology, drug action, and the diagnosis and treatment of aging and diseases such as AIDS, addiction, attention-deficit hyperactivity disorder, and multiple sclerosis.
- NUCLEAR CHEMISTRY: building upon Ray Davis's Nobel Prize-winning work, neutrino research is carried out at the Sudbury Neutrino Observatory in Canada. In addition, one of the four collaborations at the Relativistic Heavy Ion Collider (RHIC; see pages 14-17) is based in Chemistry. PHOBOS, the collaboration's detector, is searching for rare events arising from the collision of gold beams, with the goal of discovering quark-gluon plasma, thought to have last existed moments after the Big Bang.



Chemistry Department Chair Alex Harris (left, front) with other members of Chemistry's scientific staff.

Meet Morris Bullock and Vladimir Dioumaev

Though the liquid in their test tubes has a purplish-red hue, Morris Bullock and Vladimir Dioumaev see only green — a fine example of "green chemistry," that is.

"Our interest in developing readily recyclable catalysts and the use of solvent-free conditions arose out of the 'green chemistry' movement — the growing recognition of the importance of using chemical reactions that can contribute to a sustainable future by minimizing the generation of hazardous waste," says Bullock, who has been a member of Brookhaven's Chemistry Department since 1985.

"Green" chemistry is defined as the design of chemical processes and products that minimize or, ideally, eliminate the production of hazardous substances. That approach has multiple benefits, since avoiding both the production of waste and waste treatment can save the environment, lives, and money.

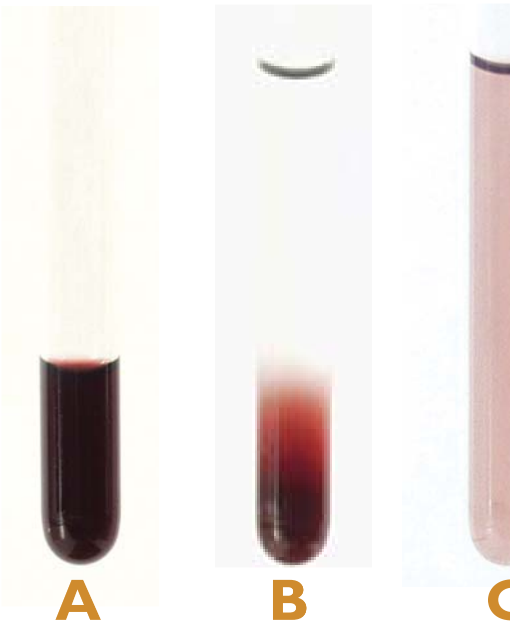
It was, in fact, the economical, practical idea of developing a self-separating catalyst that first drew the interest of Dioumaev, Bullock's postdoctoral fellow.

interact with it, and then must precipitate when the reaction is complete. If these two events do not happen, then the reactants will not generate the products properly, and the catalyst will not be easy to recover and recycle after the reaction. As a result, more steps would be needed to use up the reactants and collect the catalyst, and so the reaction would produce unwanted waste.

To solve these problems, Bullock and Dioumaev employed a tungsten catalyst that they had prepared and have shown to be effective for hydrogenation of ketones, a class of organic compounds. They found that this tungsten complex also catalyzed the reaction of ketones with organic silicon compounds to produce alkoxysilanes, which are used in the manufacture of drugs, pesticides, and other familiar organic compounds, as well as in the preparation of ceramic materials.

In earlier research, the two chemists had discovered that, while this class of catalysts could dissolve in ketones, it does not dissolve in certain other solvents. Instead, the catalysts forms oily precipitates called liquid clathrates.

Observing this, Bullock and Dioumaev wondered if using the oily substance in the reaction might be an ideal way to keep the catalyst suspended in the reactants until the reaction concluded. They postulated that the oil, when compared to a solid precipitate, might offer some advantages in the reaction because it would not obstruct the interaction between the liquid reactants in the way that a solid would.



Soluble in a reagent (A), the new catalyst remains soluble when another reagent is added (B). As the reaction goes on and the product builds up (C), the catalyst precipitates from the mixture as an oil (D), which

The researchers worked with this idea experimentally, developing a suitable catalyst, a formulation containing the metal tungsten. Because this research required knowledge of the catalyst's molecular structure, the structure of the tungsten catalyst was determined using x-rays at the National Synchrotron Light Source (NSLS; see page 18-21).

"In its ideal form, 'green' chemistry eliminates the production of hazardous waste from the start of a process."

MORRIS BULLOCK

> “In making this recyclable catalyst,
> we had to understand the details
> of each bond-making and bond-breaking step
> of the individual reactions making up
> the catalytic cycle.”
>
> VLADIMIR DIOUMAEV

continues as an active catalyst because the reagents can penetrate it. When the reagents are converted into product, the oily catalyst turns into a sticky solid (E), which can be easily separated and recycled.

CATALYST AT WORK

The new catalyst begins working as it mixes readily with the reactants. When the reaction is nearly complete, the catalyst begins to precipitate, yet it remains suspended within the reactants as an oily liquid clathrate clearly visible in the reaction tube. “The reagents penetrate the oil to keep reacting until the reactants are used up,” Dioumaev explains. When that happens, the catalyst is no longer soluble, so it precipitates out of the reaction as a solid, settling to the bottom of the test tube.

Further analysis revealed that virtually no trace of the catalyst is left in the liquid reaction products. This property is particularly desirable, for instance, in the creation of pharmaceutical compounds, which must be free of metal-based catalyst residue to be safe for use.

Now, the Brookhaven scientists will see if catalyst self-separation using liquid clathrate catalysts can employed in other reactions. “At present, we are trying to determine the scope of reactions that can be carried out using this type of catalyst,” says Bullock. “In the future, we will seek to understand the criteria that influence the behavior of catalysts and their ability to mix with different solvents, which may allow us to design more catalysts that are readily recyclable.”

MORE INFORMATION

- funding: Division of Chemical Sciences, Office of Science, U.S. Department of Energy
- paper: “A Recyclable Catalyst That Precipitates at the End of the Reaction,” Nature, 2003, 424, pp. 530-532
- contact: Morris Bullock, bullock@bnl.gov or (631) 344-4315
- Web: www.bnl.gov/bnlweb/pubaf/pr/2003/bnlpr073003.htm and www.chemistry.bnl.gov/SciandTech/PRC/bullock/bullock.html

“Morris was the first to realize the environmental ‘green’ implications when I showed him how the catalyst self-separates,” Dioumaev says.

The team’s approach to designing catalysts is to use fundamental mechanistic information about the individual steps of the reactions and then to design catalysts that use those individual reactions.

“Our long-term goal is rationally to design catalysts that have high reactivity, but that, at the same time, are used in processes that are environmentally benign,” Bullock explains.

Morris Bullock grew up in North Carolina and earned a B.S. in chemistry from the University of North Carolina at Chapel Hill in 1979, and a Ph.D. in chemistry from the University of Wisconsin–Madison in 1983. He did postdoctoral research at Colorado State University before coming to the Lab.

Vladimir Dioumaev did his undergraduate work at Moscow State University in his native Russia, before earning an M.S. in organic and organometallic chemistry through a joint program of Yale University and Moscow State University in 1988.

Dioumaev earned his Ph.D. in inorganic and polymer chemistry from McGill University in 1997 before coming to the United States. He joined the Lab’s Chemistry Department in 2001 and became a naturalized U.S. citizen in 2003.

The main problem in fighting viruses has been the evolution of drug-resistant strains. Toward the goal of developing a new approach to anti-viral therapy that may prevent drug resistance from arising, Brookhaven biologists have developed a multi-drug attack against several sites on a single, vital, viral protein: an enzyme that cleaves other proteins to complete the maturation of newly synthesized virus particles.

BY KAREN MCNULTY WALSH

New Approach to Anti-Viral Therapy

THEY CAUSE DISEASES FROM AIDS TO ZOSTER — with colds, Ebola, hemorrhagic fever, influenza, measles, mumps, rabies, SARS, smallpox, and yellow fever, among thousands of others, in between.

Ultramicroscopic, they are simply composed of a protein coat surrounding a nucleic acid core. Capable of infecting animals, plants, and bacteria, they are unable to metabolize or reproduce without these unwilling hosts.

They are viruses, and "one of the biggest challenges in modern biology is to find ways to thwart them," says Brookhaven Lab biologist Walter Mangel.

The structure of the adenovirus protease, with one cofactor in red and, in turquoise, the amino acids present in the active site.

The main problem in fighting viruses has been the evolution of drug-resistant strains: Almost as soon as scientists come up with drugs to block a virus's disease-causing effects, mutant virus particles appear that are "immune" to the drug. These resistant strains can then go on causing infection. By being able to mutate spontaneously, viruses can survive most any challenge in the environment, including the presence of antiviral agents. In other words, explains Mangel, "Viruses have evolved to secure their existence."

With funding from the National Institutes of Health (NIH) and the Office of Biological and Environmental Research within the U.S. Department of Energy's (DOE's) Office of Science, Mangel and a group of scientists in his lab have developed a new approach to anti-viral therapy that may prevent drug resistance from arising. Their idea: to stage a multi-drug attack against several sites on a single, vital, viral protein.

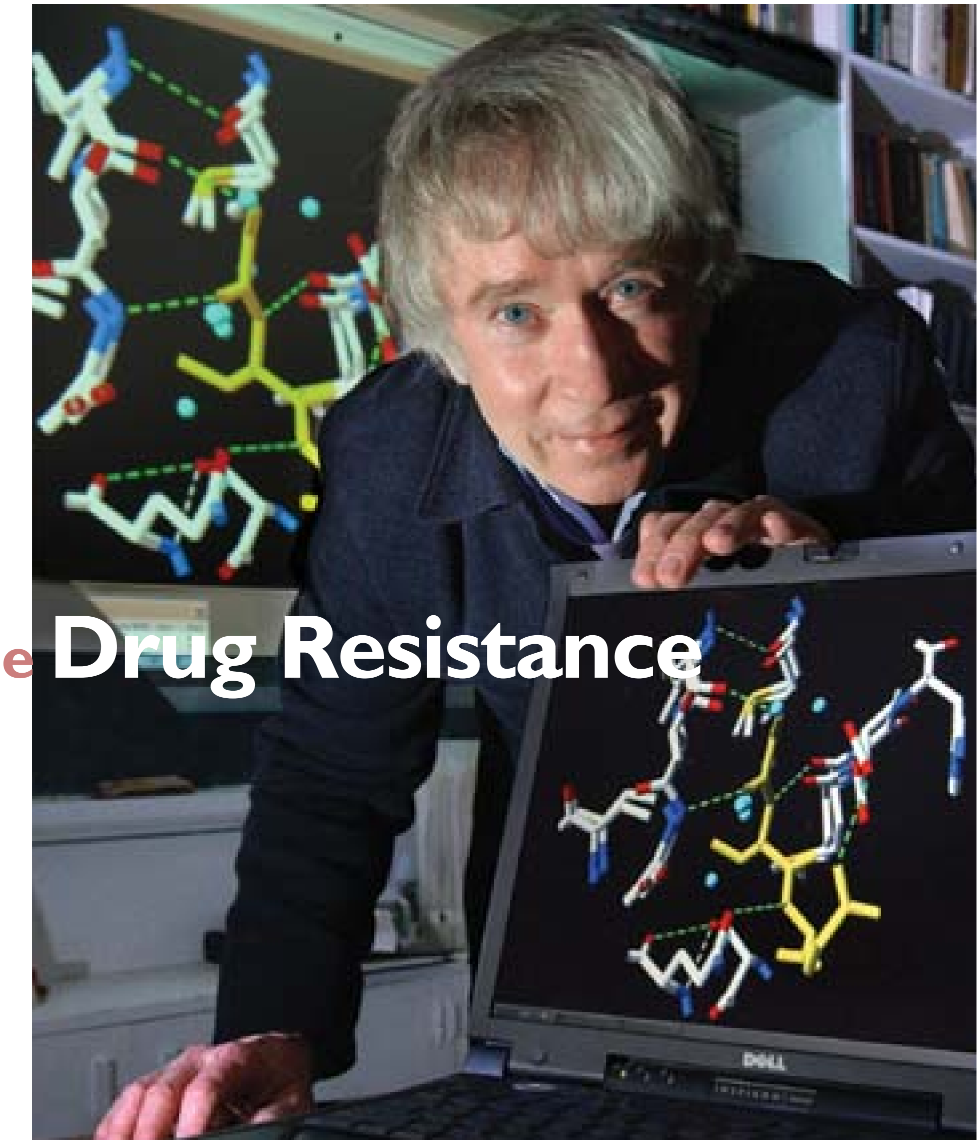
TARGET PROTEASE

The target protein is an enzyme called a protease, which cleaves other proteins to complete the maturation of newly synthesized virus particles.

Similar to the way supportive scaffolding is removed after the completion of a construction project, this protease cleaves, or cuts out, viral "construction" proteins, leaving infectious virus particles behind. Without the protease, the viruses cannot continue to produce infectious progeny. "If you can block the activity of this enzyme," says Mangel, "then you can block the infection."

The concept of blocking a viral protease is not, in itself, new. For instance, protease inhibitors have been among the most successful drugs in the struggle to treat patients infected with human immunodeficiency virus (HIV), the virus that causes AIDS, or acquired immunodeficiency syndrome. But, HIV is notorious for its ability to evolve resistant strains.

What is new in Mangel's approach is the idea of using mul-



Brookhaven biologist Walter Mangel showing the positions of some of the atoms and chemical bonds in the three-dimensional crystal structure of the adenovirus protease.

May Help Overcome Drug Resistance

tiple drugs aimed at different sites on the same enzyme.

The idea arose from x-ray crystallography studies conducted by Mangel and others at the National Synchrotron Light Source (NSLS; see pages 18-21) at Brookhaven Lab. By shining the NSLS's intense beam of x-rays on a crystal of a viral protease and recording how the x-rays scatter off the atoms in the sample, the scientists were able to produce a three-dimensional map of the protein's molecular structure.

The protease they used was from adenovirus, which causes colds and pink eye. It has features in common, however, with proteases from many other viruses, including HIV, and some bacteria, such as those that cause Chlamydia and plague.

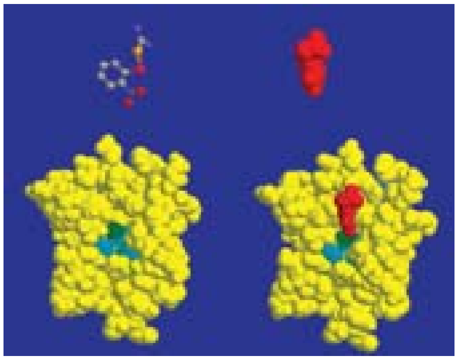
CO-FACTOR INTERACTION

Other studies by Mangel's group indicated that, in order for the adenovirus protease to be active, it must interact with several different co-factors. The x-ray technique allowed the scientists to identify the sites where the various co-factors bind to the enzyme, and the subsequent sequence of structural changes occurring between these sites that leads to the activation of the protease.

One very significant finding is that different parts of the enzyme interact with one another.

One of the co-factors, for example, binds to a site on the enzyme that is quite far from the active site — the part of the protease involved in cleaving protein. Yet, its binding produces structural changes in the active site. Its binding also produces structural changes in the binding site of another co-factor, which also attaches far from the active site. Thus, these crucial sites interact with each other.

These structural details all give the scientists a variety of targets against which to design drugs that can interfere with the active site, the co-factor binding sites, or the pathways between these sites along which signals are transmitted to produce the structural changes. The idea behind such structure-based drug design is to select small molecules that will fit into the structural nooks and crannies important to the functioning of the enzyme. The process is helped along by a powerful computer program that searches databases containing the structures of millions of small molecules, looking for ones that fit.



A small molecular weight drug (top, left and right) was predicted by a computer program to bind to the adenovirus protease (yellow) active site (green and turquoise). The drug is shown binding to the active site (bottom, right).

Using this approach, Mangel's team has already developed five potential drug candidates that block the active site of the adenovirus protease. Once characterized, these drugs will be tested by the NIH to see if they act as anti-viral agents.

MULTIPLE TARGETS

The next step will be to design drugs that block parts of the protease-activation sequence. A drug designed to block any part of this sequence could disable the viral enzyme. As Mangel explains: "The protease-activation sequence can be viewed as a road, so a drug that blocks anywhere along the road prevents the activation sequence from being completed."

Disabling this pathway is particularly appealing because the interconnectedness of the steps makes it much harder for the virus to evolve resistance to the drugs.

Why? Because any mutation in the virus protease that destroys a drug's effectiveness might also change some other part of the enzyme's structure in a way that disrupts the enzyme-activation sequence. Such changes would not be selected for because, without an active protease, the virus would be unable to pass on the drug-resistant trait to new virus particles.

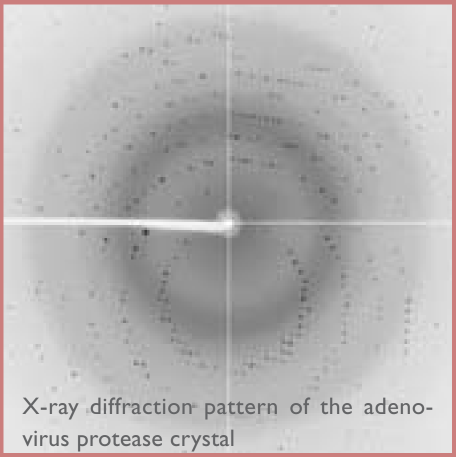
"Using multiple drugs targeted at multiple sites along this sequence would be most effective of all," says Mangel, "because the likelihood of resistance evolving to multiple drugs without altering the crucial activation sequence is infinitely small."

ANTI-PROTEASE APPROACH

Because proteases are so prevalent in infections caused by viruses and bacteria, Mangel suggests that multiple drug treatments against proteases might be effective in treating a wide variety of ailments, including those caused by hepatitis virus, herpes virus, polio virus, dengue virus, SARS virus, and bacterial diseases such as Chlamydia and plague.

In fact, Mangel has recently expanded his work to develop

Crystals of the adenovirus protease



X-ray diffraction pattern of the adenovirus protease crystal

X-Ray Crystallography at the NSLS

Finding drugs that specifically inactivate a protein essential for a disease process involves two technologies. First, the three-dimensional (3-D) atomic level structure of the protein must be known. Then, computer programs find small drugs that bind to a specific site in the 3-D atomic level structure of the protein and inactivate the protein.

The major technique for determining these structures is x-ray crystallography. At the National Synchrotron Light Source (NSLS) at Brookhaven Lab — where life scientists are the largest and fastest growing group of facility users — biologists have used the NSLS's intense x-rays to perform x-ray crystallographic studies to determine the structures of myriad proteins, including those from organisms responsible for common colds, Lyme disease, and AIDS.

In fact, work done in part at the NSLS to solve the structure of a cell-membrane protein essential to the function of all nerve and muscle cells led to a 2003 Nobel Prize in Chemistry for Roderick MacKinnon, who is a Rockefeller University professor and frequent user of the NSLS.

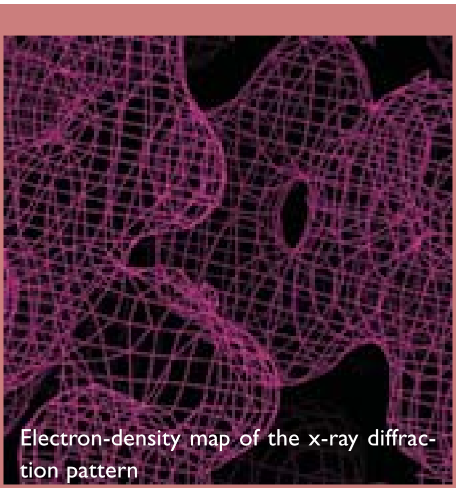
The first step in determining a protein's 3-D atomic structure is to make a crystal with many copies of the protein (see image, top left). The crystal is then mounted inside an experimental station at the end of a beam line of the NSLS x-ray ring.

When a beam of high-intensity x-rays passes through the crystal, it diffracts, or bends, as it interacts with the electrons in the atoms of the protein. These x-rays then hit a detector, which records the scattering pattern as a series of dots (see image, bottom left). Analysis of the dot pattern results in the generation of an electron-density map that bears a resemblance to the protein's 3-D shape (see image, top right).

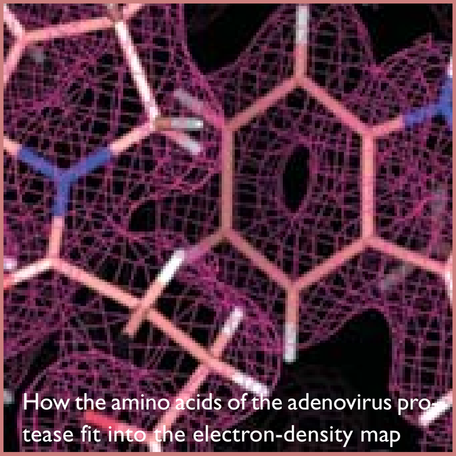
Knowing the sequence of amino acids that make up the protein, scientists then fit that sequence into the electron-density framework to yield a 3-D map of every atom in the protein (see image, bottom right).

> “Certain viruses have learned how to survive most any challenge in the environment, including the presence of anti-viral drugs. One of the biggest challenges to modern biology is to find ways to thwart them.”
>
> WALTER MANGEL

anti-viral agents for use against the coronavirus which causes SARS, or severe acute respiratory syndrome, which was first reported in Asia in 2003. Eventually, he wants to apply the technology developed in his lab to combating malaria, the parasite-caused illness that strikes 300-500 million people worldwide, causes about 1,200 cases in the U.S., and results in the death of 1 million people each year.



Electron-density map of the x-ray diffraction pattern



How the amino acids of the adenovirus protease fit into the electron-density map

‘ATOMIC BIOLOGY’

Mangel says: “The golden age of biology will peak in this century, especially at places like Brookhaven Lab, where biologists collaborate easily with physicists, chemists, and computer scientists to work on complex problems. For the last 50 years, molecular biology, a combination of biochemistry and genetics, was the major discipline in biology. Now, a new discipline is emerging — atomic biology — which is a combination of structural biology and molecular biology. Our ability to define biological molecules and the processes they undertake atom by atom using facilities like the NSLS will produce a new level of understanding of the relationship between structure and function in biology — and, ultimately, the ability to predict structures and functions. And this will lead to effective drugs against viruses, bacteria, and, possibly, even malaria.”

MORE INFORMATION

- research funding: National Institutes of Health; Office of Biological & Environmental Research, Office of Science, U.S. Department of Energy
- paper: “A new form of antiviral combination therapy predicted to prevent resistance from arising, and a model system to test it,” 2001, *Current Medicinal Chemistry*, vol. 8., pp. 933-939
- contacts: Walter Mangel, mangel@bnl.gov, (631) 344-3373
- Web: www.biology.bnl.gov/cellbio/mangel.html

Meet Walter Mangel

Walter Mangel likens protein-cleaving by viral proteases — the enzymes that he is studying in the quest for a new form of anti-viral therapy — to the final step in cathedral construction: As are viruses, cathedrals are built around an internal scaffold, which has to be removed for the final product to be functional.

Mangel’s analogy is not surprising given his interest in the arts. With a B.S. in philosophy and a Ph.D. in biophysics from the University of Illinois, Urbana, he blends science and art whenever he can. For instance, during a recent presentation on his virus studies, he concluded with drawings that he made of the people in his lab — artwork that will be on display at a Long Island gallery this summer.

Before coming to Brookhaven in 1985, Mangel did postdoctoral research at the University of California, Berkeley, and the Imperial Cancer Research Fund Laboratory in London, England. At Brookhaven, he has been working on virus-coded proteases, malaria, and SARS. Aware of the insightful power of structural biology, Mangel has, for the last seven years, been using the x-ray crystallography stations at the National Synchrotron Light Source.

As much as he enjoys literature, Mangel’s greatest passion is classical music and opera. As he explains, “My enjoyment in listening to great music and in doing science is similar.”

Brookhaven Develops Clean, Sustainable

Biofuel field testing, wind-energy design, battery-material development, natural-gas harvesting, clean hydrogen production — these are several of the alternative-energy research initiatives now underway at Brookhaven. The goal is to transfer to industry technology that solves world-wide energy challenges in an innovative, economically feasible fashion.

BY PETER GENZER

THE OIL BURNER FLARES TO LIFE with a bright blue and orange flame, illuminating the walls of Brookhaven's oil-heat laboratory. This burner, however, is fueled much differently than those typically found in homes: It is being powered by a mix of fuel oil and a vegetable oil-derived alternative known as biodiesel, thus reflecting the forward thinking of researchers in Brookhaven's Energy Sciences & Technology Department (ES&T).

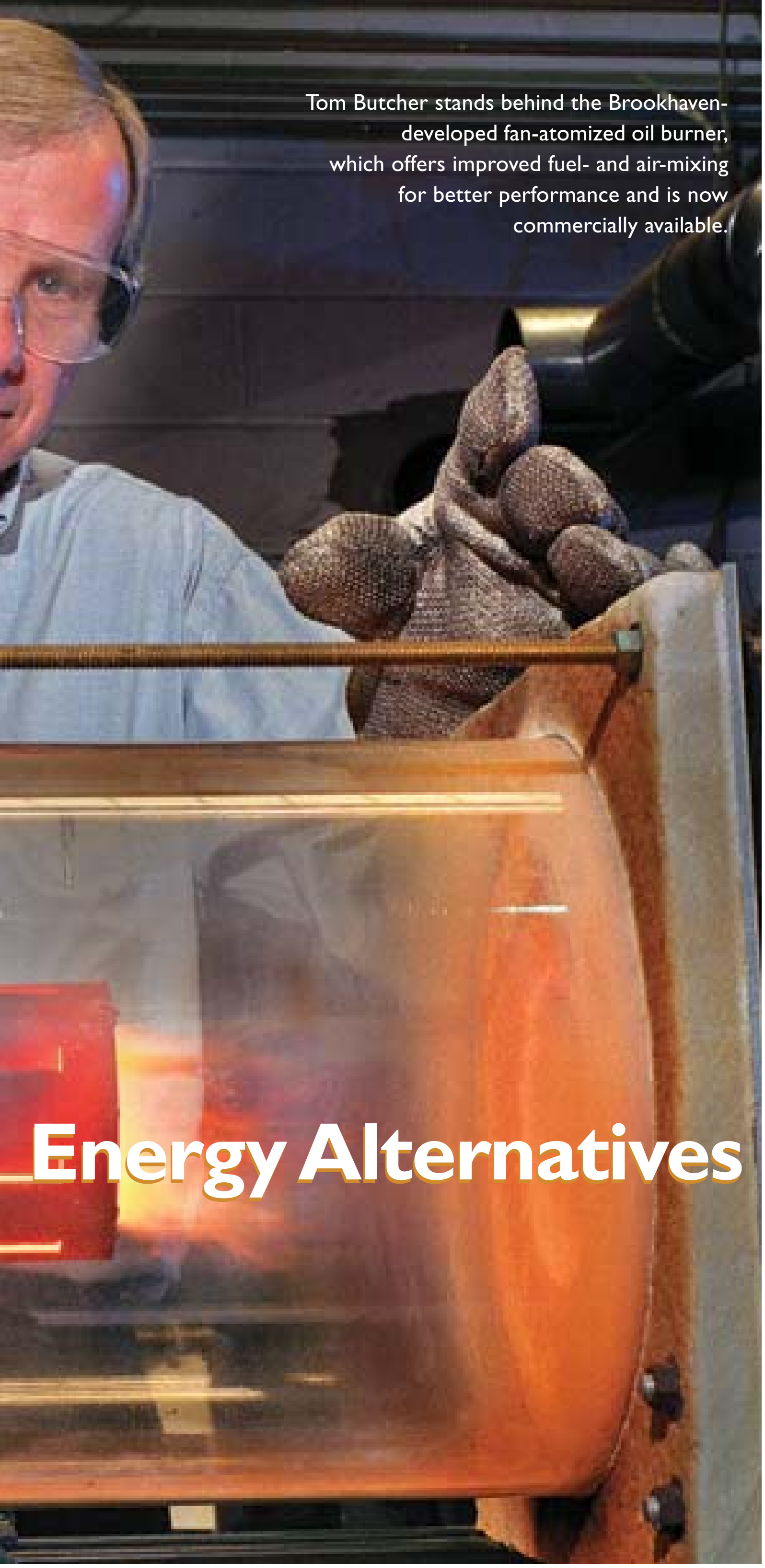
"It is important for the United States to have an alternative fuel option — we need to have a Plan-B energy source that we can turn to in the future," says C.R. Krishna, Brookhaven's lead biodiesel researcher. "So, we see biodiesel as a potential home-grown fuel for home heating."

Initially designed as an alternative for diesel-powered vehicles, biodiesel is a "biofuel" that can also be used as an additive or replacement energy source for use in a standard, oil-fired furnace or boiler. Made from new or used vegetable oils or animal fats, biofuel is biodegradable, nontoxic, and, most important, renewable. While organic materials take millions of years to transform into fossil fuels, biofuel feedstocks can be grown in just a few months, and the plants themselves consume carbon dioxide, helping to counterbalance what is produced when the fuels are burned.

Brookhaven researchers, in collaboration with the New York State Energy Research and Development Authority, have been studying the practicality of biofuel use in a two-year, 100-home field test in upstate New York, one of several such studies going on across the country. The Laboratory is also working with the National Park Service (NPS), providing technical assistance and performing monitoring as part of a test of biodiesel planned for an NPS site on Long Island.

"One of the benefits is that these biofuels burn much more cleanly than fuel oil," explains Krishna. In addition to reducing boiler buildup and the subsequent need for servic-

Energy Alternatives



Tom Butcher stands behind the Brookhaven-developed fan-atomized oil burner, which offers improved fuel- and air-mixing for better performance and is now commercially available.

ing, the burning of biofuels in residential boilers results in the release into the air of less nitrogen oxide and particulate, and no sulfur dioxide, thus reducing air emissions.

In contrast to the reduced environmental cost, biofuels are still more expensive to produce than fuel oil, costing approximately 25 to 50 cents more per gallon. However, as biofuel use becomes more widespread and production rises, Brookhaven researchers expect the price to drop.

"If we can further develop biodiesel, then one economic benefit would likely be an increase in the agricultural production of biofuel feedstock in upstate New York and elsewhere in the country," comments Tom Butcher, who heads ES&T's energy resources division. "This could lead to the expanded use of other plant-based petroleum-replacement products, such as biolubricants and biohydraulic oil, which is already in use at Brookhaven."

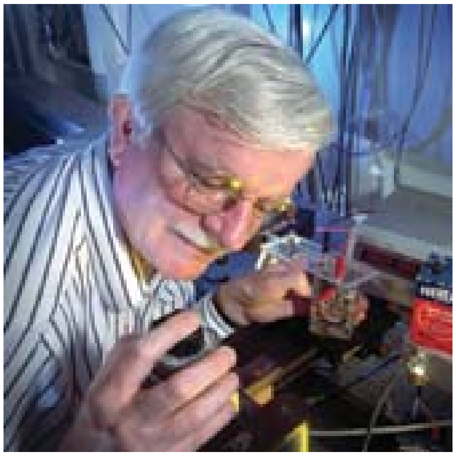
INNOVATIVE SOLUTIONS

Under DOE's energy-resource mission, the biofuel project is just one of several alternative-energy research initiatives under way within Brookhaven's ES&T Department. By focusing on basic and applied research and technology development of clean, sustainable energy products and processes, the goal is to transfer to industry technology that solves world-wide energy challenges in an innovative, economically feasible fashion.

Encompassing energy and economic modeling, energy-infrastructure reliability, proliferation-resistant reactor designs, and energy production, transmission, and storage, current projects include:

- **WIND-ENERGY RESEARCH:** Interest in wind energy in the New York metropolitan area is escalating, and several proposals for large-scale land and offshore wind turbines are under review by local power companies. Designing sturdy foundation structures is one key to the success of these projects, so Brookhaven researchers are now evaluating the dynamic response of large wind turbine systems and assessing alternative foundation materials. A computational method now under development will be a significant technical advance and may lead to a commercial software package. Alternative foundation materials being studied include concrete with high fly ash content, as well as fiber-reinforced concrete.
- **STUDY OF CORROSION-RESISTANT GEOTHERMAL MATERIALS:** Working with DOE's National Renewable Energy Laboratory, Brookhaven researchers are: performing corrosion testing of nickel-chromium-molybdenum alloys; evaluating coatings and mortars for resistance to sulfur-oxidizing bacteria; exploring non-destructive test methods; and field-testing various coatings and cements, with the goal of reducing geothermal energy costs. Brookhaven researchers received an R&D 100 Award and a Federal Laboratory Consortium Technology Transfer Award for developing a high-performance coating system that is highly effective in highly corrosive environments, such as geothermal power plants and chemical processing facilities.
- **DEVELOPMENT OF BATTERY MATERIALS:** For hybrid and electric vehicles, the focus is on advanced cathodes for high-rate lithium ion batteries. Using the material characterization abilities of the National Synchrotron Light Source at Brookhaven (see pages 18-21), researchers are also exploring novel methods of producing fuel-cell electrocatalysts that require substantially reduced amounts of platinum, the most expensive component of a fuel cell.

- COGENERATION OF HEAT AND ELECTRIC POWER: Seen as an important option for achieving large gains in energy efficiency, combined cooling, heating, and power technologies are a possible energy solution even for the individual home. Brookhaven is now serving as a host site for the demonstration and testing of integrated thermal technologies, such as gas- and oil-fired microturbine power generators, absorption chillers, and fuel cells.
- NATURAL GAS PRODUCTION AND STORAGE: Vast quantities of natural gas are trapped in ice structures known as methane hydrates, which are found in permafrost and beneath the ocean floor. Brookhaven researchers have expertise in performing structural studies of methane hydrates and so have teamed with other national laboratories to participate in a DOE effort to establish the fundamental properties of these hydrates. The goal is to permit the safe harvesting of trapped methane by 2015.
- CLEAN HYDROGEN PRODUCTION: Brookhaven researchers are studying catalysts that can streamline the hydrogen-production process and speed the implementation of hydrogen-based fuel cells in a host of transportation and other applications. A novel, low-temperature process of producing "pure" hydrogen recently patented by a Brookhaven scientist (see sidebar, below), may help address one of the most significant difficulties in developing efficient and affordable fuel cells: how to extend the life of the catalysts that make them work.


James McBreen has been working with industry in researching and developing materials for better lithium-ion batteries.

INCREASED RELIABILITY

In addition to these alternative energy projects, the Laboratory is also working to improve the reliability and diversity of existing energy sources.

For instance, Brookhaven researchers are developing an advanced oil-burner system that offers increased efficiency and reduced air emissions relative to conventional burners. This concept will be used in residential appliances and is also the centerpiece of a novel thermophotovoltaic system for electric power generation.


Marita Berndt and A.J. Philippacopoulos display samples of the high-efficiency grout they developed for use in geothermal heat-pump systems. The computer monitor shows a model of thermally induced stresses in these systems.

Scientists are also researching clean liquid fuels, such as heating oil, with ultra-low sulfur and nitrogen contents,

MORE INFORMATION

- funding: Offices of Energy Efficiency & Renewable Energy; Nuclear Energy, Science & Technology; and Fossil Energy; U.S. Department of Energy
- patent: "Method for low temperature catalytic production of hydrogen," United States patent no. 6,596,423, July 22, 2003
- contact: William Horak, horak@bnl.gov or (631) 344-2627
- Web: www.bnl.gov/est/main_e.htm

New Patented Process Produces

Fuel cells combine hydrogen and oxygen without combustion to produce direct electrical power and water. They have been pursued as a source of power for transportation because of their high energy efficiency, potential for source fuel flexibility, and extremely low emissions.

An important problem facing today's most promising fuel-cell technologies is that the same hydrogen feeding the reaction often contains high levels of carbon monoxide (CO), which is formed during hydrogen production. Within a fuel cell, CO "poisons," or degrades, the expensive platinum catalysts which convert hydrogen into electricity, deteriorating their efficiency over time and requiring their replacement.

"The commercial viability of fuel cells for power generation depends upon solving a number of manufacturing, cost, and durability issues," says Brookhaven chemist Devinder Mahajan, "including finding a simple, inexpensive method of producing hydrogen that is essentially free of carbon monoxide." Mahajan has recently done just that, by patenting a process that can produce hydrogen with a very low CO content, which results in extended catalyst life.

Fuel cell researchers have tried to solve the CO-poisoning problem in several different


Devinder Mahajan uses a gas chromatograph to analyze carbon monoxide levels in hydrogen purified using his patented process.

"Our job is to do the necessary basic science and develop the technologies that provide innovative solutions to some of the most important energy issues facing the Northeast, the nation, and the world."

WILLIAM HORAK, CHAIR
ENERGY SCIENCES & TECHNOLOGY DEPARTMENT

using microorganisms to upgrade oil, coal, and other petroleum products, plus developing advanced, proliferation-proof nuclear reactor designs. Work focused on energy conservation includes the development of advanced heating equipment and improved heating-distribution systems in buildings.

Brookhaven's research to improve fuel-oil efficiency has saved approximately $6 billion in the past decade for the 10 million Americans who heat their homes and businesses with oil.

This research has also resulted in two technologies that have been patented: a fan-atomized oil burner, which is up to 10 percent more efficient than typical burners, and a flame-quality indicator, which monitors a burner's flame for maximum efficiency.

Pure Hydrogen for Fuel Cells

ways. One way is by adding metals such as ruthenium or molybdenum to the platinum to formulate more tolerant catalysts. But even these are poisoned by 100 parts per million or more of CO, which are relatively low levels.

A second option is to send the hydrogen through an additional process to remove most of the CO before feeding it into the fuel cell. This process typically employs a high-temperature catalytic reaction known as water-gas-shift, which, because of thermodynamic constraints, leaves unacceptable levels of CO in the finished product.

In Mahajan's new process, a ruthenium trichloride or similar metal catalyst is mixed with a nitrogen complex to form a homogenous solution in a methanol and water mixture. The hydrogen feed containing CO is then introduced, and, at the relatively low temperatures of between 80 and 150 degrees Celsius, the catalyst reacts with the CO and water to convert nearly 100 percent of the CO into carbon dioxide — plus additional hydrogen. The resulting hydrogen feed contains only a few parts per million of CO and is at the correct temperature to be fed directly into a fuel cell. The process also minimizes the amount of waste produced during the reaction because of the low temperature operation, high product selectivity, and high catalytic activity.

"It's quite an economical reaction, and it happens very quickly, in just a few seconds," says Mahajan, "The process works with impure hydrogen produced by any method, including coal and biomass, and it can be easily scaled up for more substantial production."

Mahajan believes his new hydrogen production method will assist in the commercialization of proton exchange-membrane fuel cells, which are the most promising for widespread transportation use because they operate at low temperatures, produce a fast transient response, and possess relatively high energy densities compared to other fuel cell technologies.

Introducing Energy Sciences & Technology

The chair of Brookhaven's Energy Sciences & Technology (ES&T) Department, William Horak, knows that satisfying the ever increasing demand for energy is a never ending challenge. As Horak points out, "Just in the past year, we've seen a major blackout, record electrical demand, and spikes in gas and natural gas prices."

To help solve these problems, ES&T employs a staff of 100 and annually receives some $35 million in funding. This comes primarily from three U.S. Department of Energy offices: Energy Efficiency & Renewable Energy, Fossil Energy, and Nuclear Energy. ES&T also works for other sponsors, including the U.S. Nuclear Regulatory Commission, state agencies, and industry. Performing basic science, undertaking computer modeling and analysis, and developing innovative technical solutions to some of the world's most challenging energy issues, ES&T staff work toward:

- ensuring the adequate supply of clean, reliable and affordable energy
- reducing U.S. vulnerability to supply disruptions
- increasing energy efficiency
- advancing alternative and renewable energy technologies
- maintaining U.S. leadership in the science and technology of energy
- helping to educate and train the next generation of scientists and engineers working in the energy field.

At the recent Quark Matter 2004 conference, new evidence was presented that gold-ion collisions at the Relativistic Heavy Ion Collider are producing an extremely dense form of matter — which may, quite possibly, be the long-sought quark-gluon plasma.

There was also animated discussion about other intriguing RHIC results, including the likelihood that RHIC's experiments have detected the existence of an "anti-pentaquark," an exotic type of particle containing five quarks, and may have uncovered signs of another dense form of matter called color glass condensate.

BY KAREN MCNULTY WALSH

Latest RHIC Results Make News Headlines at

DOMINATING THE AGENDA of Quark Matter 2004, presentations of analyses from recent runs of the four experiments at the Relativistic Heavy Ion Collider (RHIC) created quite a media buzz during the week-long, 17th international conference on ultra-relativistic nucleus-nucleus collisions. For this meeting, more than 600 nuclear physicists from around the world gathered this January in Oakland, California.

Located at Brookhaven Lab and funded primarily by the U.S. Department of Energy's Office of Science, RHIC was built to collide gold ions at nearly the speed of light, to recreate hot, dense conditions that existed at the dawn of the universe. Under those conditions, quarks and gluons are expected to be free of the strong force which holds them confined within protons and neutrons within the atomic nucleus. Freed, they are expected to form a state of matter called quark-gluon plasma, which scientists think last existed a few microseconds after the Big Bang. Studying the freed quarks and gluons within the plasma will help scientists develop an understanding of how matter evolved over time since the Big Bang. It will also provide more insight into the strong force, which is one of the four forces in nature and the short-range attraction responsible for holding the atomic nucleus together.

At the Quark Matter conference, new evidence was presented that gold-ion collisions at RHIC are producing an extremely dense form of matter — which may, quite possibly, be the long-sought quark-gluon plasma. There was also animated discussion about other intriguing RHIC results, including the likelihood that RHIC experiments have detected the existence of an exotic type of particle containing five quarks, and may have uncovered signs of another dense form of matter called color glass condensate.

"We have intriguing results, but it may take some time to sort out their significance in relation to the search for quark-

A computer image of RHIC particle events generated by the STAR experiment.

Quark Matter 2004

gluon plasma or other new discoveries," says Sam Aronson, Chair of Brookhaven's Physics Department and a collaborator on PHENIX, one of the two larger RHIC experiments.

As reporters covering Quark Matter discovered, however, not all those at the conference were quite so circumspect. After the first day of the conference, for instance, stories in the *Oakland Tribune* and *The New York Times*, respectively, quoted scientists who all but declared that discoveries of quark gluon plasma and color glass condensate have already been made.

GOLD, DEUTERONS, PROTONS

The RHIC data presented at Quark Matter are from January through March of 2003, when beams of heavy gold nuclei were collided with beams of deuterons, which are much smaller and lighter nuclei, each consisting of one

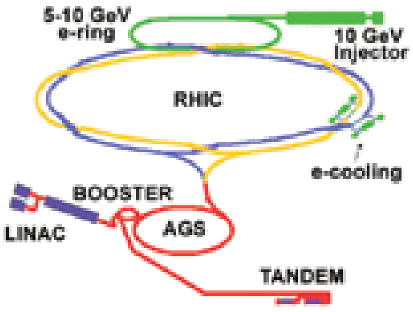
RHIC Experimental Findings Explained

While the discovery of quark-gluon plasma remains to be declared, analyses of data from previous RHIC runs have revealed the following:

- JET QUENCHING: There is more evidence that sprays of particles, or jets, produced in RHIC's gold-gold collisions are getting stuck in some sort of "goo" created by the collisions. This phenomenon, known as jet quenching, was first hinted at after RHIC's first run in 2000 and presented at the Quark Matter 2001 meeting at Stony Brook University and Brookhaven. But findings from more recent runs now confirm that the quenching in gold-gold collisions is a result of the environment created by the collisions and not some preexisting condition.
- COLLISION-ZONE SHAPE: Having mapped out RHIC's collision zone, physicists showed that it is, indeed, almond-shaped, thus giving them yet another way to examine the concept of jet quenching. They found that jets traveling the long axis of the zone are more likely to get stuck than those going the shorter distance across the almond-shaped width.
- DIRECT PHOTONS: Because photons coming directly from the collision zone are unaffected by the collision environment, direct photons serve as a thermometer. Just as the color of a hot, glowing object indicates the object's temperature, the number and wavelength distribution of direct photons are relaying the temperature of the first stage of a collision.
- J/PSI SUPPRESSION: The production of J/psi particles (co-discovered at Brookhaven in 1974) is expected to be suppressed by quark-gluon plasma. To see if J/psi suppression is occurring within gold-gold collisions, control experiments during which no plasma can be created were performed by colliding gold ions with deuterons, or hydrogen ions. Deuteron-gold results on J/psi production will be compared to J/psi production during RHIC's just completed gold-gold run.
- QUARK-STRUCTURE SENSITIVITY: At certain momentum, mesons, which are made of a quark and an anti-quark, exhibit less of a collective motion known as elliptic flow than do baryons, made of three quarks. This could be because of their different quark number, or because the most abundant mesons are lighter in mass. Comparing the elliptic flow of phi mesons and protons (a baryon), which are close in mass, the phi meson appears to have reduced flow similar to the other mesons. This indicates that this effect is, indeed, due to the quark structure, not particle mass. This may be crucial evidence that these two- and three-quark particles all came from a hot soup of strongly interacting quarks and gluons within the first moments of the collision.
- 'HEAVY FLAVOR' PRODUCTION: Physicists reported upon the ability to measure particles containing a "heavy" charm or bottom quark, which are the heaviest in the quark family. These quarks are interesting because the extent to which they mimic the behavior of lighter quarks may be an indication of the extreme conditions, such as high temperature, present in the very first moments of collision, when quark-gluon plasma is supposed to formed.
- COLOR GLASS CONDENSATE: As gold ions are accelerated to RHIC's high energies, some postulate, gluons that flit into and out of existence within the gold nucleus would appear to be longer lived. This would result in a dense collection of gluons called color glass condensate, a new type of particle suppression most evident close to the direction of the beam. A small particle colliding with such a gluon "wall" would be less likely to interact with any individual gluon in the particle's nucleus, resulting in a deficit of jets. Three of RHIC's experiments have now detected such a jet deficit in deuteron-gold collisions. While some interpret this as evidence for color glass condensate within the gold nuclei, others would like to see more data.
- PENTAQUARK PARTICLE: Known particles made up of quarks and/or anti-quarks contain either two or three of them. Indications are, however, that other, multi-quark states exist. CERN in Switzerland and Jefferson National Accelerator Laboratory have uncovered a pentaquark, a new particle composed of five quarks. Now, one RHIC experiment has seen an anti-pentaquark; if confirmed, this will be a new diagnostic tool to analyze quark structure in RHIC experiments.

The RHIC II upgrade will provide a ten-fold increase in the luminosity, or collision rate, enabling scientists to study particle collision events that happen only rarely and to explore states of matter believed to have existed during the first moments after the Big Bang.

FACILITIES FOR THE FUTURE OF SCIENCE: A 20-YEAR OUTLOOK
OFFICE OF SCIENCE, U.S. DEPARTMENT OF ENERGY



Planning for RHIC II and eRHIC

Today, the ultra-high temperatures of the early universe are approachable on Earth — but only inside the largest, highest energy particle accelerators. That is why the Relativistic Heavy Ion Collider (RHIC) was constructed at Brookhaven National Laboratory: to attempt to recreate quark-gluon plasma, a state of matter that is thought to have existed immediately after the Big Bang.

Once the existence of quark-gluon plasma is proven, however, two challenges will remain. The first is to characterize this primordial state of matter and its relationship to the fundamental features of today's universe. The second is to look for color glass condensate. It is hypothesized to be the saturated, or maximum density, state that can be achieved at high energies by particles subject to the strong force, which is the short-range attraction binding atomic nuclei.

To undertake these tasks, Brookhaven has proposed and the U.S. Department of Energy is planning for two upgrades to RHIC: RHIC II and eRHIC.

RHIC II

Although RHIC's gold-ion beams are energetic and intense enough for the plasma's discovery and initial exploration, beams of even higher intensity are needed for a detailed examination of rare processes.

By upgrading RHIC into RHIC II, the collider's luminosity, or collision rate, will

proton plus one neutron. These deuteron-gold runs, along with other data from colliding two beams of protons, serve as a basis for comparison for the gold-gold collisions at RHIC

When two gold nuclei collide head-on, the temperatures reached are so extreme — more than 300 million times the surface temperature of the sun — that the protons and neutrons inside the merged gold nuclei are expected to melt, releasing their quarks and gluons to form quark-gluon plasma. In contrast, when a much smaller deuteron strikes a large gold nucleus, only a small part of the gold nucleus is heated up, and so the matter within the gold nucleus is thought to remain close to its normal state, with distinct protons and neutrons.

In either type of collision, a pair of quarks can be knocked loose from a proton or neutron, with each of these loose quarks producing a spray, or "jet," of ordinary particles. The two jets will emerge back to back from the collision region — unless they are stopped within a dense medium. In the 2003 deuteron-gold experiments, back-to-back jets were seen; but, in head-on collisions during the earlier gold-gold runs, one of the two jets was missing. In addition, fewer highly energetic individual particles were observed coming from gold-gold than from deuteron-gold collisions.

One explanation of the missing jets is that a quark traveling through this environment would interact strongly, losing most of its energy. Thus, if a quark pair is produced near the surface of the nuclear fireball resulting from a head-on gold-gold collision, then the outward-bound quark is likely to escape, while the inward-bound quark is absorbed. As a result, only one jet is detected. This phenomenon, called "jet quenching," is predicted to occur within quark-gluon plasma. The same calculations also predicted the observed suppression of individual high-energy particles.

RHIC physicists are intrigued by these distinctions, which clearly show that head-on gold-gold collisions are producing a nuclear environment quite different from that of deuteron-gold collisions. These phenomena are new at RHIC, as they have not been observed in previous experiments at lower energies.

THE COLOR GLASS CONDENSATE DEBATE

As postulated by some nuclear physics theorists, color glass condensate (CGC) may be another extreme, universal form of matter thought to be an intrinsic property of strongly interacting particles that can only be observed under high-energy conditions such as those at RHIC. If CGC exists, then it may explain many unsolved problems, such as how particles are produced in high-energy collisions and the distribution of matter itself inside of these particles. However, there is considerable controversy among nuclear physicists about the existence of CGC and the interpretation of RHIC data regarding its existence. The debate may not be settled until after RHIC is upgraded to become eRHIC (see sidebar).

According to Einstein's theory of relativity, a high-energy particle appears to be Lorentz contracted, or compressed, along its direction of motion. As a result, the gluons inside one gold ion appear to the other ion as a "gluonic wall" traveling near the speed of light. At very high energies, the density of the gluons in this wall is seen to increase greatly. Unlike the quark-gluon plasma produced in the collision of such walls, CGC describes the walls themselves.

"Color" in the name color glass condensate refers to a type of charge that quarks and gluons carry as a result of the strong force. The word "glass" is borrowed from the term for silica and other disordered materials that act as solids over short time scales but as liquids over long time scales; in gluonic walls, the gluons themselves are disordered and do not change their positions rapidly because of Lorentz time dilation. "Condensate" means that the gluons have a very high density.

THE CONTINUING SEARCH FOR QUARK-GLUON PLASMA

"When we are convinced that we have found quark-gluon plasma, it will be a tremendous return in terms of knowledge on the nation's investment in RHIC science, as well as very satisfying for the people involved," concludes Thomas Kirk, Brookhaven's Associate Laboratory Director for High Energy & Nuclear Physics. "Although we are optimistic about being able to report that discovery soon, we are exercising due caution about interpreting the results that RHIC has produced to date."

And so the search for quark-gluon plasma and other physics continues at RHIC.

MORE INFORMATION

- RHIC Website: www.bnl.gov/rhic
- RHIC experiment Websites: www.bnl.gov/rhic/brahms.htm, www.bnl.gov/rhic/phenix.htm, www.bnl.gov/rhic/phobos.htm, www.bnl.gov/rhic/star.htm
- Quark Matter 2004 Website: www.lbl.gov/nsd/qm2004/
- contact: Thomas Kirk, tkirk@bnl.gov or (631) 344-5414

be increased by a factor of ten, thereby increasing the rate of plasma production and the ability to study rare processes associated with the substance.

After examining the science intersecting physics and astronomy, the National Research Council of the National Academy of Sciences identified the existence of quark-gluon plasma as one of the most pressing research questions to be addressed in this field. In addition, the science underlying RHIC II received the highest ranking from a future-facilities subcommittee of the Nuclear Science Advisory Committee (NSAC), which reports to DOE's Office of Science and to the National Science Foundation.

eRHIC

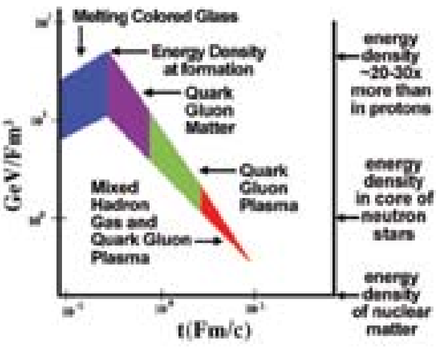
Since color glass condensate is another form of matter thought to exist in heavy nuclei accelerated to high energy, Brookhaven has proposed to turn RHIC into eRHIC, the world's only electron-heavy ion collider.

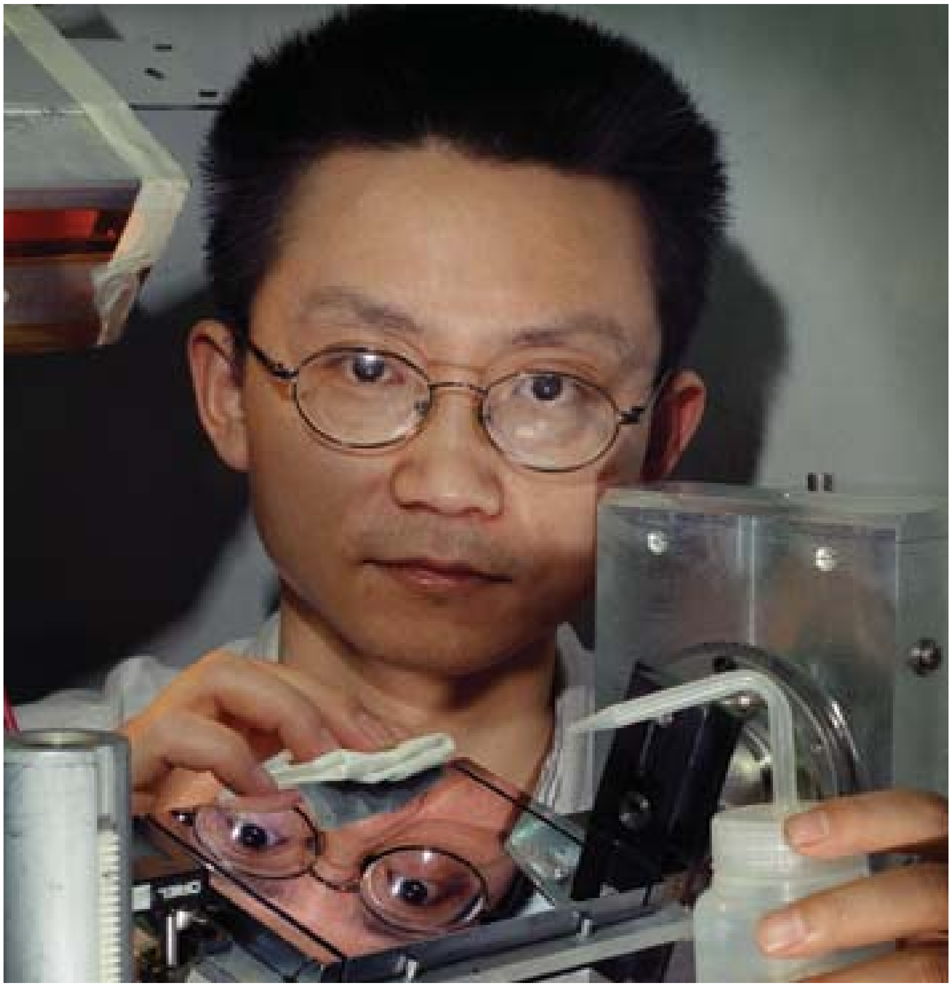
Point-like and weakly interacting, the electron is an ideal probe of nuclear structure. Evidence from lower energy electron accelerators has, in fact, resulted in the prediction of color glass condensate. Some think that, before nuclei colliding at high energy can make quark-gluon plasma, they become densely compressed — a color glass condensate — in the direction they are being accelerated. Upon impact, color glass condensate is thought to "shatter," thus forming the plasma.

Because it is "absolutely central" to U.S. science, eRHIC received the highest science ranking from a future-facilities subcommittee of DOE's Office of Science Nuclear Science Advisory Committee.

The addition of an electron accelerator to the current RHIC facility would create the world's first electron-heavy ion collider (eRHIC), enabling the creation of an enormous number of gluons and presenting a unique opportunity to probe the substructure of particles.

FACILITIES FOR THE FUTURE OF SCIENCE: A 20-YEAR OUTLOOK
OFFICE OF SCIENCE, U.S. DEPARTMENT OF ENERGY





X-rays from the National Synchrotron Light Source at Brookhaven Lab are being employed for the first time in diffraction enhanced imaging, a new, low-dose experimental technique to visualize not only bone, but also soft tissue. This new imaging technique may eventually greatly enhance the detection of cancer and other soft-tissue pathologies.

BY LAURA MGRDICHIAN AND
KAREN MCNULTY WALSH

New Medical Imaging Technique First to Use

TO LOOK BELOW THE SURFACE of the human body in search of deep-seated injury or disease, today's radiologists use an alphabet-soup of imaging techniques: computerized tomography, or CT; magnetic resonance imaging, or MRI; positron emission tomography, or PET; single photon emission computed tomography, or SPECT; whole body scanners; and ultrasound.

Despite the advancements in non-invasive medical imaging since 1895 — the year in which Wilhelm Röntgen discovered a new, higher energy, shorter wavelength form of light able to penetrate solid objects which he called the x-ray — 80 percent of radiology still involves the plain, old x-ray.

But x-ray imaging technology has not changed very much over the past 100-plus years, since the day that Röntgen made the world's first x-ray of his wife's hand, complete with wedding ring. For the most part, x-rays still produce an image that shows bone very clearly, but, if a contrast agent is not used, distinguishes poorly among non-calcified soft tissue, such as ligaments, cartilage, or blood vessels.

Now, thanks to researchers working at Brookhaven Lab, x-rays from the National Synchrotron Light Source (NSLS) are being employed for the first time in a new, low-dose experimental technique to visualize not only bone, but also soft tissue in a way that not is possible using conventional x-rays. Called diffraction enhanced imaging (DEI), the technique provides all the information provided by conventional x-rays, plus additional data on soft tissues that were previously accessible only using alternative methods such as MRI or ultrasound. Even compared to those images, DEI delivers a much sharper and more detailed view of soft tissue.

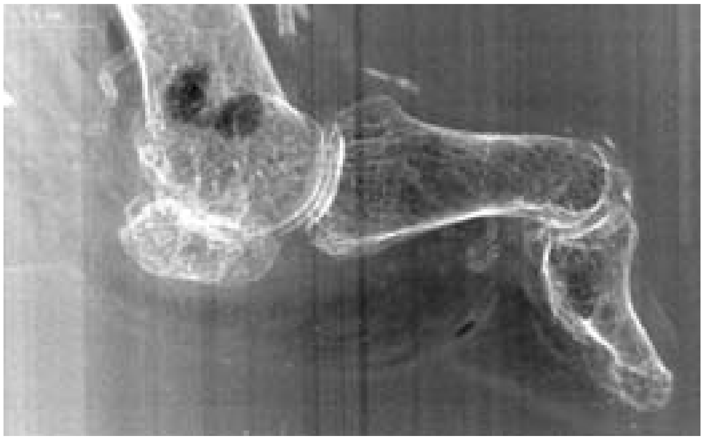
Once DEI is scaled down for clinical use, this new imaging technique may eventually greatly enhance mammography and be used in the search for breast cancer, as well as be employed for the detection of other soft-tissue pathologies such as osteoarthritis and lung cancer.

"We've previously shown that this technique can visualize tumors in breast tissue and cartilage in human knee and ankle joints, but this is the first time that we have shown it to be effective in visualizing a variety of soft tissue, such as skin, ligaments, tendons, adipose pads, and even collagen and large blood vessels," explains NSLS physicist Zhong Zhong (pictured, left), who heads this research project. "The ability to use just one technique to visualize such a range of soft tissue as well as bone has many potential diagnostic applications."

Performed with Rush Medical College, the research is funded by the National Institutes of Health, GlaxoSmithKline, Inc., and the U.S. Department of Energy.

SHADES OF GREY

DEI makes use of the special beams of x-rays available at synchrotron sources such as the NSLS. In contrast to x-rays from conventional sources, synchrotron x-ray beams are thousands of times more intense, as well as being highly collimated, or extremely concentrated into a narrow beam. In addition, synchrotron light can be tuned to be "monochromatic," or essentially of one wavelength or color.



This conventional x-ray of a human toe shows bones and a blood vessel that has been hardened by calcium deposits. Except for a faint shadow of the surrounding soft tissues and the tendon calcification, no other structures are visible.

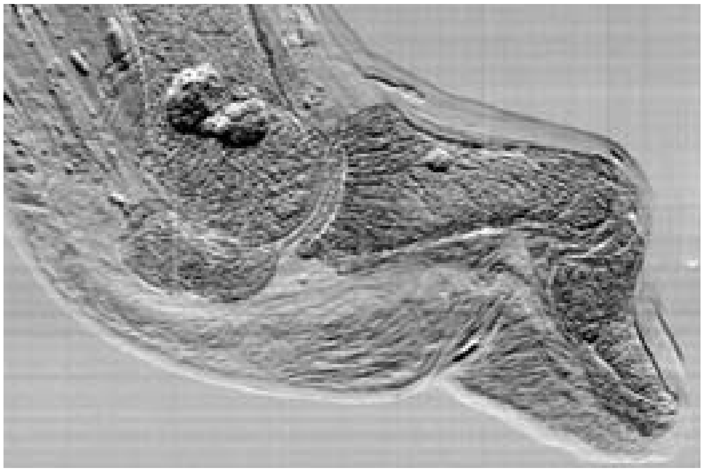
Instead of making use of absorption, DEI, as its name says, relies upon diffraction, which is the variation in the intensities of light after it scatters off structures of different densities and organization. Because DEI relies upon diffraction instead of absorption to produce contrast among various structures, the x-ray dose is lower, while the image quality is higher. "Because absorption is necessary to produce contrast in the image, the radiation dose received from traditional x-rays comes from the x-rays that are absorbed by the body," explains Zhong. "But in DEI, we do not need to use absorption as a contrast mechanism because we are only following the x-rays that pass through the tissue. Therefore, we can use higher-energy x-rays, which pass through with little absorption so the dose is lower."

To make a diffraction enhanced image, x-rays from the synchrotron are first tuned to one wavelength before being beamed at an anatomical structure, such as a hand or foot.

Low-Dose X-Rays to Reveal Soft Tissue

To make a conventional radiograph, x-rays are beamed at, say, a hand that is placed between the x-ray source and a piece of x-ray film or a digital recorder. The density of the structures being pictured and, hence, their x-ray absorption determine what the radiograph looks like.

When the negative is developed, bone and other calcified structures appear clear, or white, and metallic objects, such as Anna-Bertha Röntgen's ring, are seen as bright white. Soft tissue, because it absorbs fewer x-rays than does bone but has small differences in density, is seen as shades of grey.



This DEI scan of the same appendage in the same position, however, clearly shows skin, the fat pads beneath the bones, blood vessel, nail plate, and some tendons, which are clearly distinguishable from the surrounding connective tissue. Within one of the fat pads, the organizational architecture of the collagen framework is even visible. Moreover, the bones take on a three-dimensional appearance because of the detail available in the scans.

As the monochromatic beam passes through, the tissue within the appendage scatters the x-rays at different angles and causes the x-rays to refract, or change directions. The subtle scattering and refraction are detected by what is called an analyzer crystal, which diffracts, or changes the intensity, of the x-rays by different amounts according to their scattering angles.

The diffracted beam is passed on to a radiographic plate or digital recorder, which documents the differences in intensity to show the interior details.

> “The multi-disciplinary working environment at the National Synchrotron Light Source enabled my collaborators and me to turn what was initially a curiosity-driven physics experiment into a biomedical imaging project.”
>
> ZHONG ZHONG

Meet Zhong Zhong

During the ten years that physicist Zhong Zhong has been performing research at the National Synchrotron Light Source (NSLS), starting as a graduate student in 1993 and, since 1998, as an NSLS staff physicist, he has worked on projects that have produced two patents in the field of medical imaging.

In 1999, he and two NSLS colleagues received a patent for the new soft-tissue x-ray imaging technique called diffraction enhanced imaging (DEI), which, using x-rays, allows soft tissue to be viewed with more detail and clarity than conventional imaging methods. This year, the application of DEI to cartilage imaging was patented. Now, two additional patents are pending that will bring the new technique to medical centers.

In the future, Zhong wants to continue other research that he has begun using crystals to improve the focusing of high-energy x-rays, studies that may lead to better synchrotron light sources.

Zhong earned his B.S. in physics from Beijing University, China, in 1990; received an M.S. in applied physics from Michigan Technological University in 1992; and, in 1996, took his Ph.D. in physics from Stony Brook University (SBU). Today, he serves an assistant adjunct professor in the Department of Radiology and an assistant professor in the Biomedical Engineering Department, both at SBU.

In addition to spending his free time with his wife and two daughters, he enjoys fixing up his house, working on his two old cars, and doing vegetable gardening.

2-D AND 3-D TECHNOLOGY

Because the technique itself produces good contrast, another advantage of DEI is that it does not require the use of contrast agents, which are chemicals injected into the body before imaging to distinguish among different tissue types. “For screening, contrast agents are often undesirable since they complicate the procedure and may have side effects,” Zhong explains. Being free of the need for contrast agents, this makes DEI viable as a potential screening tool for breast cancer.

Since medical centers do not have synchrotrons, Zhong and his team are working on transferring two-dimensional DEI technology out of the Laboratory. To make three-dimensional images, they are developing a DEI computed-tomography method useful for making scans of more complex anatomy. But, even in its present form, “DEI provides far greater structural information than conventional radiography,” concludes Zhong.” And this new technology can only stimulate the further development of x-ray imaging.”

MORE INFORMATION

- funding: National Institutes of Health; GlaxoSmithKline, Inc.; U.S. Department of Energy
- paper: “Radiography of soft tissue of the foot and ankle with diffraction enhanced imaging,” Journal of Anatomy, May 2003, volume 202, issue 5, pp. 463-470
- contact: Zhong Zhong, zhong@bnl.gov or (631) 344-2117
- Web: www.bnl.gov/bnlweb/pubaf/pr/2003/bnlpr051303.htm

> “Recognizing the importance of upgrading the NSLS within the next decade, the U.S. Department of Energy is planning NSLS-II, a highly optimized storage ring that will allow synchrotron-light users to continue to push the limits of discovery at Brookhaven.”
>
> STEVEN DIERKER
> ASSOCIATE LABORATORY DIRECTOR FOR LIGHT SOURCES

Brookhaven's Light Sources Directorate

Serving about one-third of the U.S. Department of Energy's synchrotron light-source user community each year, the National Synchrotron Light Source (NSLS) at Brookhaven Lab is one of the world's most widely used scientific facilities. Each year, about 2,400 researchers from more than 400 institutions worldwide use its bright beams of x-ray, ultraviolet, and infrared light for research in the fields of biology, chemistry, geophysics, materials science, medicine, and physics. Some 60 percent of those scientists come from institutions in the northeast U.S.

A drawing of the future National Synchrotron Light Source (NSLS-II)

At the NSLS, for example, scientists have produced images of the AIDS virus as it attacks a human cell, developed a method for imaging soft tissue (see story), and created a technique to make faster, denser computer chips. In addition, the 2003 Nobel Prize in Chemistry was awarded to frequent NSLS user Roderick MacKinnon, a Rockefeller University professor, for work partially done at the NSLS to determine the structure of a specific cell protein that allows nerve and muscle cells to function.

A photograph of the present National Synchrotron Light Source (NSLS)

"Since its commissioning in 1982, the NSLS has continually updated and expanded its capabilities to remain at the forefront of science," comments Steven Dierker, who came to the Lab in May 2001 to chair the NSLS Department. Serving as Brookhaven's Associate Laboratory Director for Light Sources since July 2003, Dierker oversees 175 employees and an annual budget of $38 million.

Nonetheless, the Laboratory realized that, for the research of its formidable user community to continue to flourish, the NSLS needs to be upgraded within the next decade. And DOE agreed: In its recently released 20-year plan for Office of Science user facilities, DOE includes an upgrade to the NSLS complex, which is called NSLS-II.

To come on line in 2012, the proposed upgrade would be an advanced, third-generation x-ray storage ring, producing light that is more than ten thousand times brighter than the present NSLS x-ray ring in the energy range important for research in many fields, including nanoscience, the study of materials on the scale of a nanometer, or a billionth of a meter.

Nanoscience will be the focus of another new, DOE-funded facility at Brookhaven, the Center for Functional Nanomaterials (CFN). To be built beginning in 2005 across from the site for NSLS-II and to be operational by 2008, CFN will be an interdisciplinary facility providing state-of-the-art capabilities to tailor materials at the atomic level, thus improving the chemical or physical functioning of these materials. The resulting "functional nanomaterials" are expected to be the basis of such future technology as faster computers, improved solar energy conversion, and more efficient chemical catalysis.

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