

## BNL Lecture: The AChE-in-3-D Story — Electric Ray Torpedoes, Alzheimer's, Snake Venom and More!

What do electric ray torpedo fish off the coast of California have in common with human brain cells? How does this tie in with Alzheimer's disease, the venom of green mambas from the jungles of Africa, ancient Chinese folk medicine — and BNL's Protein Data Bank (PDB)?

The fascinating connection linking this unlikely list is the enzyme Acetylcholinesterase, AChE for short, which is one of the roughly 3,500 proteins, nucleic acids and other important biomacromolecules whose 3-D structures are stored in the PDB and easily available everywhere on the World Wide Web.

AChE works in the brain's communication system, breaking down the chemical neurotransmitter acetylcholine once it has transmitted a signal from one brain cell to another.

Since some of the symptoms of Alzheimer's disease are believed to be associated with a deficiency in acetylcholine, designing agents to inhibit AChE may be a way to alleviate the effects of this terrible disease. Using AChE in *Torpedo californica*, which is 55 percent identical with human AChE and much easier to do experiments with, researchers at the Weizmann Institute of Science in Israel crystallized the enzyme and then started to determine its structure and how it functions.

Leading the AChE research team at Weizmann was BNL's present Protein Data Bank Head, Joel Sussman, who is also a senior scientist with a joint appointment in BNL's Chemistry and Biology Departments and a professorship in the Department of Structural Biology at Weizmann. To talk about this



Joel Sussman examines the electrostatic properties of the 3-D structure of AChE.

research and some of its implications for medicine and science, and to demonstrate the latest advantages of the enzyme's structure's being stored in the PDB, Sussman will deliver the 306th Brookhaven Lecture, "AChE in 3-D: Mysteries Revealed From the Crystal Structure," on Wednesday, May 17. The talk will begin at 4 p.m. in Berkner Hall, and Sussman will be introduced by Biology Department Chairman William Studier.

In his lecture, Sussman will describe how the "incredibly beautiful" crystalline form of AChE was made; the excitement and surprise of discovering its unusual formation, with a deep, narrow gorge that the acetylcholine has to enter and penetrate to reach AChE's active site. He will also explain why, because AChE acts so extraordinarily quickly — breaking down acetylcholine at a rate of 20,000 molecules per second — the only way to see and record it was by using high-powered x-ray beams in diffraction techniques, which was done at beam lines built by Biology Department

scientists at the National Synchrotron Light Source.

These new techniques, as Sussman will note, are among the reasons why the PDB, started in Chemistry Department in the early 1970s, has expanded so rapidly in the past seven years. He will also explain the advantages to researchers worldwide of this remarkable resource.

Sussman will detail other information: the vital importance of AChE's electro-

(continued on page 2)

### BWIS Seminar

## Determining the Structure Of Tumor-Suppressor Protein p53

What do breast cancer, prostate cancer, lung cancer, bladder cancer and pancreatic cancer have in common? These and many other cancers are marked by the disruption or elimination of multiple tumor-suppressor genes, which code for proteins that inhibit cell replication.

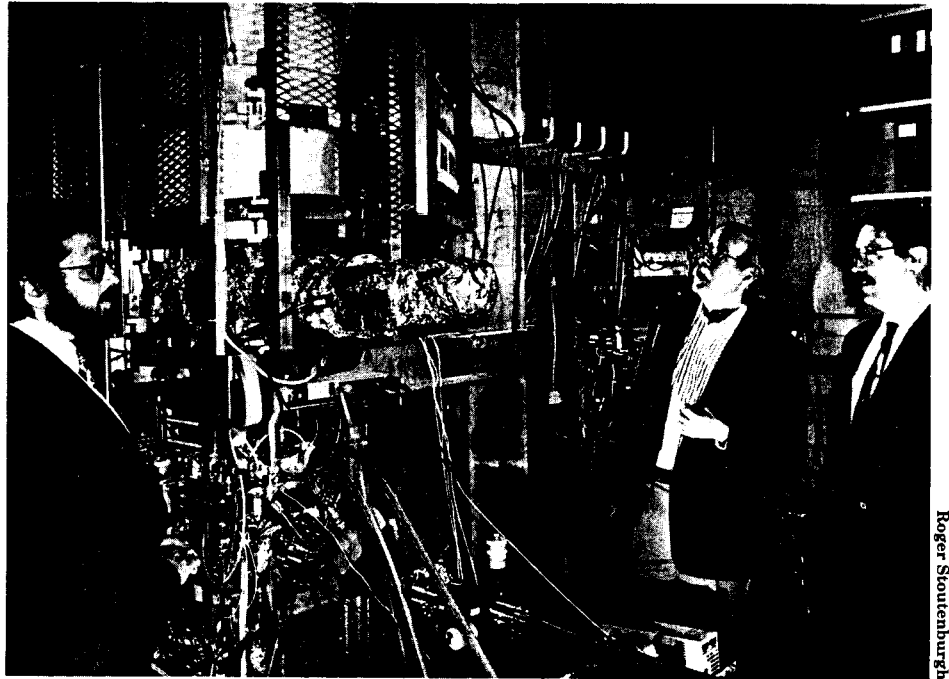
The hallmark of cancer is the uncontrollable proliferation of cells, which compress and damage normal tissue, and which may invade neighboring or-



Cheryl Arrowsmith

gans and establish distant colonies throughout the body. While the development of cancer can result from the activation of oncogenes, which code for proteins that encourage cell replication, many cancers, such as those listed above, arise because of inherited and/or accumulated defects in tumor-suppressor genes.

One such gene is p53, which resides on human chromosome (continued on page 2)



## NREL Director Visits BNL

Visiting the Lab on March 10 to discuss ongoing and possible future joint programs was Charles Gay (right above), the recently named Director of the National Renewable Energy Laboratory (NREL) in Golden, Colorado. A U.S. Department of Energy laboratory for the development of new energy conservation and solar technology, NREL collaborates with BNL in programs involving health and safety, energy planning and advanced photovoltaic energy technologies. Following discussions with BNL Director Nicholas Samios, Department of Applied Science (DAS) Chairman James Davenport and Department of Advanced Technology Chairman Romney Duffey, Gay was photographed with Paul Moskowitz, DAS (left), and Kelvin Lynn, Physics Department. They are standing in front of a unique positron annihilation spectroscopy system perfected at BNL by Lynn and Palakkal Asoka-Kumar, Physics, to detect electronic structural defects in materials. The BNL research will provide valuable data needed for large-scale manufacturing of photovoltaic modules. Gay also visited James McBreen and James Wegrzyn, both of DAS, and Margaret Bogosian, Deputy Manager of the Technology Transfer Office, to discuss other BNL/NREL technical projects in progress.

## Warming to New Oil Heat Technology



During the ninth annual Oil Heat Technology Transfer Conference and Workshop, held at BNL March 22-23, oil heat marketers, equipment manufacturers and researchers saw a demonstration of the RotriX oil burner, developed in Germany to meet new environmental regulations there. Looking at the unit are: (from left) Peter Hofbauer, Viessmann R&D; Jack Sullivan and John Carey, both from the New England Fuel Institute (NEFI); Roger McDonald, BNL's Department of Applied Science (DAS); and Harold Prell, Viessmann Manufacturing Co. The

quartz-glass combustion chamber of the demonstration unit is framing another conference participant, one of close to 200 conference attendees. The two-day meeting began with a keynote address by Sullivan, who is the newly elected Executive Vice President of NEFI. Over half of the technical agenda was devoted to transferring to industry DAS's research and development in oil-heat technology. The conference was sponsored by BNL, the U.S. Department of Energy and the Petroleum Marketers Association of America.

# New Liquid-Discharge Limitations: SEP Monitoring Stepped Up

Stricter release limits for wastewater discharges into waterways and groundwater are not only reflected in a new five-year State Pollutant Discharge Elimination System (SPDES) permit that BNL received from the New York State Department of Conservation (NYSDEC) effective March 1. They are also seen in BNL's efforts to reduce effluent releases and in stepped up monitoring of wastewater by BNL's Safety & Environmental Protection (SEP) Division.

"The new limits reflect the continuing efforts by the state and the Laboratory to reduce environmental releases, particularly those that might affect the Peconic River or the sole-source aquifer beneath the site," says Robert Casey, Head of SEP.

The U.S. Environmental Protection Agency has delegated authority to the NYSDEC to carry out provisions of the Federal Clean Water Act, which includes establishing effluent release limits and administering a permit program. In BNL's SEP, Barbara Royce and Robert Lee are responsible for implementing the new requirements of the SPDES permit.

"The revised SPDES permit establishes much more restrictive effluent release limits for discharges from the Lab's Sewage Treatment Plant [STP]," Royce said. "So all employees must be



The Safety & Environmental Protection Division's Robert Lee and Barbara Royce inspect one of the new flow-monitoring stations located along the Peconic River, downstream of the BNL Sewage Treatment Plant.

even more diligent in their efforts to prevent unacceptable materials from being poured down laboratory sinks."

Wastewater discharges from BNL operations are released to the environment as indirect discharges to the Peconic River after being treated at the STP, or, in the case of stormwater and cooling water, as direct discharges to one of seven on-site groundwater recharge basins. Water from recharge basins percolates to Long Island's sole source aquifer.

Under the new permit, monitoring requirements for discharges from the STP to the Peconic River have increased in both frequency of analysis

and in number of analytical parameters. Five chemicals used on site have been added to the list of 16 that must be monitored at the STP. In addition, effluent limits for discharges have been drastically reduced for inorganic elements such as copper, iron, lead, silver and zinc — some by a factor of four or more. For example, lead limits were reduced from 0.067 parts per million (ppm) to 0.019 ppm.

Regulations for monitoring recharge basins have also become more stringent. Previously, water in these basins only had to be tested for pH, a measure of acidity or alkalinity, and

flow. Under the new permit, routine sampling and analysis for oil and grease, volatile organic compounds, metals and other materials, and reporting of analytical results are required for all recharge basin discharges.

In addition, wastewater from certain industrial processes, including photo processing, printed circuit-board manufacture and metal cleaning, must be monitored at the locations where they originate. These processes have been targeted under the new permit because of their potential to discharge toxic organic and metallic materials.

Four additional steps must now be taken to meet the standards of the new permit: bioassay testing of STP discharge to determine the toxicological effects to freshwater organisms; an engineering study to reduce the amount of processed or cooling water discharged to the STP; rerouting floor drains connected to recharge basins to the STP; and preparing of a best-management-practices plan to reduce or eliminate contaminants in storm-water runoff.

The increased monitoring potentially may cost the Lab an extra \$40,000 per year for analytical services and the time equivalent to one-half of a full-time employee. Also, monthly paperwork required to comply with the new permit has increased from three to a minimum of 13 pages.

The SPDES environmental monitoring data and compliance status are summarized annually in the Site Environmental Report, which is available through the SEP Division, the Public Affairs Office, the BNL Research Library and local public libraries.

— Diane Greenberg

## BWIS Lecture

(cont'd.)

17. The normal protein product of this gene functions in several biochemical pathways, including those enabling a cell to repair damage to its DNA. Because of the important function of the p53 protein, its inactivation through deletions, mutations or interactions with cellular or viral proteins appears to be a key step in the development of many human cancers.

"The Structure of the Tetramerization Domain of Tumor-Suppressor Protein p53, as Determined by Multidimensional NMR Spectroscopy" will be discussed at the next seminar sponsored by Brookhaven Women in Science (BWIS). To be presented on Monday, May 15, at 4 p.m. in the Hamilton Seminar Room, Bldg. 555, the talk will be given by Cheryl Arrowsmith, a senior scientist with the Ontario Cancer Institute, a teaching hospital affiliated with the University of Toronto, Canada. All are invited.

As the speaker will relate, the tetramerization domain of the p53 protein contains a number of important functions associated with p53 activity, including transformation, oligomerization, nuclear localization and a phosphorylation site for p34/cdc2 kinase. As Arrowsmith will explain, the tetramerization domain forms a symmetric dimer of dimers.

She will conclude by presenting the results of modeling based on the observed structure, which suggests possible modes of interaction not only between adjacent domains, but also with DNA.

Cheryl Arrowsmith received her Ph.D. in physical organic chemistry in 1986 from the University of Toronto. After a stint at Stanford University as a postdoc, 1986-89, and then a research associate, 1989-91, she became an assistant professor in the Department of Medical Biophysics of the University of Toronto in 1991. She holds her present position of Senior Scientist in the Division of Molecular and Structural Biology of the Ontario Cancer Institute.

After the lecture, to dine with the speaker at 6:30 p.m. at Ladakin's in Moriches, contact Eva Bozoki, Ext. 3701, by 5 p.m. today.

## BNL Lecture

(cont'd.)

static properties; the "back door" hypothesis as a possible way out of the deep gorge and a possible aid for drugs being designed to circumvent AChE's excessive action; the significance of the discovery that toxins from green mamba venom, which paralyzes the nervous system, have a complementary structure to AChE; and that an herb called huperzine, long a folk medicine used to help elderly people in China regain their memory, may soon be tested for management of Alzheimer's disease.

Joel Sussman received his B.A. in physics at Cornell University in 1965, and his Ph.D. in biophysics at the Massachusetts Institute of Technology in 1972. He has held many visiting professorships at institutions including Duke University, University of California, Berkeley, Fox Chase Cancer Center and Rutgers University.

In 1976, Sussman had joined the Weizmann Institute, Israel, serving over the years in many capacities, including Head of the Department of Structural Chemistry, 1984-5, and Head of the Kimmelman Center for Biomolecular Structure and Assembly, 1988-9. In 1993, while a professor at Weizmann, he joined the Brookhaven Protein Data Bank Advisory Board for a year. Then, in 1994, retaining his Weizmann appointment, he came to BNL to head the PDB.

Among Sussman's honors for outstanding research were Israel's Bergmann Prize in chemistry, 1979, and the U.S. Army Science Conference Award, 1992.

After the lecture, all are invited to join Sussman for discussion and refreshments. All those wishing to have dinner with the speaker at a restaurant off site should call Minette Cummings, Ext. 4726.

## Healthline Lecture

### The Interplay of Genes, Environment in Human Disease

In recent years, research has been identifying the genetics underlying many diseases, including obesity, breast cancer and diabetes. Further findings, however, are revealing that most disease arises as a result of the interplay of human genes and people's environments. So, many of the most common diseases are thought to be preventable through healthy living.

"Genetics and Environment in Common Human Disease" will be the subject of the next Healthline lecture, on Wednesday, May 17, from noon to 1 p.m. in Berkner Hall. Sponsored by the Health Promotion Program (HPP) of the Occupational Medicine Clinic, the lecture will be presented by physician Victor Pechaszadeh. All are invited; the talk will be available on audiocassettes at the Research Library.

Board certified in pediatrics, clinical genetics and clinical cytogenetics, Victor Pechaszadeh, M.D., is the Chief of the Division of Medical Genetics in the Department of Pediatrics at Beth Israel Medical Center, New York City. He is also a member of the Panel of Experts in Human Genetics of the World Health Organization.

To register for this lecture, return the bottom portion of the Healthline flyer recently sent to all employees to Health Promotion Specialist Mary Wood, Bldg. 490. For more information about HPP and its Healthline lecture series, call Ext. 5923.

## ANS Meeting

Marshall R. Cleland of Atomic Energy of Canada, Ltd., will speak on "Food Irradiation — Its Status and Prospects," at the next meeting of the Long Island Section of the American Nuclear Society (ANS), on Wednesday, May 17, at the Radisson Hotel, Islandia. Cleland holds 15 patents to date, including one for the Dynamitron accelerator.

Following cocktails at 6 p.m. and dinner at 7 p.m., the speaker will be introduced by Frank Patti of BNL's Reactor Division.

All are welcome. For reservations, call Jeanne D'Ascoli, Ext. 2277, by Monday, May 15.

## Atlantic City Trip

A few seats remain for the next BERA-sponsored, one-day trip to the Claridge Hotel and Casino on the boardwalk in Atlantic City, on Saturday, June 10. The initial cost will be \$22, but the hotel-casino will give a \$12 coin return.

Buy tickets now at the BERA Sales Office. For more information, call Andrea Dehler, Ext. 3347; Rosalie Piccione, Ext. 3160; or Kay Dellimore, Ext. 2873.

### Note to Employees:

Attendance at lectures, meetings and other special programs held during normal working hours is subject to supervisory concurrence.

## June Bus Trip: Art, Gardens, Sculpture

On Saturday, June 24, join the Art Society-sponsored bus trip to old-world Old Lyme, Connecticut. There, relive the sparkling summers of the American Impressionists, who painted meadows, orchards and river scenes around Miss Florence Griswold's mansion-cum-boardinghouse. It is now a museum of period rooms, art works and memorabilia of over 100 painters, including landscape masters such as Childe Hassam, Willard Metcalf and William Chadwick.

After wandering in the museum gardens and the village, and having lunch, speed forward in time to the free sculpture garden of the Aldrich Museum of Contemporary Art in Ridgefield, which also has eating places nearby.

The bus will leave the BNL tennis court parking lot at 7 a.m. and return by about 9:45 p.m. The Florence Griswold Museum ticket is \$4, and the bus ticket is \$21. Call Liz Seubert, Ext. 2346 or 286-8563, evenings, for reservations.



## Clarifications

In the Brookhaven Bulletin of May 5, 1995:

- From the photograph caption headlined "First Visit of Congressman Forbes," it could be inferred that the April 19 visit by Congressman Michael Forbes was the very first time he had come to the Lab, but it was not: On November 22, 1994, then Congressman-elect Forbes came on site to be given an overview of the Laboratory. Hence, his April 19 tour was his first visit as a Congressman.

- In the story announcing the AUI Distinguished Lecture given by Lev Borisovich Okun, it was not pointed out that both T.D. Lee and C.N. Yang were summer visitors at the Lab in 1956, when they did their Nobel Prize-winning work on parity non-conservation. In fact, though C.N. Yang came from the Institute for Advanced Study, he listed Brookhaven as his affiliation on the 1956 *Physical Review* paper for which he and Lee were awarded the 1957 physics Nobel, since he was a BNL visiting senior physicist at the time they wrote and submitted the manuscript.

## Baldwin Again Wins Long Island Science Bowl

For the second consecutive year, Baldwin Senior High School has won the Long Island Science Bowl, organized by BNL's Office of Educational Programs. This regional contest involving schools in Nassau and Suffolk Counties is part of the National Science Bowl sponsored by the U.S. Department of Energy (DOE) and the Cray Research Foundation.

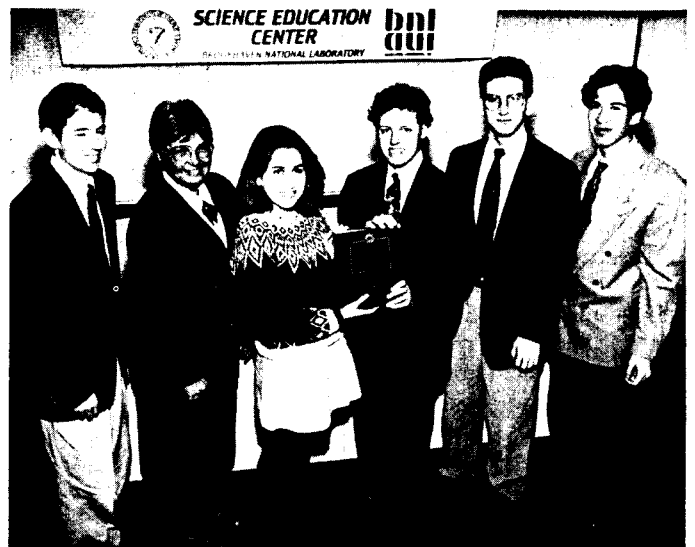
As the winner from Long Island, the Baldwin team was provided with an all-expense-paid trip to Washington, D.C., from April 28-May 1, during which it participated in the national competition.

The National Science Bowl is an academic tournament in which outstanding high school students answer science and math questions. DOE initiated the annual contest in 1991 to increase interest in science and mathematics among American pre-college students. About 8,000 students from 38 states participated in 56 regional contests this year.

The winning team in the national contest, Van Nuys High School from Van Nuys, California, has their choice of one of four prizes: two weeks of study at the International School of Physics in Sydney, Australia; a one-week science project at British Petroleum in Prudhoe Bay, Alaska; one week in a New Mexico-based, hands-on science camp sponsored jointly by Los Alamos and Sandia National Laboratories; or one week of research at two DOE facilities in Hawaii — the Kauai Test Facility Rocket Range and the Pacific International Center for High-Technology Research Ocean Thermal Energy Conversion Site.

At the regional competition held on February 12 on site, 30 BNL scientists volunteered as moderators, rules judges and timekeepers, while four BNL Museum Program staff members of the Public Affairs Office were scorekeepers.

In addition to Baldwin Senior High School, the other high schools that placed in the top eight out of 47 schools in



Roger Stoutenburgh

The Baldwin Senior High School team members who won the Long Island regional Science Bowl held at BNL are: Brian Staskowski (left), Staci Mesher (center, left) and Lee Ashendorf (center, right), who are displaying the standard reference, *Chemical Rubber Corporation Handbook of Chemistry and Physics*; and Adam Jacobs and Jason Bressner (right), with team coach Barbara Riess.

the Nassau-Suffolk regional competition were: Roslyn, taking second-place; Massapequa and Garden City, placing third; and George W. Hewlett High School in Hewlett, JFK High School in Plainview, Ward Melville High School in East Setauket and W.T. Clarke High School in Westbury, all tying for fourth place.

## 1995 Basketball Champions



Roger Stoutenburgh

Wild horses couldn't stop the Mustangs from galloping off with the regular season, nine games to one. But, by defeating the Mustangs 66 to 55, Magic won the 1995 championship game on April 13 and once again worked its wizardry to become the Basketball League champions for a second year in a row. The back-to-back champs are: (back row, from left) Albert Langhorn, co-captain Terrence Buck, Raymond Jackson, Patrick Brown, captain Mitchell Williams; (front row, from left) Edward Gregory, Troy Mayo, Fred Maier and Dennis Ryan; missing is Carlos Victoria. For leading his team's defense, Raymond Jackson was named the game's most valuable player.

## Mountain Club

The Mountain Club has reserved the Watch Hill group campground on Fire Island for Memorial Day weekend, May 26-29. All BNL surf, sun and nature lovers and their families are invited to camp with the club. Call Nancy Kuehner, 878-6947, after 6 p.m., or Nancy Nagy, 821-2652, for more information.

## Arrivals & Departures

### Arrivals

Albert B. Andrews ..... Comp. & Comm.  
Joseph A. Drozd ..... RHIC  
Maxim Y. Gorbunov ..... App. Science

### Departures

This list includes all employees who have terminated from the Lab, including retirees:  
Steven C. Bradley ..... Reactor

## Software Demo

The Rasna Corporation will present a demonstration of MECHANICA technology for design synthesis, on Wednesday, May 17, in the CCD seminar room, Bldg. 515, beginning with coffee and refreshments at 9 a.m. After a round table with BNL users at 9:30 a.m., the software demonstration will begin at 10 a.m.

Based on the geometric element analysis (GEA) technology for structural simulation and optimization, MECHANICA has applications for static, model, thermal, buckling, dynamic response and nonlinear simulations.

All are welcome to attend. For more information and to reserve a seat, call Pam Mansfield, Ext. 7286.

## AIX Meeting

The next meeting of the AIX Local Users Group will be held on Thursday, May 18, at 2 p.m. in room 2-160, Physics, Bldg. 510. For further information, contact Ronnie Evans, Ext. 2851.

## Microcomputer Club

The next meeting of the BERA Microcomputer Club will be held on Thursday, May 18, at noon in the lobby of Berkner Hall, during which a representative from Hauppauge Computer Works will demonstrate its Win/TV video overlay and capture card for the PC. The Win/TV cards show a live video overlay under Windows, OS/2 and WindowsNT; can capture high-quality video images to disk; and are used for security, medical imaging, desktop publishing and image analysis.

All are welcome to attend; bring your lunch. For further details, contact Steve Stein, Ext. 5694.

## In Memoriam

Arthur E. Nelsen, who retired from the Supply & Materiel Division (SMD) on January 28, 1977, died on March 15 at the age of 80. He joined the Lab on January 10, 1966, as a janitor in the Plant Maintenance Division. In 1968, he transferred to SMD, where he was working as a stores clerk when he retired.

Andrew Ruzicka, who had retired on June 30, 1980, died on April 29. He was 67 years old. He began his 18-year career in the Biology Department on March 19, 1962, as a field & greenhouse worker. Ruzicka retired as a senior laboratory specialist.

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### Season's Opening!

Wednesday, May 17  
11:30 a.m. to 1:30 p.m.  
in the parking lot  
opposite Berkner Hall,  
between the tennis courts and  
the Science Education Center

