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Biological and Environmental Research Program at Oak Ridge National Laboratory

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Environmental, Life, and Social Sciences

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Acknowledgments

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Role

The Oak Ridge National Laboratory (ORNL) is managed by Martin Marietta Energy Systems, Inc. (MMES), for the U. S. Department of Energy (DOE). ORNL is one of DOE's major multiprogram national laboratories. Activities at the Laboratory are focused on basic and applied research, technology development, and other technological challenges that are important to DOE and to the nation. The Laboratory also performs research and development (R&D) for non-DOE sponsors when such activities complement DOE missions and address important national and international issues.

The Laboratory is committed to the pursuit of excellence in all its activities, including the commitment to carry out its missions in compliance with environmental, safety, and health laws and regulations. The principal elements of the Laboratory's missions in support of DOE include activities in each of the following areas:

- *Energy production and conservation technologies.* The Laboratory conducts applied R&D in energy technologies–in conservation, fission, magnetic fusion, renewable resources, and fossil energy.
- *Physical, life, and social sciences.* Experimental and theoretical research is undertaken to investigate fundamental problems in physical, chemical, materials, computational, biomedical, earth, environmental, and social sciences; to advance scientific knowledge; and to lay the foundation for other technologies of national significance.
- *Scientific and technological user facilities.* ORNL designs, builds, and operates unique research facilities for the benefit of university, industrial, other federal agency, and national laboratory researchers. Currently, ten major user facilities are found at ORNL, ranging from particle accelerators to a 12,400 acre outdoor laboratory for studying large-scale environmental processes. The Laboratory brings national and international research elements together for important scientific and technical collaborations.
- *Environmental protection and waste management.* ORNL develops technologies to correct existing environmental problems, to prevent future problems, and to reduce waste generation.
- *Science and technology transfer.* The transfer of science and technology to U.S. industries and universities, a key factor in increasing the nation's international competitiveness, is an integral component of ORNL's R&D missions.
- *Education.* ORNL helps to prepare the scientific and technical work force of the future by offering innovative and varied learning and R&D experiences at the Laboratory to students and faculty members from the preschool level through post-doctoral studies.

With an annual operating budget of over $600 million, ORNL is the largest of the nation's five multiprogram, non-weapons laboratories. ORNL employs more than 4600 staff members, as well as hosting some 2300 guest researchers from universities and industries each year.

As shown in Figure 1, ORNL's funding totaled about $636 million in 1991, and was provided by a variety of DOE and non-DOE sources. Approximately 28% of this funding, or about $175 million, was supported by DOE's Office of Energy Research (OER). In turn, about 17% of the OER total was funded by the Biological and Environmental Research (BER) Program (budget code "KP") from the Office of Health and Environmental Research (OHER).

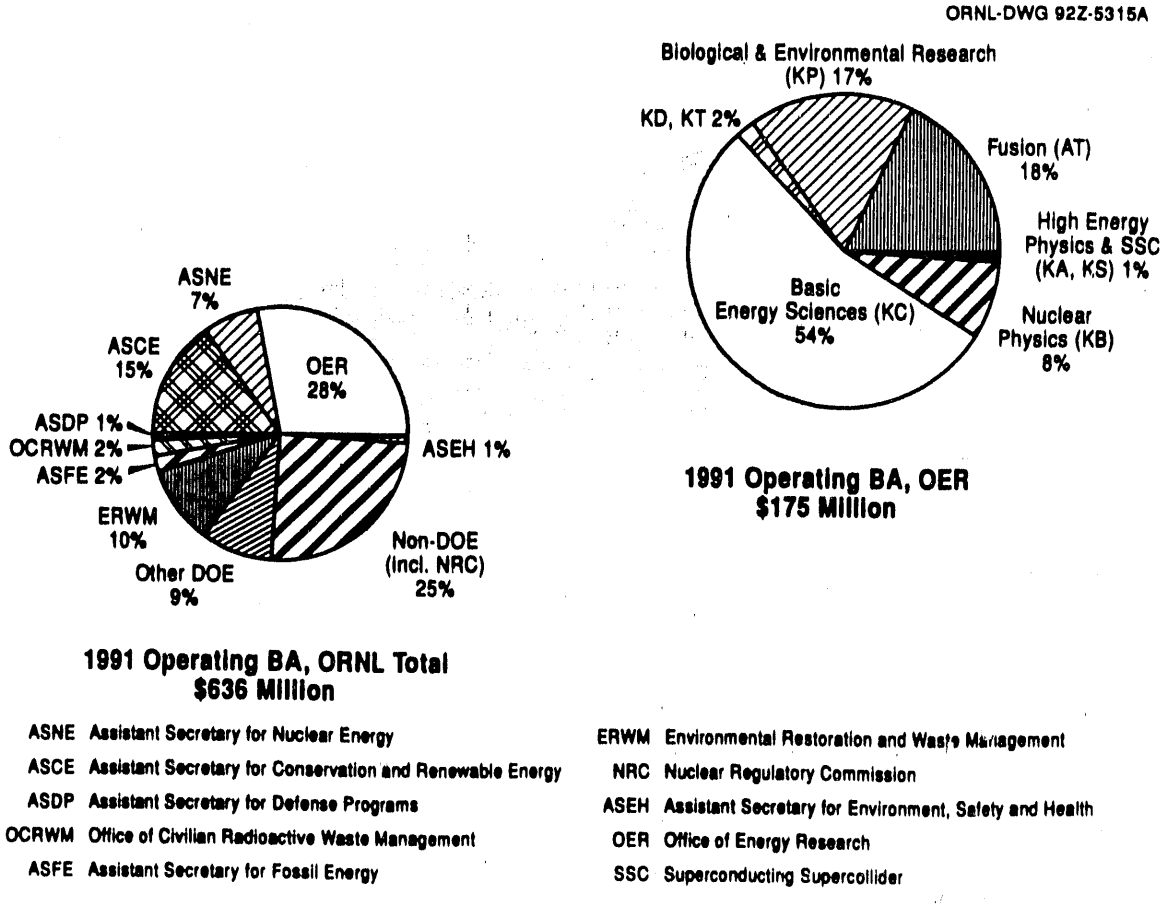

Fig. 1. 1991 annual operating budget, Oak Ridge National Laboratory

The principal mission of OHER's BER program is to provide the scientific foundation for the understanding and anticipation of the long-term health and environmental consequences of energy use and development, and for the understanding and technological solution of major problems in biology and medicine related to these issues. The research should also provide the foundation for developing solutions to environmental problems related to energy technologies. OHER is to make effective use of the unique multidisciplinary capabilities of the national laboratories, in concert with the university and industrial scientific community, for the scientific and technological benefit of the nation in areas related to biology, medicine and environmental science on problems of particular significance to energy production and use.

At ORNL, BER activities will continue to prosper as essential elements of the Laboratory's research programs. In biology, the plan is to build on the core areas of mammalian genetics, molecular biology, and protein engineering. In addition, it is planned to expand multidisciplinary research in structural biology and genome mapping. The proposed new Center for Biological Sciences (CBS) will provide modern, cost-effective space to maximize ORNL's competitiveness in biological research. Enhanced efficiency and diminished security restrictions will facilitate interactions with the external community and will be compatible with establishing user facilities for specialized techniques such as neutron scattering and insertional mutagenesis.

Health and safety research will continue its focus on the measurement and assessment of human health impacts of radiological and chemical substances. Emphasis will be on forming a new center of risk management, improving the understanding of pollutant interactions at the atomic and molecular levels, enhancing studies

of the liquid state of matter, and developing advanced photonics for environmental and biomedical applications. Progress will continue in the development of radiopharmaceutical products for routine clinical applications, advanced information management techniques, and state-of-the-art site characterization methods and instrumentation. Important goals are to continue to maintain world leadership in radiation dosimetry and to establish centers of excellence in health risk analysis and health physics instrumentation.

In the environmental sciences, the broad goal is to retain the Laboratory's status as one of the world's premier ecological-environmental research centers. The environmental sciences program will cover both energy-related environmental issues and global science. An important objective is to understand from these studies the interactions of physical and chemical agents with living organisms, including the ultimate consequences on the environment. Global environmental studies will be directed toward gaining the fundamental understandings needed to deal intelligently with the major global-change issues including global warming. One of the goals is to provide practical input to decision makers for making technology and policy decisions.

This report is the 1992-1994 Program Director's Overview Report for ORNL's BER Program, and as such it addresses KP-funded work at ORNL conducted during FY 1991 and in progress during FY 1992; it also serves as a planning document for the remainder of FY 1992 through FY 1994. Non-BER funded work at ORNL relevant to the mission of OHER is also discussed. The second section of the report describes ORNL facilities and resources used by the BER program. The third section addresses research management practices at ORNL. The fourth, fifth, and sixth sections address BER-funded research in progress, program accomplishments and research highlights, and program orientation for the remainder of FY 1992 through FY 1994, respectively. Work for non-BER sponsors is described in the seventh section, followed by a discussion of significant near and long-term issues facing BER work at ORNL in the eighth section. The last section provides a statistical summary of BER research at ORNL. Appendices supplement the above topics with additional detail.

ORNL/OHER Facilities and Resources

This section describes the facilities and resources at ORNL that are applied to OHER funded research. Included are organizational information, funding types and levels, user facilities, and personnel information.

The administration and management of the ORNL BER Program are the responsibility of the Associate Laboratory Director for Environmental, Life, and Social Sciences, who reports directly to the ORNL Director. (Fig. 2).

As can be seen, seven ORNL divisions representing a wide range of expertise were involved in BER work during FY 1991: Analytical Chemistry, Chemistry, Engineering Physics and Mathematics, Instrumentation and Controls, Biology, Environmental Sciences, and Health and Safety Research (the Global Environmental Studies Center was also involved in BER work during FY 1991, but the extent of involvement is included in the divisional totals).

The divisions noted above were involved in BER work to varying degrees, as measured by the percent of total KP funds authorized to each (Fig. 3). The principal divisions involved were Biology (40%), Environmental Sciences (30%), and Health and Safety Research (23%); combined, these three divisions account for about 93% of the BER funds authorized at ORNL during FY 1991. Consequently, for the remainder of this report, details of these three divisions are emphasized more than other ORNL divisions involved in the BER Program. Organizational charts for these three divisions are presented in Figures 4-6.

The BER programmatic funds are distributed in six subprograms, noted as KP01 (Analytical Technology-Dosimetry Research and Measurement Science), KP02 (Environmental Research), KP03 (Health Effects), KP04 (General Life Sciences), KP05 (Carbon Dioxide Research), and KP06 (Nuclear Medicine).

Figure 7 presents the distribution of the total BER funds authorized at ORNL during FY 1991 by KP subprogram. The combined total of KP02 through KP05 funds accounted for about 85% of the KP funds at ORNL during FY 1991. Funding supplied to BER divisions by non-BER sources is highlighted in the seventh section of the report.

Two of ORNL's ten major user facilities are of principal interest to the BER Program: the Bioprocessing Research Facility (BRF) and the National Environmental Research Park (NERP). The BRF integrates physical resources from the Biology and Chemical Technology Divisions to include laboratories for the investigation of advanced bioprocessing concepts using stirred-tank and columnar bioreactors and a fermentation pilot plant for large-scale batch and columnar experiments. Other research and support laboratories are available on-site. The NERP, located on the DOE Oak Ridge Reservation (ORR), provides 5008 ha (12,400 acres) of protected land for research and education in the environmental sciences. Lying in the heart of an eastern deciduous forest area of streams and reservoirs, hardwood forests, and extensive upland mixed forests, the research park offers the unique advantages of a large information base, a close proximity to educational institutions, and on-site resources, such as the services of environmental scientists at ORNL and the field and laboratory facilities.

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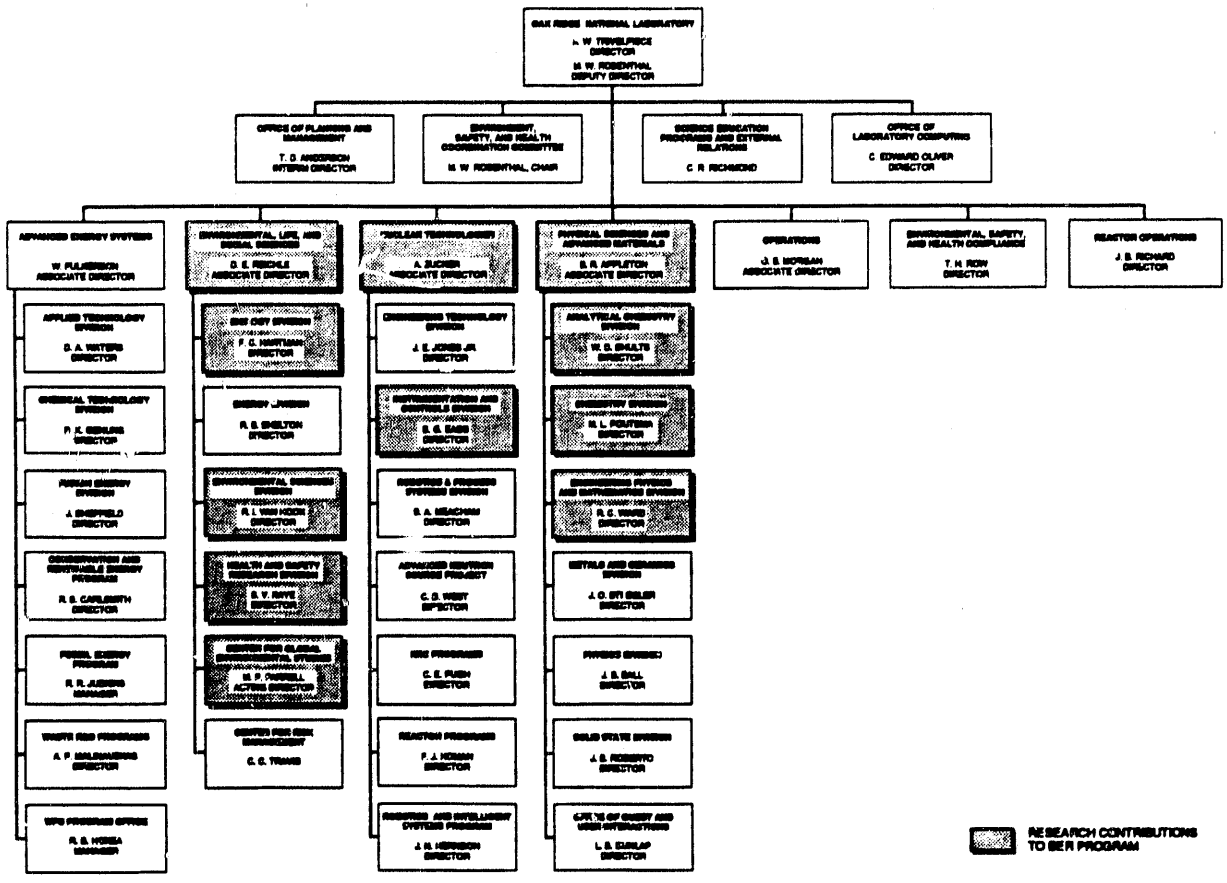

Fig. 2. Simplified organizational chart of Oak Ridge National Laboratory showing involvement in the Biological and Environmental Research Program during FY 1991.

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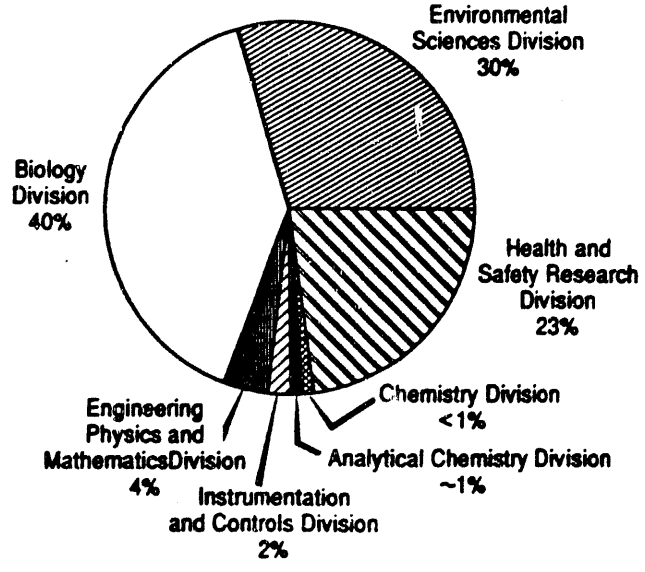

Biological and Environmental Research Program (KP)
FY 1991 Operating BA
$30 million

Fig. 3. KP authorization by ORNL divisions during FY 1991

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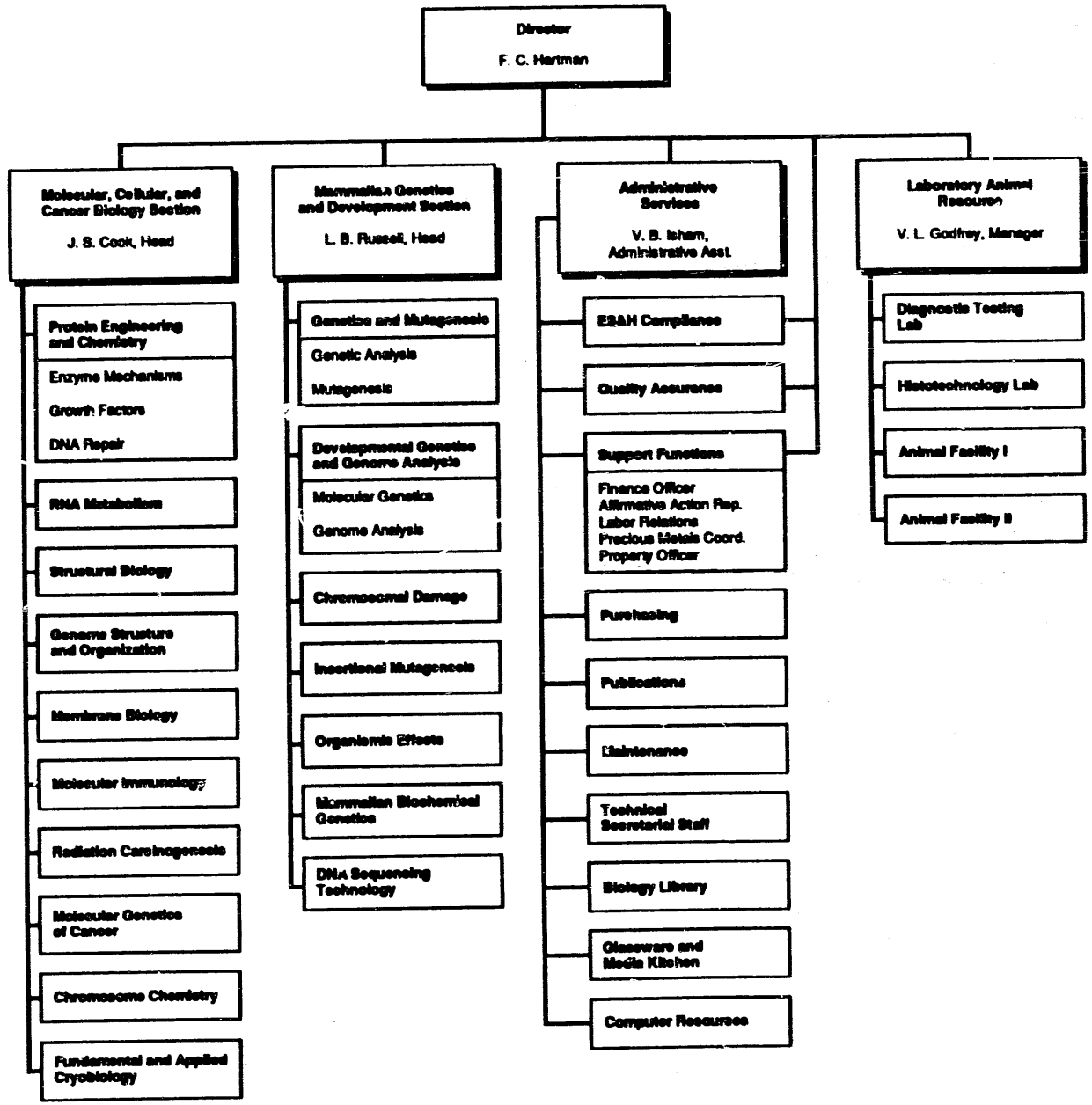

Fig. 4. Organizational Chart for the Biology Division.

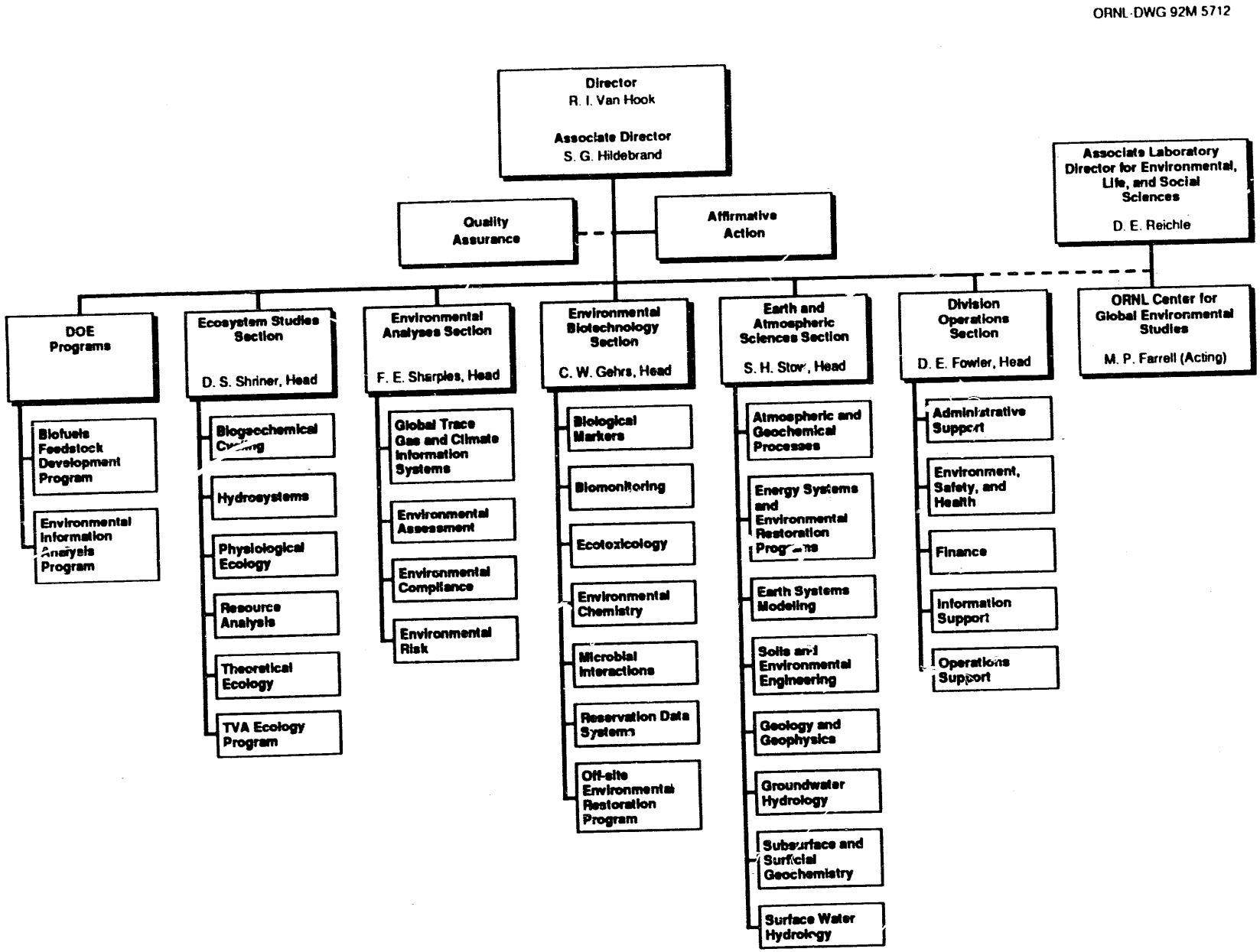

Fig. 5. Organizational Chart for the Environmental Sciences Division.

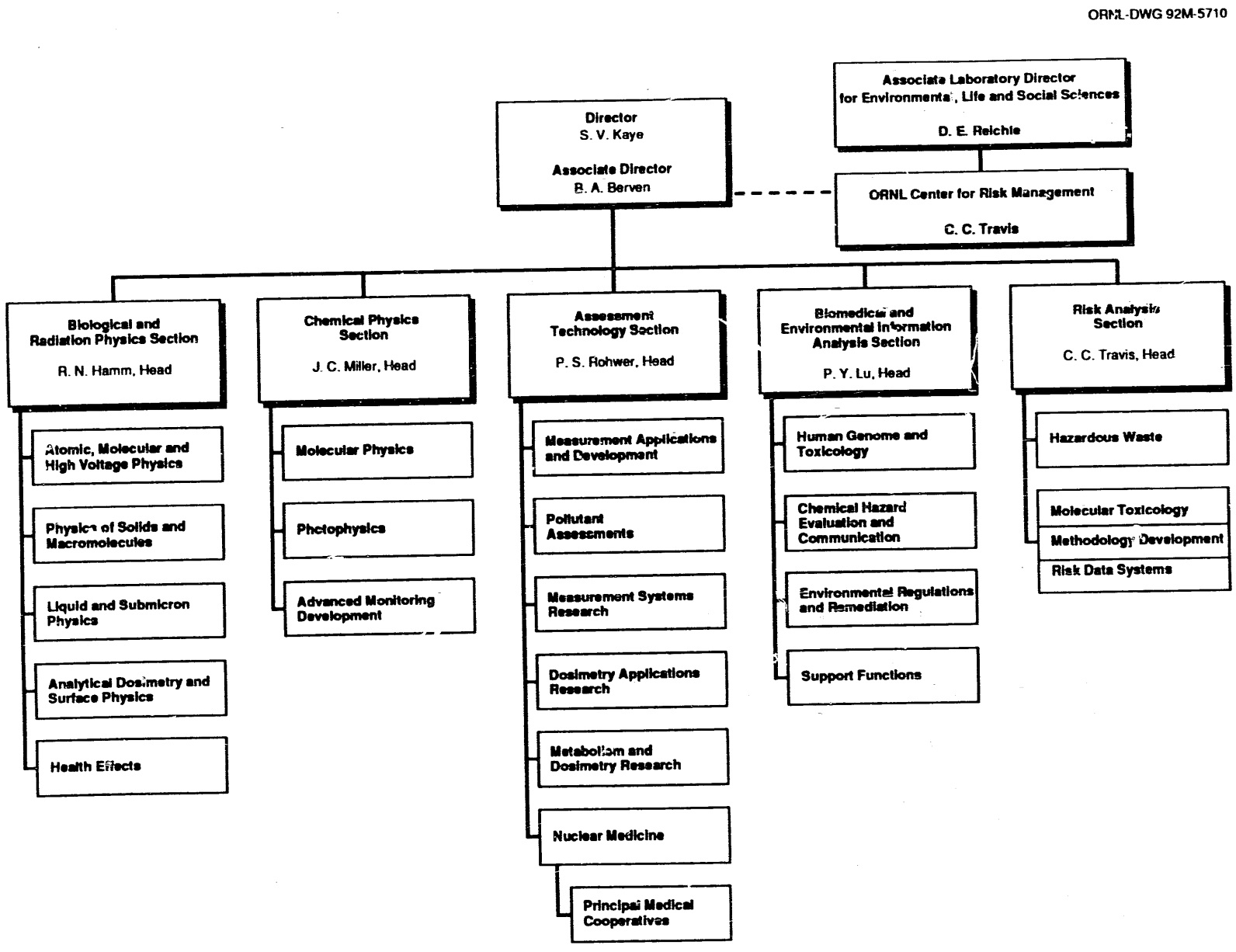

Fig. 6. Organizational Chart for the Health and Safety Research Division.

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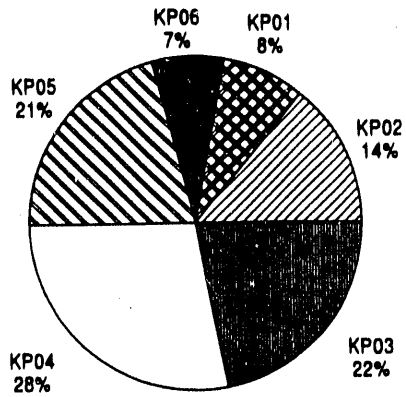

KP01 = Analytical Technology - Dosimetry Research and Measurement Science
KP02 = Environmental Research
KP03 = Health Effects
KP04 = General Life Sciences
KP05 = Carbon Dioxide Research
KP06 = Nuclear Medicine

Biological and Environmental Research Program (KP)
FY 1991 Operating BA
$30 million

Fig. 7. Distribution of total BER funds authorized at ORNL during FY 1991 by KP subprogram

Table 1 shows current personnel numbers categorized by principal investigators, scientific support personnel, and others for the BER program at ORNL. The personnel totals primarily reflect Biology, Environmental Sciences, and Health and Safety Research divisions, which, as previously described, represent about 93% of the BER funding authorized in FY 1991 at ORNL. As can be seen, a total of 77 research scientists are currently working in the program, and they are supported by 84 scientific support (postdoctorates, technicians, and animal care staff) personnel. In addition, professional (administrative), clerical (administrative), and maintenance, reflect another 42 personnel. Table 2 shows changes in professional personnel that occurred during FY 1991 and that are anticipated in FY 1992. Arrivals and departures are expected to decline in FY 1992. The net change in professional staff anticipated for FY 1992 is relatively flat (increase of one), which still represents an increase over estimated FY 1991 changes.

Table 1. Current Personnel[a] Numbers for Biological and Environmental Research Program

Principal Investigators		77
Scientific Support Personnel		84
Other		42
	Total	203

[a]Estimated FY 1992 totals.

Table 2. Changes in Biological and Environmental Research Program professional personnel

	FY 1991	[a] FY 1992
Arrivals	25	13
Departures	29	12
Net Change	-4	+1

[a]FY1992 changes are based on current statistics and open requisitions and may not reflect actual changes.

A decrease in the KP0302 budget required an adjustment in the number of Biology Division staff members associated with the programs involving health effects and radiation carcinogenesis. Management responded by relocating one staff member within the Biology Division, placing eight members in other ORNL divisions, and reducing the work force by four members. These changes, coupled with retirements and resignations of other senior staff, resulted in the need to reorganize ORNL's Biology Division from four sections into two (as noted in the organizational chart presented in this report). Several key new staff were hired by Biology Division during FY 1991 who have high potential to make significant contributions to the BER program.

In early FY 1992, the Environmental Sciences Division (ESD) reorganized. Three areas relate directly to OHER: (1) M. P. Farrell has left the position of Section Head in the Division to work on developing the Laboratory-wide Global Environmental Studies Program; (2) S. G. Hildebrand, whose most recent responsibilities included oversight of the CO_2 exposure work sponsored by Roger Dahlman, has become Associate Division Director; and (3) P. Kanciruk has been named Program Manager for Environmental Information Analysis in the Division with oversight responsibilities for Carbon Dioxide Information Analysis Center (CDIAC), Atmospheric Radiation Measurement (ARM) Archiving, and other environmental data activities. Paul also serves as the Division's interface with the Laboratory's recently announced supercomputing initiative. R. M. Cushman has taken over day-to-day responsibilities for CDAIC. This new organizational structure places ESD in a much better position for both responding to and initiating new activities with OHER, and with other DOE and non-DOE organizations. ESD will continue to be a major component of the pending ORNL Global Environmental Studies Program.

Research Management Practices

Research projects under the auspices of the BER Program continually undergo review procedures to ensure quality, productivity, and efficiency. To help accomplish the desired results, appropriate management measures are applied at various levels of the organization. This section describes the methods and criteria used for establishing and reviewing laboratory program priorities, quality, direction, and personnel.

Staff Recruiting and Development

To ensure continuity in both staff quality and capability, it is necessary for ORNL to attract and hire outstanding personnel. The increased competition for outstanding scientists and engineers has necessitated enhanced recruiting efforts by ORNL to reach high quality professionals. To ensure the continued high caliber of those being hired, the Laboratory has established a set of hiring guidelines that defines the academic and professional characteristics being sought in new hires. Additionally, an ad hoc review process has been reinstituted for prospective Ph.D. new hires and for experienced B.S. and M.S. technical candidates.

Formal yearly reviews are conducted for each staff member according to the Performance Planning and Review (PPR) system. Figure 8 illustrates the organizational performance planning process and the progression from the company's strategic plan to performance plans for individual salaried employees. The reviews are augmented by informal reviews that occur several times during the year.

The career review program identifies employees with high potential to fill key scientific and management positions, and works in concert with an aggressive affirmative action program to provide equal opportunities for women, minorities, and the disabled. Employee development plans are prepared for these individuals. The plans are monitored by division directors, associate directors, and the ORNL Director. Periodic reviews of some are conducted by the Professional Managers Improvement Committee.

Among the special personnel programs sponsored by the Laboratory, the Educational Assistance Program remains an effective tool for helping employees achieve their academic and career goals. This program helps ensure the proper availability, optimum utilization, and continuing welfare of Laboratory employees. In addition, selected management and staff with high potential are given the opportunity to attend management training seminars conducted by outside organizations, including universities.

The Laboratory also provides in-house development designed to meet the specific education and training needs of its current population. In addition, the Laboratory is responding to a heightened emphasis on environmental, safety, and health issues by expanding specialized technical training programs. Finally, the cadre of courses offered as a part of ORNL's management training is being expanded to include courses that present strategies for communicating across cultural barriers and cultural diversity. This area of management training is crucial in preparing managers for the changing work force in the 1990s.

The Laboratory recognizes that it is also necessary to retain outstanding personnel. ORNL strives to provide opportunity for growth, and to reward excellent performance. Several financial and nonfinancial incentive and recognition programs have been established to reward

outstanding contributions and significant achievements. ORNL participates in Energy Systems annual awards night to recognize outstanding performance in various categories: publications, technical achievement, management support service, inventions, operational performance, and administrative/technical support.

Environment, Safety, and Health

ORNL is an active participant in major programs instituted by Energy Systems to promote a clean environment and health and safety. In an ongoing effort to monitor and to audit internally, Energy Systems management has several programs to encourage corporate ethics, security, and safety and environmental activities.

These activities include the following:

- The Environmental, Safety, and Health Coordination Committee is staffed by management at all levels. Teams have been formed to monitor activities such as Occupational Safety and Health Act compliance, plant safety evaluation for potential hazards and associated risks, and personnel records protection.
- The Central Safety and Health Committee tracks and reviews performance and injury records of all Energy Systems personnel, promotes general safety and health on and off the job, encourages thoughtful safety suggestions from all staff, and holds mandatory quarterly safety meetings for all personnel. In addition, the committee has organized emergency preparedness teams at all facilities and oversees fire protection, industrial safety, Quality Department activities, and personnel radiation monitoring.

Quality Assurance, Conduct of Operations, and Occurrence Reporting

Quality assurance (QA) is a high priority at ORNL; it is accomplished through close working relationships among divisional QA representatives, ORNL, Energy Systems, and the QA staff. Manuals and procedures have been developed for Energy Systems Conduct of Operations and Occurrence Reporting. All employees are involved in the implementation of these high priority policies.

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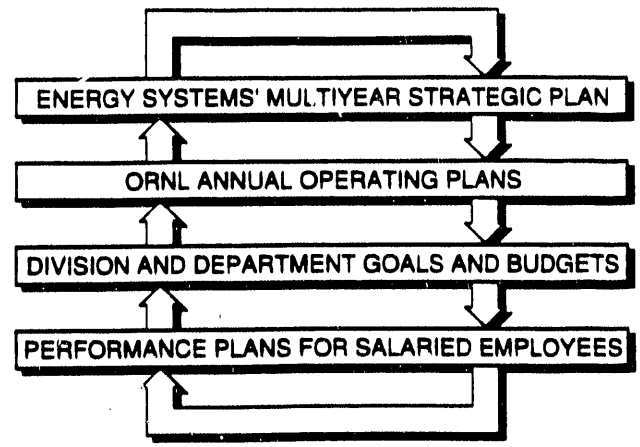

Fig. 8. The organizational performance planning and review process at Oak Ridge National Laboratory, managed by Martin Marietta Energy Systems, Inc.

The Total Quality Management Plan Committee has as some of its goals an increased ownership by line management at every level of the organization; a focus on continuous improvement, empowerment, and quality planning and assurance; and a thorough integration in daily operations of performance improvement, quality, values, and education.

ORNL recently formed an Operations Committee whose functions are to identify and solve operations problems, improve communications between research and development and operations activities, address factors which will enhance ORNL's ability to be more productive in its R&D mission, monitor operations activities, and address other operations issues as appropriate.

Internal Peer Review

All scientific publications and technical reports receive an internal peer review. This process serves as a quality control check and is closely monitored by ORNL management.

Performance Improvement Process

In FY 1985, Energy Systems initiated the Performance Improvement Process (PIP). PIP is designed to (1) measure improvement, activities, or projects; (2) identify and implement opportunities for improvement; and (3) enhance recognition and awards programs. Formal training in the PIP concept is provided to all monthly employees to ensure awareness of, and total participation in, PIP.

Animal Care and Use

The care of laboratory animals at ORNL meets or exceeds the requirements of the U.S. Department of Agriculture, the policies of the National Institutes of Health (NIH) and DOE, and the principles of humane care of the American Veterinary Medical Association. The facilities are accredited by the American Association for Accreditation of Laboratory Animal Care (AAALAC) and are supervised by a laboratory animal veterinarian. In February 1991, the AAALAC attached provisions to ORNL's accreditation based on a review of the program at that time. ORNL implemented a number of improvements to address the concerns of the AAALAC, and in November 1991, the AAALAC restored full accreditation and commended ORNL staff on the positive actions taken. Table 3 lists the membership of the ORNL Animal Care and Use Committee as of July 1991.

Human Studies

Research involving human subjects at ORNL meets the requirements of the Federal Policy for the Protection of Human Subjects promulgated as a final rule and as a U.S. Department of Energy regulation (10 CFR Part 745) on June 18, 1991. For all research activities involving human subjects, the research proposals, consent forms, research practices, and research progress are reviewed and approved by a Committee on Human Studies that serves both ORNL and the Oak Ridge Associated Universities (ORAU). Table 4 lists the current members. In FY 1991, the committee reviewed over 30 research proposals for the two institutions. The committee meets two times per year.

Table 3. Members of Oak Ridge National Laboratory's Animal Care and Use Committee, FY 1991–1992

Name and degree	Affiliation
S. Marshall Adams, Ph.D.	Environmental Sciences Division, ORNL
Kathleen R. Ambrose, M. S.	Chairperson, Health and Safety Research Division, ORNL
Virginia L. Godfrey, D.V.M.	Biology Division, ORNL
Donald W. Goodwin, Ph.D.	Retired minister (nonscientist member)
Stephen J. Kennel, Ph.D.	Biology Division, ORNL
Eugene M. Rinchik, Ph.D.	Vice Chairperson, Biology Division, ORNL
Edward C. Schroeder, D.V.M	College of Veterinary Medicine, The University of Tennessee, Knoxville

Table 4. Members of the Oak Ridge Associated Universities-Oak Ridge National Laboratory Committee on Human Studies, FY 1991- FY 1992

Name and degree	Affiliation
William H. Calhoun, Ph.D.	The University of Tennessee
James E. Crook, M.D.	Oak Ridge Associated Universities
Howard R. Friedman, Ph.D.	Martin Marietta Energy Systems
R. J. Michael Fry, M. D.	Consultant
Shirley Fry, M.B., B.Ch. (MPH)	Oak Ridge Associated Universities
A. Seaton Garrett, Jr., M. D.	Oak Ridge National Laboratory
Karl F. Hubner, M.D.	The University of Tennessee
Melvin E. Koons, J. D.	Tennessee Innovation Center
Robert Lange, M.D.	The University of Tennessee
Ten-Ching Lee, Ph.D.	Oak Ridge Associated Universities
Fun Fong, M.D.	Oak Ridge Associated Universities
Edward D. Aebischer, B.S.	Oak Ridge National Laboratory
Helen Vodopick, M.D.	Oak Ridge Medical Clinic
Fred C. Hartman, Ph.D.	Oak Ridge National Laboratory
Glenn Davis, M.D.	Oak Ridge Associated Universities

Long-Range Plans

ORNL participates in the DOE multiprogram laboratories institutional planning cycle. Components of the planning cycle include submission of preliminary data, completion of the on-site review, and approval of the Institutional Plan. The plan includes the five-year baseline of program projections and the 15-year strategic view for ORNL. The plan is an integration of DOE guidance and laboratory planning for R&D.

Five-year R&D plans are prepared by each division on a regular schedule to coincide with Advisory Committee reviews. The division plans address research directions and goals. In addition, the plans identify future resource needs and a strategy for achieving the stated goals. ORNL's senior management reviews and approves division plans.

In late FY 1991–early FY 1992, ORNL formed an R&D Strategic Planning Committee, whose mission is to provide strategic planning for ORNL focused specifically on R&D issues and opportunities. The committee will be concerned with charting R&D directions, with the climate for doing R&D, and with the vitality and quality of the scientific and technical professional staff.

Office of Planning and Management

The ORNL Office of Planning and Management (OPM) is responsible for a number of key ORNL functions dealing with research management practices. Responsibilities include long-range and strategic planning, R&D initiatives, laboratory performance monitoring and assessment, director's staff functions, capital assets planning and management, procedures, honors and awards, special publications, and logistical support for the DOE Oak Ridge Field Office.

ORNL Advisory Board

The ORNL Advisory Board was chartered to critique and to provide advice on ORNL's goals and missions and to give general guidance to

future directions. Convened for the first time in June 1984, the board meets semiannually. Dr. Robert Barker, provost of Cornell University, is the member of the board who closely reviews the BER Program. Table 5 presents the composition of the Advisory Board in FY 1991.

Division Advisory Committees

Each division undergoes a regularly scheduled review by an outside advisory committee that constructively critiques research activities, long-range and strategic planning, and future directions. The committees present their recommendations directly to the ORNL Director. Table 6 gives the membership of the advisory committees for each of the key divisions in ORNL's BER Program.

Laboratory Directed Research and Development Program

The principal objective of the Laboratory Directed Research and Development (LDRD) Program is to provide financial support for innovative research and development ideas that, while within the general mission of the Laboratory, have no direct programmatic funding. Such ideas could lead to productive new technical directions for the Laboratory, DOE, and the nation. The program obtains its funds through a charge to all Laboratory programs. The program operates under the authority of DOE Order 5000.4, "Laboratory Directed Research and Development," dated February 28, 1991. Previously the program was operating under DOE Order 5000.1A, "Institutional Planning by Multiprogram Laboratories," dated September 12, 1986.

There are two major activities within the ORNL LDRD Program, the Seed Money Fund and the Director's R&D Fund. Proposals for Seed Money projects are accepted directly from the Laboratory's scientific and technical staff (with management concurrence) at any time of year and are selected for funding with the assistance of a Proposal Review Committee composed of representative scientific and technical staff. A Seed Money project is funded for 12 months, which often spans two fiscal years. Director's R&D Fund proposals are solicited from staff in June, reviewed through line management, and most are selected by the Laboratory's Executive Committee (five percent

Table 5. ORNL Advisory Board, FY 1991

Name	Affiliation
Dr. Robert Barker	Provost Cornell University
Dr. William F. Brinkman	Executive Director of the Physics Division AT&T Bell Laboratories
Mr. Floyd L. Culler	Electric Power Institute
Dr. John M. Deutch	Provost Massachusetts Institute of Technology
Dr. Robert G. Morra	Vice President, Technical Operations Martin Marietta Corporation
Mr. Robert Polutchko	Senior Vice President, Technical Operations Martin Marietta Corporation

Table 6. Division Advisory Committee members for FY 1991 and FY 1992

Committee member	Year (FY)	Affiliation
		Biology Division
Dr. Irwin Fridovich	1991-93	Department of Biochemistry Duke University Medical Center Durham, North Carolina 27710
Dr. David E. Housman	1991-93	Professor of Biology Center for Cancer Research, E17-543 Massachusetts Institute of Technology 40 Ames Street Cambridge, Massachusetts 02139
Dr. H. Ronald Kaback	1992-94	Professor, Department of Physiology University of California at Los Angeles 405 Hilgard Avenue Los Angeles, California 90024-1570
Dr. William J. Schull	1988-91	Director, Center for Demographic & Population Genetics The University of Texas Health Science Center Post Office Box 20334 Houston, Texas 77225
Dr. Shirley M. Tilghman	1988-91	Howard A. Prior Professor of the Life Sciences Department of Molecular Biology Princeton University Princeton, New Jersey 08544
Dr. Joseph J. Villafranca	1988-91	Professor, Department of Chemistry 152 Davey Laboratory Pennsylvania State University University Park, Pennsylvania 16802
Dr. Arthur Weissbach	1988-91	Associate Director, Retired Roche Institute of Molecular Biology Post Office Box 168 Sanibel, Florida 33957
		Environmental Sciences Division
Dr. J. F. Franklin	1990-92	Bloedel Professor of Ecosystem Analysis College of Forest Resources University of Washington Anderson Hall (AR-10) Seattle, Washington 98195

Table 6. (continued)

Committee member	Year (FY)	Affiliation
Dr. G. M. Hornberger	1990-92	Professor, Department of Environmental Sciences University of Virginia Charlottesville, Virginia 22903
Dr. Gene E. Likens	1989-91	Director, The New York Botanical Garden Institute of Ecosystem Studies The Mary Flagler Cary Arboretum Box AB Millbrook, New York 12545
Dr. A. P. Malinauskas	1990-91	Director of Waste R&D Programs Oak Ridge National Laboratory Building 4500S, MS-6135 P. O. Box 2008 Oak Ridge, Tennessee 37831
Dr. R. H. Olsen	1991-93	Professor, Microbiology and Immunology Department University of Michigan Ann Arbor, Michigan 48109-0620
	Health and Safety Research Division	
Dr. Eugene Merzbacher	1992-95	Professor Department of Physics and Astronomy University of North Carolina Chapel Hill, North Carolina 27599
Dr. Genevieve Roessler	1990-93	Associate Professor Department of Nuclear Engineering Sciences University of Florida Gainesville, Florida 32611
Dr. Robert Snyder	1990-93	Professor and Director Department of Pharmacology and Toxicology College of Pharmacy, Busch Campus Rutgers University Piscataway, New Jersey 08854
Dr. F. Ward Whicker	1990-93	Senior Scientist Savannah River Ecology Laboratory Drawer E Aiken, South Carolina 29802

of the LDRD Program is allocated by Laboratory Associate Directors through the Director's R&D Fund). Financial support for a Director's R&D fund project is provided by fiscal year. Provision of two routes of access to exploratory funds maximizes the likelihood that novel and seminal ideas will be recognized and supported. Additional descriptions of ORNL's LDRD Program can be found in DOE (1986), DOE (1987), and DOE (1988).

In FY 1991, the ORNL LDRD Program allocated substantial funds to projects related to the mission and interests of OHER. This section summarizes the LDRD activity.

Seed Money

In FY 1991, ORNL funded 15 seed money projects relevant to the BER Program at a total level of about $693,000. Table 7 provides a summary of the principal investigator, division, and title of these projects.

Director's Research and Development

In FY 1991, there were eight Director's R&D projects relevant to the BER Program, with a combined budget of about $1.6 million. Table 8 provides a summary of the principal investigator, division, and title of these projects.

Summary

ORNL actively supported a large number of wide-ranging innovative R&D ideas related to the mission and research goals of OHER. The total FY 1991 funding allocations and budget for these projects exceed $2 million. The results of these projects should provide new insights to issues of key interest to OHER, thereby leading to new technical directions for the BER Program.

Science Education

BER-funded divisions at ORNL are heavily involved in a number of key educational activities that support DOE's initiatives in science education. The following paragraphs describe some of these activities for FY 1991.

Table 7. ORNL Seed Money projects active in FY 1991 and relevant to the BER Program

Principal Investigator	Division	Title
L. G. Christophorou	Health and Safety Research	Dielectric Liquid Pulsed Power Switch
R. N. Compton	Health and Safety Research	Multiply Charged Negative Ions
K. B. Jacobson	Biology	DNA Sequencing by Hybridization to Oligonucleotides Synthesized on Solid Supports
M. G. Payne	Health and Safety Research	A Soft Ionization Mass Spectrometer for the Simultaneous, Real-Time Analysis of Biogenic Non-Methane Hydrocarbons and Nitrogen Oxides in the Forest Canopy Airspace
G. M. Brown	Chemistry	Luminescent Lanthanide Ions as Labels for DNA Sequencing and Mapping
R. J. Luxmoore	Environmental Sciences	Fractal Characteristics of Percolation Clusters in Heterogeneous Porous Media

Table 7. (continued)

Principal Investigator	Division	Title
J. S. Cook	Biology	Cellular Responses to Mutants of Epidermal Growth Factor
F. T. Kenney	Biology	Molecular Chaperones
W. K. Yang	Biology	Isolation of Endogenous Retroviral Genes from Human Cancers
D. W. McPherson	Health and Safety Research	Radioiodinated Altanserine, A Potential Radioligand for the Imaging of Cerebral S2 Serotonin Receptors by Nuclear Medicine Techniques
S. S. Stevens	Energy	Long Path Infrared Spectrometer to Measure the Distribution of Atmospheric Trace Gases
D. K. Solomon	Environmental Sciences	Validation of groundwater dating and recharge determination using 3H and He isotopes
R. N. Compton	Health and Safety Research	Studies of Buckyballs
G. D. Griffin	Health and Safety Research	Practical Biological Monitor for Electromagnetic Fields Employing Liposomes
H. Yoshida	Health and Safety Research	Identification and Characterization of Radiation-Induced Products of Thymine, Thymidine, and Related Compounds

Table 8. ORNL Director's Research and Development projects open in FY 1991 and relevant to the BER Program

Principal Investigator	Division	Title
K. B. Jacobson	Biology	Human Genome Initiative: Methods for DNA Sequencing Using Stable Isotopes
S. B. McLaughlin	Environmental Sciences	Stratospheric Ozone Depletion and UV-B Radiation: Response of Biotic Resources in Natural and Managed Ecosystems
R. C. Mann	Engineering Physics and Mathematics	High Speed Exploratory DNA Sequence Pattern Analysis Using Concurrent Processing

Table 8. (continued)

Principal Investigator	Division	Title
V. H. Dale	Environmental Sciences	Land Use and Global Environmental Problems: Integrating Approaches from the Social and Environmental Sciences
D. C. White	Environmental Sciences	Monitoring Critical Microbial Processes *In Situ* Degradation/ Immobilization of Complex Wastes
R. P. Woychik	Biology	Targeted Mutagenesis and Transgenic Mice
C. C. Travis	Health and Safety Research	Molecular Risk Analysis R&D Initiative
R. B. Shelton	Energy	Evolutionary Energy/Environmental/Economic Modeling

As part of an increased focus on precollege activities, ORNL continues to expand the Ecological and Physical Sciences Study Center (the Study Center), which is one of the most visible and successful precollege programs. The Study Center consists of 40 study modules that provide students with the opportunity for hands-on learning in both the life sciences and physical sciences. The units are offered generally as half-day field activities and are tailored for the academic level of elementary, junior high, or senior high school students. The Study Center operates year-round, including Summer Science Saturdays for adult community members and children. During FY 1991 nearly 20,000 students participated, with a continuing special emphasis on students with physical and/or sensory disabilities.

On the graduate level, master's degree and Ph.D. candidates, others performing thesis or dissertation research, and postdoctoral applicants are appointed to ORNL through various graduate education programs. Their goal is to enhance the educational experiences of these students by providing opportunities to work in laboratory situations and with advanced equipment not readily available on their home campuses. A major consideration in the selection of these students is the compatibility of their background and interests with research projects in ORNL divisions. Postdoctoral and the Laboratory graduate participation (thesis research) participants must be accepted by ORNL's Graduate Fellowship Selection Panel or through national panels established by OHER and DOE's Office of Fusion Energy. ORNL is actively seeking candidate fellows for two new programs introduced by OHER in FY 1991 in parallel with the Alexander Hollaender Distinguished Postdoctoral Fellowships now in their fifth year. These programs support work in the areas of human genome research and global environmental change.

In FY 1991, ORNL's BER divisions hosted a total of six DOE Hollaender Fellows (not necessarily concurrently): two in the Biology Division and four in the Environmental Sciences Division. The Laboratory's Wigner Fellowship Program also sponsored scientists in the key BER divisions during FY 1991. Both of these fellowship programs help the Laboratory attract top quality research staff, which benefits BER-funded research. Additional details on graduate students, post doctoral staff, and other educational aspects of the BER Program are presented in the "Resource Quantitation" section of this report.

ORNL hosted one of the DOE National High School Science Honors Workshops in FY 1991. More than 125 staff members from Energy Division, ESD, Health and Safety Research Division (HASRD), and the Hazardous Waste Remedial Actions Program provided the Environmental Sciences workshop with research experience and student lectures and served in other capacities. Fifty-nine high school students representing 48 states, the District of Columbia, Puerto Rico, Italy, Canada, France, Germany, Great Britain, Japan, Mexico, and the U.S. Department of Defense Dependents School in Seoul, Korea, spent two weeks at ORNL. During their stay at ORNL, these students were involved in experimental studies dealing with the effects of contaminants and pollutants on the environment.

The Special Honors Study Program implemented in FY 1986 allows exceptional high school students to conduct a study project in an area in which they have a special interest at ORNL under the supervision of an ORNL staff member.

Another key science education activity is the collaboration of ORNL and the University of Tennessee-Knoxville (UTK). Perhaps the least known, yet strongest, ORNL-UTK joint programs are the two UTK graduate schools located at ORNL. The Oak Ridge Graduate School of Biomedical Sciences (ORGSBS) is more than 20 years old and the Graduate Program in Ecology is in its second decade. Both programs at ORNL provide a home for several UTK faculty.

Housed in the Biology Division at ORNL, ORGSBS offers full-time graduate study for M.S. and Ph.D. degrees and for postdoctoral training. Student support is provided by UTK through research assistantships and federal grants. Most of the school's teaching and research training is provided by Biology Division staff. Current enrollment stands at 40 graduate students and postdoctoral appointees.

Similarly, the UTK Graduate Program in Ecology, closely aligned with ESD, offers full-time graduate study for M.S., Ph.D., and postdoctoral students and is largely supported by ESD programmatic funds. About 20% of the research training is provided by ESD staff, who also teach courses under adjunct appointments. Enrollment totals about 15 graduate and post-graduate students.

Distinguished Lecturer Series

The Distinguished Lecturer Series in the Life Sciences is a joint program of Oak Ridge National Laboratory and UTK. Now entering its 10th year, the program is designed to bring noted life scientists to give a seminar and to meet with life science staff and management at the two institutions. Researchers in ORNL's BER Program benefit from interaction with distinguished life scientists who visit as part of the series. The speakers (and seminar topics) who participated in this program during FY 1991 are as follows: (1) Dr. James R. Mahoney–"The National Acid Precipitation Assessment Program: Findings and Implications," (2) Dr. George H. Hitchings–"Biochemical Basis for the Discovery of New Drugs," and (3) Dr. Jacqueline K. Barton–"Site Specific Recognition of DNA by Metal Complexes."

Technology Transfer

Technology transfer is a primary purpose of Oak Ridge National Laboratory. A new contracting tool, termed a Cooperative Research and Development Agreement (CRADA), is now available to facilitate technology transfer by creating partnerships between government laboratories and outside parties. Martin Marietta Energy Systems was the first DOE managing and operating contractor authorized to enter into CRADAs with private industries.

In FY 1991, ORNL staff working in the BER Program contributed to a number of CRADAS. Staff members working in HASRD were most active in FY 1991 in the CRADA process, primarily in three technological areas: (1) the optical detection of charged particles; (2) surface enhanced Raman Optical Data Storage; and (3) organic compound analysis based on surface enhanced Raman spectroscopy. In addition, other ORNL divisions have initiated CRADAs in topical areas relevant to the BER Program, such as the global assessment of chlorofluorocarbons and the viability of alternative hydrochlorofluorocarbon blowing agents developed by ORNL's Energy Division.

ORNL divisions working in the BER program have been engaged in technology transfer activities outside of the CRADA mechanism. ORNL's

ESD and Instrumentation and Controls Division developed a radiation detector that will enable a California company, through a licensing agreement, to produce equipment capable of detecting radioactive pollutants in surface water, water treatment plants, liquid waste discharges, or groundwater.

Other

Other management tools such as retreats, performance measures, commitment systems, and subcontract and financial tracking systems, help to ensure sound management of ORNL BER program activities. Such widely used tools as the electronic mail system and computerized tracking systems help expedite communication for managers as well as staff.

The Performance Evaluation Committee, (PEC) which consists of representatives from the DOE Oak Ridge Field Office and the Laboratory, monitors ORNL's performance in a number of areas for the purpose of determining the award fee to be given to Energy Systems under its contract with DOE. Items considered in the PEC process include major R&D milestones, publication of peer reviewed journal articles, and technology transfer.

Research in Progress

This section presents a qualitative overview of the status of the BER program at ORNL. Discussions are organized by major subprogram.

KP01–Analytical Technology - Dosimetry Research and Measurement Science

These activities include (1) development of radiation exposure-dose relationships; (2) development of models describing the biokinetics of radionuclides; (3) development and application of cost-effective chemical and biological screening techniques; (4) development of biological and chemical sensors for studying effects of chemicals; (5) advanced photonics for environmental needs (development and application of lasers); and (6) studies of fundamental liquid phase behavior to predict new phenomena and improve technologies.

Metabolism and Dosimetry Research

Research in metabolism and dosimetry is directed toward understanding the relationship between radiation exposure and the dose to organs of the body. These relationships are defined through the modeling of both the metabolism of radionuclides taken into the body and the deposition of ionizing energy within the radiosensitive tissues from these intakes or from exposures to radiation external to the body. Such relationships provide a cornerstone for development of radiation protection guidelines for the numerous radionuclides encountered in the workplace and environment. They also serve an important role in the evaluation of diagnostic procedures involving radiopharmaceuticals and diagnostic X-ray machines.

Staff members provide much input to organizations such as the International Council on Radiation Protection (ICRP) and the National Council on Radiation Protection and Measurements (NCRP) through participation on councils, commissions, committees, and working groups. In particular, Part I of Publication 56 of the ICRP, entitled "Age-dependent Doses to Members of the Public from Intake of Radionuclides," was largely based on the age-specific dosimetric methodologies and biokinetic models developed by the staff. Part 2 of the publication will contain age-specific biokinetic models for the alkaline earth elements and lead developed by staff. Staff members prepared ICRP Publication 61, which tabulates secondary radiation protection quantities corresponding to the 1990 ICRP recommendations. This publication provided interim quantities which serve the radiation protection community until a full revision of Publication 30 is completed. Staff have begun the efforts to revise Publication 30.

Problems encountered in reconstruction of the dose to members of the public located around nuclear facilities and dose reconstruction for epidemiological studies of occupationally exposed populations have highlighted the needs for further dosimetry methods. The need to address special characterizations of exposed individuals or segments of the population requires further developments in the biokinetic and dosimetry models. Methods and experience gained in the reassessment of the dosimetry for survivors of the atomic bombings of Hiroshima and Nagasaki, and the interpretation of occupational bioassay data, are being applied to these problems.

Instrument Development

Emphasis is placed on developing techniques that provide advanced instrumentation for characterizing and sensitively detecting a wide variety of radiological species, chemical species, and related bioindicators of human exposure and health effects. Included in this effort are unique applications of laser optical techniques, ultraviolet and soft X-ray spectroscopic techniques, electron-beam microlithography, scanning tunneling microscopy, antibody-based biosensors, surface-enhanced Raman spectroscopy, advanced neutron dosimetry and microdosim- etry, photon-electron-rejecting alpha liquid scintillation, and mass and photoelectron spectroscopy.

A continuing research activity is the development of new instruments and measurement techniques to support evaluation of the potential health and environmental impacts of developing energy technologies. This research includes advanced studies on monitoring chemical exposures of humans through instrumentation and biological indicator systems. Results of this research have led to cost-effective luminescence techniques for rapid screening of samples containing polynuclear aromatic compounds, as well as portable instrumentation for on-site use at operating facilities.

Continued development of derivative ultraviolet absorbance and synchronous fluorescence field methods has produced faster, more cost-effective screening of organic contaminants in soil and groundwater at below federal regulatory levels. Improved field concentration procedures were produced as part of these methods. A new luminescence technique for free cyanide in groundwater has also been developed, with sub-parts per billion (ppb) detection capability. Work is underway to convert this into a fiberoptic, *in situ* monitoring device for use at DOE sites. A companion method for simultaneously detecting cyanide and other important anionic contaminants is being developed based on surface-enhanced Raman spectroscopy.

The OHER-funded developmental research has resulted in support from other agencies and organizations for applied studies. Transferring this technology to the commercial sector is an important objective that has met with noteworthy success in the past five years.

Radiation Calibration Laboratory

The Radiation Calibration Laboratory (RADCAL) has been made operational with beta, gamma, neutron, and X-radiation sources. Since becoming operational, RADCAL has been used for radiation dosimetry research, testing dosimeter compliance with performance standards, personnel dosimetry intercomparison studies, calibration of operational instruments, and radiobiology research.

The list of collaborative organizations which benefited from RADCAL in FY 1991 is quite lengthy. It includes ORNL dosimetry and radiobiology researchers, ORNL and Energy Systems applied health physics personnel, ORNL instrumentation developers, and about 70 dosimeter processors from a variety of facilities in the United States and around the world.

ORNL's HASRD has requested that the National Institute of Standards and Technology (NIST) certify RADCAL as a Secondary Standards Calibration Laboratory under a program announced by NIST in mid-FY 1991. Such certification is being pursued on a source-by-source basis.

Health Physics Research Reactor

The Health Physics Research Reactor was permanently disassembled and the fuel was removed from ORNL early during FY 1991. The reactor was a small, unmoderated fast reactor which was used for radiobiology and dosimetry research, criticality alarm testing, weapon radiation simulation, and training.

KP02–Environmental Research

These activities include environmental biogeochemistry; ecosystem function and response, including biogeochemical cycling at watershed scale; theoretical ecology, including quantification of regional landscape patterns and processes affecting ecosystems at large spatial scales; subsurface research–defining, understanding, and predicting the movement of energy-related contaminants in humid regions with highly organic natural waters; biotechnology–molecular biology, toxicology, and environmental monitoring; NERP; and radon–subsurface source, trans-

port, and entry of radon-bearing soil gas into residences.

Transport and Transformation

The ORNL atmospheric sciences research project concentrates on quantifying several aspects of atmosphere/biosphere exchange that are likely to be critical in understanding and predicting the effects of global change. These include wet and dry removal processes and surface emission rates of both natural and pollutant constituents important to tropospheric chemistry and biogeochemical cycling. Major emphasis is placed on determining the interactions of these materials with forest canopies, particularly in complex terrain. New issues being addressed include testing methods for measuring biogenic emissions, determining the sensitivity of global trace metal cycles to climate change, and developing models for scaling up surface exchange rates from point measurements. This work supports DOE tasks in the areas of dry deposition, precipitation scavenging, deposition modeling, landscape scaling, biogenic emissions, and biogeochemical cycles.

Coastal Transport and Accumulation Processes

This research involves the measurement of naturally occurring and man-made radionuclides to trace and to quantify transport and accumulation processes within the coastal zone. The high correlation between the transport and deposition of radionuclides and many other trace substances—such as hazardous organics, trace metals, and pesticides—makes it possible to infer the distribution and biogeochemical fate of a large number of substances from relatively simple and inexpensive analyses of radionuclides. These techniques have been combined with measurements of other sedimentary parameters to show that coastal bays and estuaries are dominated by sediments in substances transported landward from oceanic sources. In addition, the effects of major storm events on sediment deposition and source are also being evaluated.

Naturally occurring ^{7}Be, ^{35}S, delta $^{18}0$, and delta D have been used to trace the combined chemical and physical interaction between snowmelt and soils in an Arctic watershed. Preliminary results indicate that the majority of snowmelt physically bypasses the soil system on hillslopes but converges on, and infiltrates into, the soil in the riparian zones adjacent to streams. This research places added emphasis on defining geochemical processes in the riparian zone, in particular with regard to acid neutralization.

Subsurface Transport Processes

Research in the subsurface sciences is directed toward defining, understanding, predicting, and controlling the movement of energy-related contaminants in the subsurface in humid regions with highly organic and inorganic natural waters. Association with natural organic colloids may alter the transport and fate of contaminants. The program consists of field and laboratory studies that are integrated with development and application of hydrologic and chemical transport models. Complex hydrogeochemical models, such as HYDROGEOCHEM, that simulate the transport of energy-related contaminants require supercomputing capabilities.

ORNL researchers have demonstrated that the new generation of hypercube computers that use parallel processing provide better price-to-performance ratios than traditional supercomputers. These computers are ideally suited for contaminant transport simulations. New areas of emphasis include the use of isotopic tracers to determine residence time of shallow groundwater, research on the role of colloids and microbial populations in affecting subsurface transport, and transformation of energy byproducts. ORNL will continue to support OHER's Site-Directed Subsurface Initiative. Major emphasis will be directed at understanding the origin and transport processes for microorganisms in the deep subsurface. Unique field facilities consist of fully instrumented watersheds in which chemicals can be released and traced as they move through the soils in one, two, or three dimensions. Field-derived data are used in model development and validation.

Biological Responses to Stress

The productivity and biogeochemistry of forest ecosystems are highly dependent on the growth and physiology of component forest tree species, and OHER-sponsored research is addressing the processes governing the response

of terrestrial vegetation to environmental stresses of natural and anthropogenic origin. Using a combination of field and laboratory studies, research is focusing on the mechanisms controlling (1) exchange (deposition and emission) of trace gases of the atmosphere-biosphere interface,(2) photosynthetic carbon dioxide assimilation and water use efficiency, and (3) interactive effects of multiple stresses on terrestrial vegetation. The research focuses on forest tree species on Walker Branch Watershed (WBW) (located on the ORR), but is designed for application to a variety of forest landscapes. Each of these tasks is being addressed from the perspective of whole-plant physiology.

Development and application of molecular markers for evaluating the status of ecosystems affected by energy-related activities remain an important component of our research efforts, and we expect it to expand in the work that we conduct for OHER. Major funding for environmental restoration and waste management activities is expected. The interest in restoration, coupled with the expected level of funds for accomplishing cleanup, gives rise to a need for faster and more cost-effective methods for evaluating efficacy of actions taken. Basic research relating molecular markers [such as deoxyribonucleic acid (DNA) adducts] to population and ecosystem responses will ultimately allow cost-effective monitoring systems to be employed. The utility of aquatic biomarkers will continue, and will expand with new research directed at the development of plant biomarkers. Microbial markers and gene probes will receive new emphasis.

National Environmental Research Park

The 5500-ha (13,585-acre) Oak Ridge NERP continues important long-range research planning within the framework of DOE's interactive ParkNet system, which involves six other National Environmental Research Parks. The Research Park is also an integral component of the biosphere reserves in the United Nations Educational, Scientific, and Cultural Organization's Man and Biosphere's (MAB's) Southern Appalachian Man and Biosphere (SAMAB)–the only official regional program in the United States. Additionally, it serves as an important resource for information on plants, animals, and special habitats (particularly wetlands) necessary for on-site characterization and remediation activities. Providing opportunities for environmental research and education are primary objectives of the Research Park.

Requests from other projects and organizations for surveys and information on wetlands and rare plants on the ORR to comply with the National Environmental Policy Act has continued to increase. A preliminary document "Wetlands of the Oak Ridge Reservation," will be published in early 1992. Management of wildlife on the ORR through the Tennessee Wildlife Resources Agency has included not only deer hunts, but also restoration of species such as wild turkey and osprey. A wildlife management plan for the ORR has been completed and will be published in early 1992. Educational activities have included the creation of posters, international tours, local school involvement, publication of a report on environmental education resources in the SAMAB area, and workshops. Educational activities are conducted in coordination with other divisions of ORNL, ORAU, neighboring federal agencies, and SAMAB. Research has recently addressed tree drought stress tolerance, tree nutrient use efficiency, seedling changes by site in response to unusual weather events, and modeling of soil moisture gradients on a watershed basis. Research involves support from several agencies.

Interactive ParkNet activities have included participation in a video on the DOE Research Parks, the provision of data for ParkNet workshops, and the organizing of a preliminary workshop at Oak Ridge on "Remote Sensing and Landscape Connectivity." Currently, digital maps are being prepared from the ORR, H.J. Andrews Long-Term Ecological Reserve (LTER), and Pacific Northwest Laboratory (PNL) Arid Lands Ecology Reserve that will be used in a workshop at Oak Ridge in June 1992 to analyze and interpret results from landscape pattern models.

SAMAB activities include data management cooperation, climate change assessments, and studies of the processes causing red spruce decline. The Temperate Directorate of MAB is funding a large cooperative study on comparative land-use change between ORNL/U.S. Department of Agriculture Forest Service/

SAMAB and the University of Washington/ Olympia Peninsula.

Future plans call for development of a long-term integrated approach to understanding important biological and physical processes associated with environmental stress. Selected soil and hydrologic processes involving cations, carbon, and nitrogen are being considered as common denominator expressions of stress physiology, ecosystem functions, and landscape alterations. This work should lead to modeling the effects of diverse environmental change scenarios, evaluating environmental risk, and assessing the effectiveness of human-directed responses in resource management and policy changes.

Integrated Watershed Research

Since 1967, WBW on the ORR has been the site of intensive research on the biogeochemistry of forested watersheds. The first two decades of research on WBW have been synthesized and published (Johnson and Van Hook, eds. 1988); this has further enhanced the reputation of WBW as one of the premier watershed research sites in the world. The long-term record of streamflow volume and chemistry, atmospheric deposition, and forest growth from WBW makes it an irreplaceable resource for studying the effects of energy technologies on the natural environment.

Following over twenty years of detailed research mechanisms of chemical cycling and transport, the WBW Project is moving into a new, experimental phase in which the project's data and computer simulation models are being used to address an issue of urgent national and international concern–the effect of global climate change on forests, which has major economic and ecological implications. Changes in forest productivity, or the replacement of one tree species by another, will affect the value of forest timber products, as well as alter wildlife habitat and biological diversity. A large-scale experiment is being initiated to investigate the response of a forest ecosystem to changes in rainfall amount. Of all the components of carbon dioxide-induced climate change, increases or decreases in precipitation are likely to have the most significant effect on agricultural and forest productivity. Unfortunately, the predictions of the effects of climate warming are not sufficiently precise to determine whether a particular area will receive an increase or a decrease in precipitation.

The Walker Branch Climate Change Experiment is designed to investigate the effect of both increased and decreased precipitation on a deciduous forest ecosystem. The experimental treatments will be accomplished by intercepting 25 percent of the total rainfall in troughs before it reaches the forest floor and transferring the water from one plot (the dry treatment) across a control plot to a third plot (the wet treatment). Each of the plots will be approximately the size of three football fields, and the decrease in precipitation on the dry plot will be equivalent to that received during the worst drought year of the 1980's. Continuation of these treatments for at least five years will simulate a significant change in climatic rainfall pattern.

The responses of the forest to this change in climate will be monitored using methods previously developed and tested on WBW, and evaluated using computer simulation models developed on this, and other, projects. Spatial and temporal patterns of soil moisture will be intensively monitored, as will tree growth and fluxes of carbon dioxide and other "greenhouse" gases. Changes in root growth and nutrient uptake will be compared among the wet, dry, and control treatments. One key to the future of the forest is the germination and growth of tree seedlings. Failure of certain species to regenerate will be an early indicator that the forest is likely to change significantly in response to this type of climate change. Other sensitive indicators may include genetic changes, alteration of carbon storage patterns, changes in soil nutrient concentrations, and altered gaseous fluxes.

The results of the Walker Branch Climate Change Experiment will help evaluate the potential impacts of climate change on forest ecosystems, as well as the effect of climate change on forest sensitivity to stresses that may result from acidic precipitation, ozone and other gaseous pollutants, and heavy metal deposition. As the first experiment of this type, the Walker Branch Climate Change Experiment will also serve as the prototype for the experimental investigation of altered precipitation in other types of forests in North America and elsewhere.

Theoretical Ecology

Landscapes are complex ecological systems that operate over broad spatial and temporal scales. Hierarchy theory conceptualizes such systems as composed of relatively isolated levels, each operating at a distinct time and space scale. Our theoretical research has explored some basic properties of scaled systems with a view toward taking advantage of the scaled structure in predicting system dynamics.

Biotic potential and environmental limits form constraint envelopes within which the landscape system must operate. Such constraint envelopes (operating at a number of scales) should be reflected in scaled patterns on the landscape.

Landscape Patterns and Processes

For the past decade, ORNL has conducted a series of studies on the fundamental properties of natural systems and the response of these systems to natural and human disturbances. The scale of these studies has ranged from microcosms held under laboratory control to discrete watersheds in the southeastern United States. Our research indicates that detailed site-specific problems are not readily extrapolated to broader spatial scales, while broad-scale analyses have lacked the resolution necessary to incorporate detailed studies of spatial heterogeneity. Therefore, there has been a growing need to coalesce these widely disparate studies to develop first-order principles that address landscape problems.

We are currently conducting theoretical, modeling, and field studies designed to develop methods for measuring ecological patterns of natural and managed landscapes, relating these patterns to processes, and estimating how these patterns will change as a result of broad-scale disturbances. Research results will be used to organize information from laboratory and site-specific studies for extrapolation to landscape scales. Extrapolation will provide several applications and may lead toward a general theory of landscape ecology with application to site management issues.

Radon Dynamics

Radon continues to be the principal focus of our indoor air quality programs. Indoor radon surveys in two Alabama communities have shown atypical seasonal patterns in that summer concentrations were found to exceed winter concentrations. Among typical U.S. homes, the reverse seasonal pattern is found. In addition to our OHER-funded work, we have been providing technical assistance to military and other federal agencies in their screening studies of radon in federally-owned or controlled buildings.

An increasing body of data suggests an association between karst terrain and elevated indoor radon levels. Because of the abundance of limestone and karst terrain in eastern Tennessee, our experiments have involved studies of this phenomenon in occupied homes near Oak Ridge, Tennessee. For example, experiments at a home with unusually high winter radon levels compared to summer levels are exploring processes affecting gaseous transport between the home and a nearby cave.

In support of renewing interest in indoor air quality, a continuous monitor for formaldehyde vapors has been developed. The device being tested is an inexpensive fiberoptic chemical sensor to which many probes can be attached for multipoint sampling in large buildings.

Chernobyl Research

Research related to Chernobyl was conducted in FY 1991 in ESD under OHER funding provided through Lawrence Livermore National Laboratory. The work involved validation of environmental assessment models using Chernobyl data. The models use the concentrations of radionuclides in primary media (e.g., water) and then follow the radionuclides through pathways that concentrate the radionuclides in the human body. Also in FY 1991, the Cherynobyl work was merged with the International Atomic Energy Agency efforts on the Validation of Assessment Model Predictions (VAMP) and with the International Biospheric Model Validation Study (BIOMOVS).

KP03, KP04–Health Effects and General Life Sciences

Common themes within these activities are interactions of animals, cells, and molecules with their respective environments. In the analytical technology area, physical properties of materials of biological or environmental importance,

mechanisms that govern transport and chemical transformations of pollutants, and the details of direct interactions of harmful agents with biological materials are studied through a variety of theoretical and experimental techniques. The efforts encompass interactions at the atomic, molecular, and macroscopic levels in solids, liquids, and gases; on surfaces; and at solid-liquid interfaces. Special emphasis is given to interactions in the liquid including Monte Carlo modeling of radiation effects on biological molecules in irradiated matter. Strong emphasis is given to development of techniques that provide advanced instrumentation for characterizing and sensitively detecting a wide range of chemical species and related biomarkers of health effects. Included in this effort are unique applications of laser optical techniques, ultraviolet and soft X-ray spectroscopic techniques, electron-beam microlithography, electron microscopy, scanning tunneling microscopy, mass spectrometry, and picosecond laser techniques. ORNL's new program for experimental studies of picosecond processes in liquids, gases, and molecular clusters concentrates on studies of structure and dynamics relevant to energy deposition. Programmatic areas of emphasis include mammalian genetics, protein engineering, and cell biology. Another major area of interest is the Human Genome; work involves the analyses of mammalian genomes using new DNA sequencing technologies, development of computer-based gene sequence analysis methods, and operation of the Human Genome Management Information System. ORNL also continues to support OHER's Radon Research Program with the publication of an international newsletter *Radon Research Notes*, which is now in its seventh issue. It describes radon research conducted by DOE, other federal agencies, and the Commission of European Communities, and is distributed to over 2200 interested persons.

Chemical and Radiological Physics

The physical and technological research activities under OHER support are directed toward increasing knowledge of the interactions of potentially hazardous agents with biological and environmental systems, and toward ensuring a technical capability for characterizing and quantitatively measuring such agents in various settings. The research consists of studies of the structures and properties of materials of biological or environmental importance; the physical and chemical mechanisms that govern the formation, transport, and chemical transformation of radiation products in gaseous and condensed media; and the pollutants in the atmosphere, hydrosphere, and biosphere. Strong emphasis is given to the development of advanced instrumentation needed to satisfy the requirements of OHER.

Included in the scope of this work are theoretical and experimental studies of interactions at the atomic, molecular, and macroscopic levels in solids, liquids, and gases and on solid surfaces and solid-liquid interfaces. Also, detailed Monte Carlo studies are made of the physical and chemical evolution of radiation-induced products in natural media and in biological materials.

Investigations focus on genetic and somatic effects of radiation and chemicals. Goals include identification and qualification of these effects, elucidation of pathways by which the effects are expressed, assessment of risk associated with radiation and chemical exposures, and establishment of strategies for extrapolation of risk data from animals to humans. Concurrent basic studies in genetics, biochemistry, molecular biology, and cell biology illuminate normal life processes as prerequisites to comprehending mutagenic and carcinogenic effects of environmental agents. ORNL continues to expand and integrate its activities in genome research, which includes physical and functional gene mapping, new strategies for DNA sequencing, and informatics. Ongoing upgrade of protein crystallography in the Biology Division will complement the core program in protein engineering.

Mammalian Genetics

Added strength in molecular biology has provided new dimensions for the continuing research in basic genetics and mammalian germ-cell mutagenesis. Mutations that are generated in experiments with radiation or chemicals, and subsequently propagated in breeding stocks, are furnishing extremely useful genetic tools for correlated DNA-structural/functional analysis of selected genomic regions. In turn, the molecular analyses serve to characterize the nature of

mutations; this elucidates the manner of action of different mutagenic treatments. The generation of mutations by inserting foreign DNA into the genome (using transgenic mouse technology) has been added to physical and chemical methods of mutation induction (Appendix B). Capabilities have been added for targeted mutagenesis using embryonic stem-cell technology.

There are four objectives shared by our classical and molecular-genetic studies. They are to (1) explore the structural nature of induced mutations and of the normal gene from which they arose, (2) identify hitherto unknown genes and gene products that are important for normal mammalian development, (3) correlate defined DNA sequences with physiologically significant heritable types, and (4) analyze directly the function of homologous regions of the human genome.

In the area of germ-cell mutagenesis, an objective is to elucidate the mechanisms for, and assess the risk from, the induction of heritable mutational damage. This includes the development of methods for efficient detection of such damage, the exploration of factors that affect mutation yield, the analysis of the structural nature of mutations, and the identification of anatomical and physiological damages caused by mutations. Current areas of emphasis include characterization of the molecular targets for chromosomal breakage, exploitation of recently discovered female-specific mutagens, and the phenotypic effects of chromosome rearrangements. Mutagenesis experiments are further serving to discover chemicals and protocols for "manufacturing" specific, desired types of mutations, especially those that provide the genetic tools for molecular-structure/function studies.

Molecular Genetics

Areas of emphasis in molecular genetics include genomic structure, regulation of gene expression, and structure and function of gene products. Visualization of higher-order chromatin structure and the three-dimensional structure of nucleosomes (the core particle of chromatin) utilize special techniques in electron microscope tomography developed locally and neutron and X-ray diffractometry. Cloning of segments of the eukaryotic genome and their subsequent sequencing will provide insights about the nature of regulatory elements of DNA and the propensity of small regions of DNA to undergo spontaneous mutations.

Model systems being used to study the regulation of gene expression include oncogenes (associated with the conversion of normal cells to cancer cells), mammalian genes that are under hormonal control, and mouse globin genes that provide an experimental system for thalassemia, a human genetic disorder. Gene products under close scrutiny include ribulosebisphosphate carboxylase (a determinant of biomass yield), epidermal growth factor (a polypeptide intimately involved in cellular growth and differentiation), enzymes involved in transcription of DNA, enzymes involved in the repair of chemical and radiation-damaged DNA, and membrane transport proteins that are responsive to environmental perturbations. In addition, the analysis of mutations at the DNA level is being studied by the use of shuttle plasmid systems following exposure to radiation or chemical agents.

Protein Engineering

Protein engineering (site-directed mutagenesis), an emerging program that is unique among DOE laboratories, integrates many activities in molecular genetics. The ability to program specific mutations into cloned genes will permit (1) the systematic design of new gene products as mechanistic probes of protein function and (2) the tailoring of operons to alter the regulation of gene expression. Molecular modeling with three-dimensional computer graphics will guide the selection of mutant gene products to be constructed, and will serve as a predictive tool of the probable structural consequences. Because protein engineering provides an avenue for optimizing functional properties of enzymes, it impinges on bioprocessing.

Cancer Biology

Change in gene expression is central to development, differentiation, and malignant transformation. Differentiation and the normal function of cells are dependent on controlled gene expression. The objectives of the research in this field are to define in molecular terms the mechanisms of controlling specific genes, especially by hormones. Carcinogens alter genes and their

expression, and the changes induced in the cell genome are being studied with emphasis on endogenous retrotransposable genes and protooncogenes involved in cell growth and differentiation. One of the changes that occurs with malignant transformation is in the cell surface proteins. A tumor specific protein on the surface of the cells from human lung and colon tumors and on murine lung tumors has been identified as a member of the integrin family.

A program has been initiated to study the effects of alpha-particle radiation that includes activation of oncogenes, gene rearrangement involving mobile gene elements, malignant transformation of tracheal cells, and determination of radiation biological effectiveness for alpha particle-induced cancer of the tracheal epithelium.

ORNL Genome Program

The Laboratory is strongly committed to an integrated effort to analyze the mouse genome and, through that, the human genome. New methods that will increase the rate and accuracy for sequencing, as well as unique informatics for pattern recognition in new sequence data, are being developed in parallel with the generation and molecular analysis of new germline mutations in the mouse. The major objective is to explore the structural and functional characteristics of the mammalian genome using experimental molecular genetics. Because many parallels exist between the human and the mouse in anatomy and physiology, mutations in the mouse are powerful tools for analysis of the structure and function of the human genome.

New DNA sequencing technologies needed to provide rapid analyses for use in conjunction with analyses of the mammalian genomes, fall into three categories:

- For conventional gel electrophoresis, methods are being developed to increase the rate of sequence analysis 10- to 100-fold by replacing radioisotopes with stable isotopes and the use of resonance ionization spectroscopy to detect DNA labeled with these isotopes. This employs state-of-the-art organometallic chemistry to synthesize the labels and new modification of resonance ionization spectroscopy to detect them.
- To eliminate the gel electrophoresis step, other methods are under development. One is sequencing by hybridization; others involve various mass spectrophotometric methods of analyzing directly the DNA fragments that are usually subjected to electrophoresis.
- By employing new detection techniques, sensitive and rapid DNA analysis can occur including single molecule detection of luminescence species; mass spectrophotometric detection methods, and synchronous luminescence, phosphorescence, and Raman detection techniques.

A recent initiative that traverses several divisions (Biology; Chemistry; Engineering, Mathematics, and Physics; and Health and Safety Research) includes the application of stable isotopes to novel strategies for sequencing DNA at increased rates and sensitivities.

Some of these procedures may also be adapted for genome mapping and for analysis of gel blots of DNA. The analysis of the mammalian genomes should be expedited when some of the techniques are available.

The analysis of mammalian genomes will proceed on several fronts. The analysis of the mouse genome and the interaction with studies on the human genome will proceed as follows:

- develop complete molecular maps and refined functional maps of several specific regions of the mouse genome as models for the human genome program,
- perform fine structure point mutagenesis and physical mapping of the mouse chromosomes,
- create molecularly tagged mutations throughout the murine genome by insertional mutagenesis using both pronuclear injection and embryonic stem cell techniques,
- use efficient mutagens to generate chromosomal rearrangements for expansion of genomic regions accessible to fine structure molecular structure analyses,
- use mutagenesis techniques to create models of important human genetic disorders that can be analyzed molecularly,
- establish a national data base for transgenic mouse mutants that can be accessible by all researchers, and

- employ artificial intelligence and neural network techniques to identify important DNA sequence patterns.

Unique computer-based sequence analysis methods for identification of biologically important regions in newly sequenced DNA are being developed based on neural network, artificial intelligence, and parallel computational techniques. An expert system is under construction for rapid and reliable localization of gene components such as exons, introns, and gene control elements and the automated assembly of these components to describe whole genes. Not only is a portion of this system being used currently at ORNL to localize genes in mouse studies, but other laboratories are also beginning to submit sequence data to be searched for important human disease genes (Appendix B).

The U.S. Human Genome Project is a joint venture by the DOE and the National Institute of Health (NIH) to identify human gene location and ultimately function. The DOE Human Genome Program, under OHER, created the Human Genome Management Information System (HGMIS) in the Biomedical and Environmental Information Analysis Section, HASRD, to facilitate communication among the DOE program contractors and to serve as a forum for members of the human genome research community.

To fulfill this mission, HGMIS, which is under contract with DOE and NIH, prepares and disseminates information to researchers in academia, government, and industry. HGMIS produces a bimonthly newsletter, DOE Human Genome Program reports, an information database, and technical reports. HGMIS updates and maintains the mailing list database compiled for the human genome programs of both DOE and NIH. Additionally, HGMIS acts to orient and refer those persons seeking assistance to sources that can provide appropriate information. The documents/services are available to all persons upon request and provide both the interested scientist and lay person information in this rapidly moving multidisciplinary project.

- The newsletter, *Human Genome News*, provides readers with technical and general interest articles, meeting reports, news items, funding announcements, and meeting and training calendars. In collaboration with the international Human Genome Organization, HGMIS also reports international genome project news.
- The status of the DOE Human Genome Program is described in the *Human Genome 1990-91 Program Report*, which includes research highlights, narratives on major DOE research efforts, abstracts of research in progress, and figures and captions provided by investigators.
- The information database is being developed as a text management and user-conferencing/communications mechanism. It contains text from program reports and newsletters, bibliographic data from both scientific and popular literature, and current awareness items.
- Technical reports will be commissioned and produced by HGMIS as recommended by the DOE Human Genome Program.

KP05 - Carbon Dioxide Research

These activities are comprised of five principal components: the Global Carbon Cycle Research Program, the Resource Analysis Program, and the Carbon Dioxide Information Analysis Center, ARM Data Archive, and Computer Hardware, Advanced Mathematics, and Model Physics (CHAMMP) research. In addition, ORNL's Center for Global Environmental Studies (described in "Program Orientation") provides a unique, interdisciplinary base for exploring research activities under the KP05 program.

Global Carbon Cycle

The objective of the Global Carbon Cycle Research Program is to estimate potential increases in atmospheric CO_2 concentrations associated with different fossil fuel use patterns. This activity includes the coordination of program planning and research integration among ESD investigators addressing carbon cycle issues. There are substantial inconsistencies in our understanding of fossil fuel era changes in the global carbon cycle. These are addressed from three standpoints: (1) the oceans may in fact take up carbon more readily, (2) decreases in terrestrial carbon storage caused by land use may

be compensated for by other ecosystem responses, or (3) estimates of historical carbon releases from vegetation and soil may be wrong. Uncertainty about further increases in atmospheric CO_2 concentrations also arises from a lack of understanding about the effects of environmental changes caused by rising greenhouse gas concentrations.

Recent activities and accomplishments include:

- publication of a major review of the results in carbon cycle research from the last decade;
- publication of modeling studies to investigate the potential for increasing oceanic carbon uptake by adding iron to stimulate primary productivity;
- completion of a comparison of one-dimensional models of carbon turnover in the atmosphere and oceans;
- analysis of land use patterns in Brazil and Southeast Asia; and
- design and initial implementation of a geographically explicit model of carbon cycling in terrestrial ecosystems with explicit treatment of the influences of environmental conditions, including temperature, moisture, and atmospheric CO_2.

Resource Analysis

The purpose of the Resource Analysis task is to develop techniques and databases for investigating the potential consequences of increasing atmospheric CO_2 and of the resulting changes in climate and sea level, especially as they affect human and environmental resources. This involves:

- the collection, automation, computation, and quality assurance of multisector environmental data for use in regional climate and environmental resource studies;
- the development of a Global Coastal Hazards Database to identify those coastal areas that are especially vulnerable to climate-induced rising sea level; and
- the refinement of methods for using climate model output in regional-scale climate and environmental impact studies.

Recent accomplishments have included (1) acceptance of a paper for publication in a refereed journal that describes some of the challenges in interpreting the output from general circulation models as climate-change scenarios for climate-impact studies; (2) analysis of the relative vulnerability of the U.S. East and Gulf Coasts to inundation and erosion from rising sea levels, based on seven relevant variables; (3) compilation of a global storm (hurricanes, extratropical cyclones, monsoons, etc.) database for integration with the Global Coastal Hazards Database; and (4) publication of an environmental atlas displaying agricultural and hydrologic data for use in a collaborative research project (with Pacific Northwest Laboratory, Resources for the Future, and Sigma Xi) that analyzes the sensitivity of the Missouri-Iowa-Nebraska-Kansas region to climate change.

Carbon Dioxide Information Analysis Center

The purpose of the Carbon Dioxide Information Analysis Center (CDIAC) is to archive, compile, evaluate, and distribute CO_2-related information. CDIAC's activities include:

- serving as an archiving depository for CO_2-related computer models and numeric data;
- evaluating the quality and usefulness of CO_2-related databases that are assembled and updated as needed as computerized numeric data and computer model packages (packages consisting of written documentation and magnetic media);
- fulfilling requests for bibliographic searches, reports, and data;
- publishing a semiannual newsletter, *CDIAC Communications*;
- publishing a document, *TRENDS*, that presents recent findings and patterns in long-term temperature records and trace-gas emissions and atmospheric concentrations;
- maintaining a directory of approximately 6400 CO_2 researchers, educators, and policymakers;
- establishing links between national and international data centers; and
- providing training and research experience for visiting scientists and students through participation in special data analysis projects.

Recent accomplishments include (1) filling more than 8600 requests for data, reports, and other information during the last fiscal year; (2) documenting long-term, Chinese proxy and instrumental climate records obtained through a continuing joint U.S.-China project on the effects of increasing atmospheric CO_2 on climate; (3) documenting atmospheric CO_2 concentrations from four U.S.S.R. flash sampling sites under the auspices of Working Group VIII of the U.S.-U.S.S.R. Joint Committee on Cooperation in the Field of Environmental protection; (4) collaborating with the National Climatic Data Center in compiling a long-term, climate data set with global coverage suitable for climate analyses; and (5) participating in the Interagency Working Group on Data Management.

ARM

The ARM Program is a DOE-sponsored field project which will obtain precise measurements of atmospheric radiation-related phenomena needed to improve present General Circulation Models (GCMs) used to predict future climate. It is DOE's premier global change research program, and is the second largest U.S. global change research program next to NASA's Earth Observing System. Two principal ARM activities at ORNL are the Data Archive and Instrumentation Support.

Data Archive ORNL (ESD) has been designated as the long-term archive for the ARM Program. The ARM Archive will store, manage, process, and make data collected during the ARM project available for use by the ARM scientists, and the wider science community including atmospheric physicists, chemists, meteorologists, and climatologists. Further information on the ARM Archive is given in Appendix A.

ARM Instrumentation Support Work currently being performed by the Instrumentation and Controls Division in support of the ARM program consists of two distinct development tasks: (1) creating a pointing shortwave/near-IR radiometer and (2) devising mathematical means by which spectrally resolved solar radiation measurements can be inverted to recover concentrations of atmospheric gaseous constituents and sizes of particular matter.

The first task recognizes the need for a pointing short-wave/near-IR radiometer at the ARM CART sites with which to make solar extinction and aureole observations. The multifunction instrument being developed will operate in four modes: as a solar tracking radiometer, a solar aureole radiometer, a sky radiance radiometer, and as a zenith radiometer. Target design specifications initially established in cooperation with ARM management are as follows:

- Field of view: 0.2 degree and 1.5 degrees (selectable)
- Pointing accuracy: 0.5 degree or better in two axes
- Pointing resolution: 0.2 degree or better in two axes
- Spectral wavelength range: 0.35 to 3.5 m
- Stray light rejection: 106 to 107
- Duration of measurement: 1 minute or less for solar aureole measurements
- Number of pixels for aureole measure ment: in the range 100 to 600

ORNL, in concert with other ARM program measurement experts, is currently refining and assessing the workability of the above tentative specifications. Additional design constraints imposed by the intended service include (1) a hermetically sealed optical system, (2) a temperature-controlled environment for the photodetectors and other sensitive electronic components, and (3) ruggedized design suitable for extended field use with minimal maintenance.

The second task recognizes that the solar spectrum observed from Earth is influenced by the constituents of our atmosphere through two principal mechanisms–light absorption and scattering. Each particle or molecule absorbs the sun's light only at certain wavelengths characteristic of that particle or molecule, and the amount of light absorbed will depend upon the particles' concentrations. The scattering process is more complex, depending upon whether the incident light photon is scattered once (single scattering) or many times (multiple scattering). Scattering is dependent upon the wavelength of

the light and the shape and size of the scattering particles.

When solar spectra are measured, the effects of both absorption and scattering are combined and integrated into the spectral data. The retrieval of information from data on each of the processes (scattering or absorption for a particular species) that occur is called reconstruction or inversion. The aim is thus to devise methods for extracting information (principally, concentrations and size distributions) concerning atmospheric constituents of special interest.

Computer Hardware, Advanced Mathematics, and Model Physics (CHAMMP)

The CHAMMP program seeks to provide climate researchers with an advanced modeling capability for the study of global change issues. Current general circulation models have coarse spatial resolution and minimal coupling between ocean, atmosphere and biosphere. As a first goal in the program, current state-of-the-art models are being implemented on massively parallel computers, allowing an increase in spatial resolution. Accomplishment of this task will lay the groundwork for the second goal which is to couple oceanic and atmospheric models.

A collaborative relationship between researchers at the National Center for Atmospheric Research (NCAR), ORNL and Argonne National Laboratory was established in 1990 to tackle the challenges posed by the CHAMMP program regarding the atmospheric component of the climate. From broad definition of the issues in using massively parallel computers for climate modeling, the group has moved to providing solutions to some of the more difficult specific problems of the parallel computation of atmospheric dynamics. The specific focus of the collaboration, to date, relates to CHAMMP's first goal. The NCAR Community Climate Model, (CCM2), currently under development at NCAR for the CRAY Y-MP computer will also be offered in two massively parallel implementations. One implementation will use the computational power of distributed memory Multiple Instruction, Multiple Data (MIMD) parallel computers like the Inter Delta and PARAGON. The other implementation will take advantage of the Single Instruction, Multiple Data (SIMD) programming environment of Thinking Machines CM-2 and CM-5.

KP06–Nuclear Medicine

The Nuclear Medicine Program focuses on the design and development of new tissue-specific radiopharmaceuticals for diagnostic and therapeutic applications in nuclear medicine. This program continues to receive international recognition for the innovative design and development of new radiopharmaceuticals and of improved radiolabeling techniques. A major resource is the ORNL High Flux Isotope Reactor (HFIR) which provides parent radioisotopes for generator development and other radioisotopes for R&D.

The major areas of emphasis and progress include (1) agents for the evaluation of heart disease, and (2) a variety of radiolabeled agents and radionuclide generator systems which provide radioisotopes for tumor detection and therapy. The development of the first large-scale, clinical prototypes of the tungsten-188/rhenium-188 generator has received widespread recognition, and several new cooperative programs have been established to pursue the use of this radioisotope. Rhenium-188 is a potential replacement for many of the radioisotopes currently used for attachment to tumor-specific antibodies for radioimmunotherapy. The first osmium-194/iridium-194 generator system has been developed in this project, providing carrier-free iridium-194 as a potential new candidate for radioimmunotherapy and other therapeutic applications.

Another important area of research is the development of radiolabeled nucleoside analogues for the potential localization and therapy of tumors. A variety of structurally-modified nucleoside analogues have been developed and are in various stages of testing for tumor specificity in various *in vitro* and *in vivo* systems. The radioiodinated and fluorine-18 radiolabeled acyclonucleosides are of particular interest for single photon emission tomography (SPECT) and positron emission tomography (PET), respectively.

A major important component of the Nuclear Medicine Program is collaboration through the Medical Cooperative Programs with university hospitals, clinics, and other research institutions for further preclinical research and clinical evaluation of new radiopharmaceuticals developed at ORNL. Over 20 programs are currently

active with institutions in the U.S. and abroad. Several ORNL agents are currently in clinical trials, and clinical studies will soon be initiated in the areas of the diagnosis of various types of heart disease with the iodine-123-labeled fatty acid imaging agents. The concept of "metabolic trapping" of fatty acids developed in the ORNL program has now evolved to the commercial development of several agents. Additionally, a new radioiodinated agent developed in the ORNL Nuclear Medicine Group for the evaluation of pancreatic function entered clinical trails at the Clinic for Nuclear Medicine at the University of Bonn, Germany. Therapeutic agents radiolabeled with therapeutic radioisotopes available from ORNL-developed generator systems will soon enter clinical trials. The success of these international collaborative programs continues to be documented in a large number of joint publications. The balance between basic research and development at ORNL and interaction with key programs at other institutions thus continues to form the basis for a strong Nuclear Medicine Program.

Program Accomplishments

ORNL BER Program accomplishments include advances toward understanding potential health and environmental impacts of energy technologies and fundamental biological processes, as well as continued growth in development of innovative research techniques and instrumentation. These research findings have resulted in numerous publications and awards. Numbers and types of publications are presented in Table 14 in the Resource Quantitation section.

Appendix C lists the OHER-supported publications by ORNL staff during FY 1991. Included in this section are the most significant BER accomplishments at ORNL for FY 1991, organized by KP subprogram. Appendix B details the major research highlights for ORNL's BER Program in FY 1991.

KP01–Analytical Technology - Dosimetry Research and Measurement Science

- Successfully used a scanning probe microscope to provide the first reliably routine images of DNA.
- Installed an Atomic Force Microscope (AFM), which allows a wide range of surface conditions favorable for immobilizing and imaging DNA, and used the AFM to observe supercoiling of the DNA strands.
- Made and characterized the doubly negative charged ion of Buckyball, C_{60}^{-2}, and initiated investigations of other novel physical and spectroscopic properties of this exotic species and related fullerenes.
- Initiated investigation of laser ablation of tagged genomic material, followed by laser ionization and mass spectrometric detection for rapid sequencing of DNA bases.
- Completed operational readiness of the Radiation Calibration Laboratory (RADCAL) and used the facility for radiation dosimetry research and testing, instrument calibration, and radiobiological research.
- Prepared ICRP Publication 61, which is a tabulation of secondary radiation protection quantities corresponding to the 1990 ICRP recommendations utilized extensively by the radiation protection community.
- Examined the effect of laser wavelength, matrix, and instrumental factors for the structural characterization of normal and modified oligonucleotides by matrix-assisted laser desorption Fourier transform mass spectrom etry (FTMS).
- Initiated construction of a laser desorption time-of-flight mass spectrometer to aid in the development of laser desorption conditions for large oligonucleotides.
- Used gas phase deuterium exchange reactions to characterize alkylated nucleosides and to provide isomeric differentiation.
- Constructed an electrospray ionization source and interfaced it to a quadrupole mass spectrometer, thus allowing the ionization source to be optimized for vacuum pumping and ion transmission requirements prior to interfacing with an FTMS.
- Used the results obtained for matrix-assisted laser desorption FTMS to establish collaborative research with Dr. Jean Cadet (Grenoble, France) for the examination of nucleoside photodimers and with the American Health Foundation for the characterization of polycyclic aromatic hydrocarbon adducts of nucleotides.

KP02–Environmental Research

- Examined differences in the stable isotope composition of ammonium (NH_4-N) and nitrate (NO_3-N) in bulk precipitation and throughfall at Walker Branch Watershed by utilizing ^{15}N:^{14}N ratios; and identified the potential importance of atmospheric NH_4-N inputs to nitrogen cycling in the N-deficient forest.
- Completed the seventh measurement since 1967 of the 298 permanent biomass inventory plots (10,000 individual tree observations) on Walker Branch Watershed, thus demonstrating the division's commitment to the integrity of this valuable data record.
- Led an effort to develop for HQ the basic R&D plan in support of environmental restoration (DOE, 1990), based on contributions from over 100 scientists at all national laboratories and many universities. The plan describes the fundamental scientific challenges that must be faced for the environmental restoration of the DOE facilities.
- Examined the transport of natural organic matter (NOM) and inorganic colloids in a sandy aquifer to improve predictions of the role of these materials in enhancing the mobility of contaminants, and demonstrated that components of NOM are rapidly transported through an aquifer and that mobile NOM also solubilizes and enhances the transport of iron sorbed to the aquifer.
- Studied mechanisms controlling contaminant mobility in heterogeneous soils through unsaturated transport studies in undisturbed soil columns, and demonstrated progress on quantifying the thermodynamic and kinetic controls on solute transport.
- Used ^{7}Be and ^{35}S as natural traces of hydrological flow through watersheds and into streams to study snowmelt processes in the Arctic, which is an improvement over the conventional methods using chemical comparisons.
- Developed a revised concept of landscape equilibrium which incorporates the space and time scales of disturbance and which predicts the resultant dynamics of a landscape at any scale of observation.
- Developed the first model for dry deposition of mercury to a forest in collaboration with NOAA, and found that dry deposition, which was previously ignored, is comparable to wet deposition and may be the dominant input process in the summer.
- Demonstrated, through 'proof of principle' experiments, the ability to follow microbial genetic material in groundwater *in situ* through the use of a genetic probe.

KP03, KP04–Health Effects and General Life Sciences

- Demonstrated vulnerability of germ cells to chemical mutagens absorbed through the skin.
- Constructed new cloning vectors for co-expression of two genes, and thereby facilitated protein engineering of oligomeric proteins.
- Established that at low doses, the dose-response curve for neutron-induced tumors is linear.
- Proved that amplification of certain DNA repair genes is responsible for development of resistance to an antitumor drug.
- Identified receptor binding recognition sites of epidermal growth factor by use of site-directed mutants.
- Demonstrated the feasibility of combining chemical modification with site-directed mutagenesis as an approach to designing enzymes with altered substrate specificities.
- Developed a multiplexing method for rapid DNA sequencing that relies on stable isotopes of organometallics. These can differentially label DNA and be detected by a mass spectrometer coupled to sputter-initiated resonance ionization spectroscopy.
- Generated 50 transgenic mouse lines, several of which carry insertional mutations that may facilitate the characterization of developmental disorders in humans.
- Discovered through a novel extension of protein engineering, the mechanistic basis for the *in vivo* regulation of the CO_2-fixation enzyme by atmospheric CO_2 during photosynthesis.

- Successfully applied artificial intelligence to the identification of coding and regulatory regions of DNA based solely on nucleotide sequence information.
- Discovered that mutagenic and cytotoxic effects of certain anticancer agents are gender-specific.
- Provided molecular access to genes associated with human genetic diseases, e.g., the complex Prader-Willi and Angelman syndromes, through structure/function studies of genomic regions surrounding specific-locus markers.
- Demonstrated that the mouse mutation *scurfy* produces a defect in the thymic microenvironment that shapes the developing immune system, thus furnishing an animal model for testing hypotheses concerning causes of certain human immune system diseases.
- Developed the capability for targeted mutagenesis using ES (embryonic stem-cell) technology.
- Demonstrated very low mutation rates from mouse oocytes irradiated around the time of birth, when the state of the nucleus most resembles that of the human arrested oocyte.
- Demonstrated that the hematological indices of murine and human beta-thalassemias are similar.

KP05–Carbon Dioxide Research

- Demonstrated with box models that significant increase in carbon dioxide uptake through iron fertilization of antarctic oceans is not possible because ocean mixing, not iron, is the limiting factor regulating ocean carbon dioxide uptake.
- Further analyzed the effects of iron fertilization on phytoplankton production and ocean sequestering of atmospheric carbon dioxide.
- Participated in planning and advising for several national and international research programs addressing global change.
- Continued development and analysis of a spatially explicit, global terrestrial ecosystem model for carbon cycling that examines the effects of differences in vegetation type, temperature, moisture, and atmospheric carbon dioxide on regional and global carbon dynamics.
- Continued collection, collation, and analysis of data describing global patterns in soil carbon concentrations, and initiated publication of several papers describing global soil carbon dynamics.
- Examined eastern North American forest responses to climate changes.
- Developing preliminary capability to integrate landscape scale carbon dynamics to the global terrestrial carbon cycle.
- Refined global estimates of carbon emissions to finer spatial scales.
- Gregg Marland and CDIAC compiled emission estimates showing that global total CO_2 emissions for 1989 reached the largest annual emissions ever (5.954×10^6 metric tons of carbon). U.S. emissions were found to grow by 1.14%, down from the 4.78% growth seen in 1988, which marks the third consecutive year the nation's growth rate was higher than the global average growth rate. By contrast, emissions from Western Europe were found to be still 12% below the 1979 maximum and virtually unchanged since 1982.
- Published *Trends '91: A Compendium of Data on Global Change*, the second in the *Trends* series.
- Produced the first two issues in the new series *DOE Research Summary*, which highlights recent DOE-sponsored research on global climate change.
- Completed the quality-assurance of important data bases contributed by colleagues in the People's Republic of China and the former Soviet Union for distribution as numeric data packages.
- Gregg Marland and CDIAC collaborated with the United Nations Statistical Office to produce a world energy statistics data base, updated through 1989, that includes annual CO_2 emissions estimates by country.
- Developed a Global Historical Climatology Network, a long-term data base of temperature, precipitation, and atmospheric data useful for detection and analysis of climate change and the improvement of climate models.
- Developed and implemented algorithms for: (1) an efficient Legendre transform on MIMD and SIMD architectures, (2) parallel Fast Fourier Transforms tailored for global modeling on both MIMD and SIMD computers, (3) distributed semi-Lagrangian transport calculations on MIMD computers, and

(4) accurate spectral transform methods on a reduced grid.

- Made significant progress in understanding issues relevant to the design of massively parallel climate models. In particular completed: (1) studies of parallel scalability of the spectral transform and other numerical methods, (2) study of load balancing strategies and vertical parallelization for climate models, and (3) implementation of the CCM2 (PLX12 library) in a massively parallel version on the Intel iPSC/860.

Together, this work provides both a technical basis for developing parallel spectral climate models on MIMD and SIMD machines, and a scientific basis for the design of future parallel climate models.

KP06–Nuclear Medicine

- Developed the first osmium-194/iridium-194 radionuclide generator system. It provides carrier-free iridium-194 as a potential new candidate for radioimmunotherapy and other therapeutic applications.

Awards and Appointments

Table 9 lists awards received by BER Program Staff at ORNL in FY 1991, and Table 10 lists achievements and appointments for BER Program staff at ORNL in FY 1991.

Table 9. Professional, corporate, and organizational awards received by BER-supported personnel[a] at ORNL in FY 1991

Recipient(s)	Award
Bunick, G. J.	Martin Marietta Energy Systems, Inc., Technical Achievement Award
Chen, C. H.	Health and Safety Research Award, Excellence in Research Award
Christensen, S. W.	Certificate of Appreciation, National Acid Precipitation Assessment Program
Christophorou, L. G.	Alexander von Humboldt Foundation Senior U.S. Scientist Award; Senior Corporate Fellow, Martin Marietta Energy Systems, Inc.
Cushman, R. M.	Award of Merit for Whole Periodicals, East Tennessee Chapter of the Society for Technical Communication
Gunderson, C. A.	Distinguished Technical Achievement Award, Environmental Sciences Division, Oak Ridge National Laboratory
Kanciruk, P.	S16 Achievement Award, Martin Marietta Energy Systems, Inc.
Lindberg, S. E.	Nominated for the DOE E. O. Lawrence Award
Miller, J. C.	Fellow, American Optical Society
O'Neill, E. G.	Science Alliance Graduate Upgrade Award, Science Alliance, University of Tennessee
Owens, J. G.	Five-Year Service Award for Site Operation, National Atmospheric Deposition Program
Post, W. M. III, Peng, T.-H.; Emanuel, W. R.; King, A. W.; Dale, V. H.; and DeAngelis, D. L.	Technical Award, Martin Marietta Energy Systems, Inc.; Award of Excellence for Scholarly/Professional Articles, Technical Publications Competition, Society for Technical Communication; Award of Excellence for Scholarly/Professional Articles, Technical Publications Competition, East Tennessee Chapter of the Society for Technical Communication
Turner, M. G.	Annual Scientific Achievement Award, Environmental Sciences Division, Oak Ridge National Laboratory; Award for Distinguished Scientific Achievement, Tennessee Chapter of the Association for Women in Science
Van Hook, R. I.	Director's Award, Oak Ridge National Laboratory (awarded to Environmental Sciences Division for scientific and technical excellence)
Vo-Dinh, T.	Appointed Senior Research Associate Board Member, Environmental Research Center, University of Nevada, Las Vegas

[a]Personnel who received at least 25% of their support from the BER Program during FY 1991 are shown, as are other key managerial and scientific staff.

Table 10. External achievements and appointments received by BER-supported personnel[a] at ORNL in FY 1991

Name	Achievement/Appointment
Bunick, G. J.	Special Interest Committee on Small-Angle Scattering, American Crystallographic Association (1991-); Applications Software Working Group, National Energy Research Supercomputer User Group (1991-)
Compton, R. N.	Publications Committee, American Physical Society (1991-); Member, Publications Committee of American Physical Society
Cook, J. S.	Publications Committee, American Physiological Society (1986-1989); Chairperson (1989-1992); Member of the Corporation, Mount Desert Island Biological Laboratory (1962-); Special Study Sections, National Institutes of Health (1987-1989); External Review Committee, Biomedical Sciences Program, Wright State University (1991); *American Journal of Physiology*, editorial board (1987-1993); *Current Topics in Membranes and Transport*, advisory board (1983-); *News in Physiological Sciences*, associate editor (1986-), chair, managing board (1989-1992)
Emanuel, W. R.	Member, Working Group on Integrated Global Change Modeling, Committee on Global Change, National Research Council (1989-1991)
Fry, R. J. M.	*Radiation Research*, editor-in-chief (1988-); *Advances in Radiation Biology* (1990-1993), editorial board
Generoso, W. M.	Committee on Toxicology, National Research Council (National Academy of Sciences) (1989-1991); Member, Organizing Committee, First Latin-American Symposium on Environmental Mutagenesis, Laxambu, Brazil (1991); *Teratogenesis, Carcinogenesis, and Mutagenesis* (1979-), editorial board; *Mutation Research* (1985-), editorial board
Hartman, F. C.	Invited Speaker, Nobel Symposium entitled "CO_2-fixation and CO_2-Reduction in Biological and Model Systems"; Executive Committee, Division of Biological Chemistry, American Chemical Society (1989-1991); *Journal of Protein Chemistry* (1982-1992), editorial board; *Journal of Biological Chemistry* (1983-1995), editorial board
Jardine, P. M.	*Soil Chemistry*, associate editor (1991-1994)
Kaye, S. V.	Member, Advisory Committee, ORAU/DOE Health Physics Faculty Research Award Program (1991–)
Kennel, S. J.	Study Section on Health Effects Research, U.S. Environmental Protection Agency (1982-); Ad hoc member, National Cancer Institute Site Visit Committees (1989, 1990)

Table 10. (continued)

Name	Achievement/Appointment
Lindberg, S. E.	Member, U.S. and Soviet Scientists Delegation to select research sites in the Siberian Arctic as part of the Joint U.S.-U.S.S.R. Bilateral Agreement on Environmental Protection; U.S.-Poland Joint Research Committee on Status and Trends of Forest Ecosystems: Climate, Pollution, and Forest Health (1991); Advisory Panel, Air and Deposition Monitoring Group of the EPA program Environmental Monitoring and Assessment (1988-1991); Honorary Steering Committee, International Conference Series: Heavy Metals in the Environment (1983-); Technical Organizing Committee, Eighth International Conference on Heavy Metals in the Environment (1991); Planning Committee, International Conference on Atmosphere/Surface Exchange Processes (1991); Executive Committee, NADP/NTN (1983-); MAP3S/RAINE Precipitation Chemistry Network (1981-); Habilitation Committee, D. Godbold, University of Göttingen (1990-1991); Organizing Committee, Second International Conference on Mercury as an Environmental Pollutant (1991-1992); *Advances in Environmental Science* (1986-), editorial board
Marland, G.	Advisory Committee, National Institute Global Environmental Change-South (1990-); Policy Implication of Greenhouse Warming (1988-1992); U.S. Agricultural and Global Climate Change, Council on Agricultural Science and Technology (1990-1992)
Mazur, P.	Publications Committee (Chairman), Society for Cryobiology (1974-); Board of Governors, Society for Cryobiology (1967-); *Cryobiology* (1967-), editorial board
Mitra, S.	Consultant, National Cancer Institute (1987-)
Mulholland, P. J.	*Ecology and Ecological Monographs* (1990-1993), editorial board
Niyogi, S. K.	Scientific Expert, United Nations Industrial Development Organization, and External Advisor to Indian Jute Industries' Research Association, Government of India (1989-)
Olson, R. J.	Interagency Committee on Environmental Trends, Council on Environmental Quality (1991-); GCDIS Catalog Services Subgroup, NASA (1990-1991); Advisor, President's Council on Environmental Quality
O'Neill, E. G.	Treasurer, Soil Ecology Society (1989-)
Palumbo, A. V.	*Ecotoxicology* (1991-), editorial board
Parr, P. D.	Member, Southern Appalachian Man and the Biosphere, Environmental Education; Treasurer, Association of Southeastern Biologists (1990-)
Popp, R. A.	Mouse Hemoglobin Nomenclature (1984-)

Table 10. (continued)

Name	Achievement/Appointment
Reichle, D. E.	Council Member, American Institute of Biological Sciences (AIBS) (1990); Council Member, International Union of Radioecologists (1991–); Member, Ecological Society of America (1961–); Member, Association of Ecosystem Research Centers (1988–); *Pedobiologia*, (1975–); *Journal of Soil Biology and Ecology* (1987–); Forum for Applied Research and Public Policy (1990–); Springer-Verlag, consulting environmental editor (1978–); Member, Biology Review Panel, U.S. Environmental Protection Agency (1986–); Member, Board of Directors, The Nature Conservancy, Tennessee Chapter (1989–)
Rinchik, E. M.	Chairman, Committee for Mouse Chromosome 7, International Mammalian Genome Society (1990-)
Ritchie, R. H.	Member, Executive Council, Southeastern Section, American Physical Society, 1986 - present
Rohwer, P. S.	President, American Academy of Health Physics (1992); Treasurer, Health Physics Society (1991–); Member, Advisory Committee, ORAU/DOE Health Physics Faculty Research Award Program (1991–)
Russell, L. B.	Nominating Committee, Environmental Mutagen Society (1991-); International Committee on Standardized Genetic Nomenclature for Mice (1977-1990); Board on Environmental Science and Toxicology, National Academy of Sciences (1986-1990); Environmental Health Institute, Fellow (1987-); Awards Nomination Committee (1991-); *Mutation Research* (1976-), editorial board; *Mouse Genome* (formerly *Mouse News Letter*) (1987-1990), editorial board
Sega, G. A.	*Environmental and Molecular Mutagenesis* (1985-), editorial board
Skinner, D. M.	Board of Governors, The Crustacean Society (1987-); Selection Committee, Miller Research Fellows, Miller Institute for Basic Research in Science, University of California, Berkeley (1987-); Member of the Corporation, Marine Biological Laboratory, Woods Hole (1971-); Member, Advisory Committee, Department of Biology, Georgetown University (1983-); DOE Review of Laboratory Programs for Women (1990); *Gene* (1986-); *Physiological Zoology* (1989-), editorial board
Stevens, A. L.	Biomedical Sciences Study Section, National Institutes of Health (1985–)
Terzaghi-Howe, M.	Member, Metabolic Pathology Study Section, National Institutes of Health (1990-)

Table 10. (continued)

Name	Achievement/Appointment
Turner, J. E.	Radiation Dosimetry Advisory Committee, National Research Council (1988-present); Comprehensive Certification Panel of Examiners, American Board of Health Physics (1987 - present); Consociate Member, National Council on Radiation Protection and Measurements (1983 - present); President-elect, American Academy of Health Physics; *Radiation Research*, associate editor (1991-)
Turner, M. G.	Directorate for Temperate Ecosystems, U.S. Man and the Biosphere program; *Climate Research*, editorial advisor (1991-)
Van Hook, R. I.	Head of Research Subcommittee, Southern Appalachian-Man and the Biosphere (1988–); Member, Executive Committee, Southern Appalachian-Man and the Biosphere (1988–)
Vo-Dinh, T.	Chairman, Commission V.4 on Spectrochemical Methods, International Union of Pure and Applied Chemistry (IUPAC); Chairman, Subcommittee on Fiberoptics, ASTM Committee E.13 (1989–); *Analusis*, associate editor (1991–); *Polycyclic Aromatic Compounds*, topical editor, (1989–)
Von Damm, K. L.	Member, Ocean Drilling Program's preliminary explorations of the East Pacific Rise aboard the Atlantis II and the research vessel Alvin; Alvin Review Committee, University National Oceanographic Laboratories (1990-1993); Alvin Review Committee, University--National Oceanographic Laboratory System (1991-1994)
Yang, W. K.	Member, Cancer Biology and Immunology Contract Review Committee, National Cancer Institute (1987-1991); Outstanding Investigator Award Review Committee, National Cancer Institute (1989-1991)

[a]In addition to BER-supported personnel (as defined for Table 9), other key managerial and scientific staff are listed.

Program Orientation

The ORNL–OHER budget proposal for FY 1991–1994 is summarized in Table 11. Significant planned activities summarized by subprogram research category follow. Major facility construction and planned BER-related foreign meetings are also described. Appendix A details the major ORNL initiatives in the BER Program in FY 1991.

KP01–Analytical Technology - Dosimetry Research and Measurement Science

OHER support of the physical and technological research activities is directed toward delineating interactions of potentially hazardous agents with biological and environmental systems and toward ensuring that an adequate technical capability exists for characterizing and quantitatively measuring such agents under various circumstances.

In this program, a variety of theoretical and experimental techniques are used to study the following: (1) structures and properties of materials of biological or environmental importance, (2) physical and chemical mechanisms that govern transport and chemical transformations of pollutants in the atmosphere-hydrosphere-biosphere, and (3) the details of direct interactions of harmful agents with biological materials. The efforts encompass interactions at the atomic, molecular, and macroscopic levels on solid surfaces; in solids, liquids, and gases; and at solid-liquid interfaces.

In the technological research areas, strong emphasis is given to development of techniques that provide advanced instrumentation for characterizing and sensitively detecting a wide variety of chemical species. Included in this effort are unique applications of laser optical techniques, UV and soft X-ray spectroscopic techniques, electron beam microlithography, electron microscopy, scanning tunneling microscopy, mass spectrometry, and picosecond laser techniques.

ORNL's new program for experimental studies of picosecond and subpicosecond processes in liquids, gases, and molecular clusters concentrates mainly on studies of the kinetics of radiation-induced reactive radicals and ions under controlled ambient conditions. The experimental data have direct bearing on problems of early-time chemistry in radiological insult to solid and liquid biological materials and to numerous highly reactive chemical species of atmospheric interest. Increased emphasis in atomic and molecular studies will be on interaction of electrons with electronically excited molecules, an important area of which little is currently understood.

Detailed Monte Carlo calculations are also performed to simulate the fast physical and chemical processes that occur in materials of biological interest following irradiation. These calculations are then compared with experimental measurements to identify the fundamental mechanisms of damage to biological molecules due to different types of radiation, including that from radon and its progeny. We are also studying basic physical and chemical properties of radon and its progeny as they relate to particulate formation and transport in the atmosphere.

A growing emphasis will be placed on combined physical, chemical, and biological research directed at fundamental chemical dosimetry and

Table 11. Oak Ridge National Laboratory–Office of Health and Environmental Research budget proposal for FY 1991-1994 (thousands of dollars)

Budget	FY1991	FY 1992[b]	FY 1993[b]	FY1994[b]
Total ORNL-OHER in-house budget	23,480	23,600	24,900	26,100
Total subcontracts	2,767 (10.5)[a]	2,700 (10.3)[a]	2,600 (9.5)[a]	2,700 (9.4)[a]
Total ORNL–OHER budget	26,247	26,300	27,500	28,800

[a]Percent of total ORNL–OHER budget.
[b]Budget estimates are incomplete at this time.

dose concepts that are relevant to human health protection. One focus will be on events occurring at the ultimate target molecule or cell. Current work has involved studies of the binding of electrophiles (such as toxic metal ions) to basic sites of target ribonucleic acid (RNA) and DNA molecules. Research will be expanded to include organic adducts, distorted conformation, and changes in gene expression. The active ongoing collaboration between HASRD and the Biology Division will continue and will emphasize newly initiated experimental studies that will contribute to OHER's human genome initiative. One aspect of that effort uses scanning tunneling microscopes capable of single-atom resolution. Emphasis will be placed on studies of the structures of biological systems, particularly DNA. Another combines lasers and mass spectrometry in an effort to develop a new technique for genome sequencing.

Research will also include methodologies and devices that can be used for problems relating to radiological, hazardous chemical, and mixed wastes; fugitive emissions; exposure monitoring (including skin biological monitoring); and chemical dosimetry. Existing portable instruments and cost-effective monitoring techniques will become more focused on analyzing workplace samples in ways that reflect the degree of potential hazard to the worker. Clinical-biological as well as exposure-monitoring techniques will be included. These activities will require concomitant studies of the nature of fugitive emissions vis-a-vis process stream materials and field characterization of hazardous chemical wastes. Parallel research will be conducted to develop dosimetry concepts at both the applied and fundamental levels. Several of these projects will be carried out jointly with the Analytical Chemistry, Biology, and Environmental Sciences divisions.

A continuing research activity is the development of new instruments and measurement techniques to support evaluation of the potential health and environmental impacts of energy technologies and other DOE operations. Results of this research have led to cost-effective luminescence techniques for rapid screening of samples containing polynuclear aromatic compounds as well as portable instrumentation for on-site use at operating facilities. The OHER-funded developmental research has resulted in support from other agencies and organizations for applied studies. Transfer of this technology to the commercial sector is an important objective.

The RADCAL is the primary research tool of the Dosimetry Applications Research Group. Beta, gamma, X-ray, and neutron sources are available for use to support research, calibration, compliance testing, and training activities. The source-by-source process of NIST certification of RADCAL as a Secondary Standards Calibration Laboratory began in late FY 1991. Such

certification will relieve the radiation calibration backlog at NIST and generate additional research and calibration service work from a variety of organizations outside ORNL.

KP02–Environmental Research

In ORNL's OHER environmental research program, stable funding is anticipated during the next several years. Basic ecological research in terrestrial and aquatic systems in the Southeastern and Appalachian regions is being maintained. Research on ecosystem processes will continue to be concentrated on WBW. Studies designed to increase the understanding of the mechanisms whereby the environment modifies contaminants, and how such materials move through and affect the receiving ecosystems, are receiving emphasis.

We expect continued and increasing involvement in the subsurface science program, enhancing our investigations of the role of colloids in modifying the transport of materials in the subsurface environment. Investigations related to field scale transport continue at the Georgetown, South Carolina, site. Additional effort will be directed at understanding heterogeneity (hydrologic, geologic, and microbial) in the subsurface and in focusing on the origin of microorganisms in the deep subsurface.

Focusing on quantification of landscape patterns and on investigation of relationships between pattern statistics and environmental processes, research on landscape systems analysis continues. Use of remote sensing for regional evaluation of factors such as land use, pollution damage, vegetation cover, vegetation productivity, geology, and hydrology and for testing and developing hypotheses concerning landscape dynamics and structure, is increasing. Studies of organism responses to habitat pattern on the ORR have been initiated. The understanding developed in such studies continues to be valuable input for assessing the potential ecological effects associated with the future development proposed for this region. ORNL is prepared to participate in the initiatives directed at detecting change in ecological systems.

Research capabilities related to nuclear technologies were redirected. Emphasis will continue to center on chronic releases and the long-term behavior of the radionuclides in typical Eastern environments. Radiotracers ^{35}S and ^{7}Be are being used to investigate the biogeochemical cycling and ecological phenomena that govern element transport in forest ecosystems. Expertise is being developed in geosciences to conduct research more effectively and to analyze waste management issues.

Continued development in environmental chemistry and efficient utilization of simulation modeling will provide more accurate predictions concerning transport, fate, and ecological effects of organic contaminants. This research provides technology transfer to the site-specific cleanup activities and waste management upgrades at the Oak Ridge, Portsmouth, and Paducah facilities. The extension of this research toward new applications in environmental risk analysis is being pursued.

Research in earth sciences related to energy residues will emphasize geology, hydrology, and environmental chemistry. These areas will continue to emphasize research on contaminant transport in the geosphere. The emphasis will include research on mechanisms of sorption/desorption and matrix diffusion processes with host media. This will be combined with continued development of analytical capabilities to predict the mobility of contaminants in these systems. Analysis of regional landscapes is emphasizing the development of new mathematical approaches for quantifying spatial patterns in terms of physical and biological attributes. Spills to aquatic systems are being studied under emergency response needs.

The WBW Project has successfully completed the first phase of its ten-year research plan and is in the process of initiating the first large-scale ecosystem experiment in the history of the project. During the past year, several major site characterization tasks have been published or completed and preparations have been made to initiate a major large-scale climate change experiment on a portion of WBW. The Walker Branch Climate Change Experiment is designed to simulate the changes in rainfall amount that are expected to accompany global climatic warming. The effects of both increased and decreased precipitation on a forest ecosystem will be investigated for processes ranging from soil structure and nutrient dynamics to canopy photosynthesis. Issues of particular importance

include the adaptation or adjustment of the forest to minimize the effects of climatic stress, as well as the identification of sensitive indicators that the ecosystem is being affected by climate change.

Over the last year, ESD staff have become increasingly involved in basic research support for Environmental Restoration R&D effort. The division coordinated the preparation of the basic R&D plan supporting environmental restoration for OER/OHER (DOE 1990). This was a major undertaking that involved representation from all national laboratories and many universities. The plan will provide the technical foundation for research that will be essential for properly addressing restoration issues at DOE sites.

HASRD's indoor air quality research is focusing on radon entry and development of effective mitigation measures. Our broad-based assessment of this complex exposure problem has been supplemented by new studies focused on reduction of dosimetric and risk uncertainties. Such studies may lead to better exposure guidance.

KP03, KP04–Health Effects and General Life Sciences

During the past several years, a major consolidation of effort has taken place to strengthen and to focus our research on experimental genetics. The effort, which started prior to FY 1987 to integrate significant molecular genetics initiatives into the mammalian genetics program, will continue in FY 1992. Well established in 1989, work with modern molecular tools such as insertional mutagenesis will continue during FY 1992 and beyond. A targeted-mutagenesis program was added in FY 1991, as was expertise for long-range physical mapping of mouse chromosomes. Concurrently, with the shift of emphasis within mammalian genetics, protein engineering has unified heretofore diverse activities in enzymology, molecular biology, and structural biology. Succinct descriptions of research in genetics, protein engineering, and cancer biology follow.

A number of approaches are being taken to explore the structural and functional characteristics of the mammalian genome by use of experimental molecular genetics. Experimental plans include (1) development of complete molecular maps and refined functional maps of several specific regions of the mouse genome using sets of overlapping deletions, (2) definition of mouse-human genomic homologies with the objective of using mouse mutants as models for human genetic diseases, (3) analysis of the molecular structure and effects of heritable agent-induced mutations, (4) creation of molecularly tagged mutations throughout the murine genome by insertional mutagenesis techniques, and (5) utilization of mutagenesis protocols that generate deletion mutations to expand the genomic regions accessible to molecular-structure analyses.

A noteworthy feature of this initiative is the integration of genetic functional analyses with molecular mapping. Indeed, molecular chromosomal mapping of mouse genes will not stand alone as a sterile catalog; all structural information will be correlated with functional information including the early developmental events that lead to mutation-associated abnormal phenotypes. Because the mouse and human genomes contain numerous extended regions of homology, some of our studies should make it possible to assign functions to human DNA sequences that might otherwise be characterized only at the DNA-sequence level. To complement our current approaches of exploiting mutations for genomic analyses, we have recently added staff members with expertise in embryonic stem cells and homologous recombination. These techniques are used to generate mutations in genes for which cloned probes are available, but in which there have been no agent-induced or spontaneous mutations to date.

Recognizing that the mouse can provide a valuable experimental model system for the study of human genetic disease, part of the mammalian genetics effort is devoted to detailed phenotypic studies of spontaneous, agent-induced and insertional mutations and chromosome rearrangements. Examples are polycystic kidney disease, frontonasal dysplasia, globin gene mutations that provide models for human thalassemia, and a defect in the thymic microenvironment that provides a very useful model for immune-system-mediated diseases in humans.

Mutagenesis studies contribute to genome characterizations by generating highly useful

genetic tools. The wisdom of having preserved mutant stocks generated in past experiments has now been amply demonstrated. Further, mutagenesis experiments are leading to the discovery of agents and protocols for high-efficiency induction of specific desired mutational types. Thus, chlorambucil and melphalan mutagenesis, which produce high frequencies of deletions, will provide necessary tools for making regions throughout the genome accessible to DNA-structure/function analyses.

A number of ongoing studies are designed to provide information on the mechanisms of induction of point mutations and chromosome alterations of various types. Also under investigation are the actions of certain chemicals on zygotes that result in high frequencies of congenital anomalies; the possibility that these result from disturbances in gene expression will be investigated.

Because of the importance of studying not only mechanisms and frequencies of mutation induction but also the organismic impacts of induced mutations, combined indicators of dominant genetic damage are being used in experiments that will eliminate most of the uncertainties presently associated with the direct method of estimating human genetic risk. The phenotypic effects of translocations (both in the balanced and unbalanced state) are also being determined. Several of these provide models for some common human developmental anomalies.

Protein engineering, a new initiative in 1985, has made significant strides. Protein engineering uses recombinant DNA technology to change protein structure systematically. This provides a powerful tool for elucidating enzyme mechanisms and potentially for altering the properties of enzymes in predictable and desirable fashions. The two major objectives were to establish this newly emerging expertise within the Biology Division, and subsequently, to apply this expertise to questions concerning the mechanism of action of proteins relevant to DOE missions.

Initiated with partial support from the ORNL LDRD Fund, this program represents a collaborative effort that involves eight senior staff members of the Molecular, Cellular, and Cancer Biology Section (Biology Division) and integrates activities in enzymology, molecular and cellular biology, and structural biology. Research is focusing on the structure/function correlations of three proteins: ribulose bisphosphate carboxylase (a determinant of biomass yield), DNA-O^6-methylguanine methyltransferase (a DNA repair enzyme), and human epidermal growth factor, EGF, (a polypeptide that regulates cell growth and differentiation).

Ubiquitous among photosynthetic organisms, Rubisco is essential for net conversion of atmospheric CO_2 into carbohydrates. Thus, this enzyme is a major cornerstone of living processes and serves a critical role in the production of biomass for energy and in the global CO_2 issue (i.e., the greenhouse phenomenon). The enzyme is bifunctional: in addition to catalyzing the carboxylation of D-ribulose-1,5-bisphosphate to yield two molar equivalents of D-3-phosphoglycerate (i.e., the CO_2-fixation reaction), it also catalyzes the oxidation of ribulose bisphosphate by molecular oxygen to yield one molar equivalent each of phosphoglycolate and 3-phosphoglycerate. Although multiple substrate specificities among enzymes are not unusual, the bifunctionality of Rubisco is perhaps unprecedented in that the two reactions catalyzed are the initial steps in competing metabolic pathways—photosynthetic assimilation of CO_2 and photorespiration (the latter being an energy-wasteful process that results in the release of previously fixed CO_2).

Primary goals are (1) to understand the mechanism of this complex enzyme, especially the precise catalytic roles of active-site residues, and (2) to evaluate the feasibility of improving the carboxylase:oxygenase activity ratio and thereby provide an approach to enhancing biomass yields. A large number of Rubisco mutants have been constructed in which specific amino acids within the catalytic site have been replaced by other amino acids. Examination of the ability of mutant proteins (devoid of carboxylase activity) to catalyze discrete partial reactions in the overall process will provide a powerful avenue for defining the function of active-site residues. Chemical rescue, in which an exogenously added small organic compound mimics the missing amino acid side chain of the catalytically deficient mutant, provides a new approach for establishing structure-function relationships. As a potential approach to altering

the carboxylase:oxygenase activity ratio, chemical modifications, in concert with mutagenesis, will be undertaken to replace active-site lysines with aminoethylcysteine and active-site glutamic acids with carboxymethylcysteine; thus subtle changes may be introduced into the active-site microenvironment.

DNA-O^6-methylguanine methyltransferase is a protein that repairs mutagenic lesions in DNA caused by a variety of environmental chemicals. Specific structural alterations have been introduced into this enzyme by site-directed mutagenesis to explain the process of alkyl-group transfer between the DNA and protein. Insights have been gleaned into the regulation of gene expression for this repair enzyme, initially in bacteria and now more recently in human cells. The gene has been cloned, and sufficient enzyme has been isolated for physical and structural analysis. Similar studies are under way with another DNA repair protein, N-methyl- purine-DNA glycosate.

A shuttle plasmid system based on SV40 has been utilized to study the mechanism of induction of mutations by radiations and chemical agents. In addition, because mutations are identified by DNA sequencing, it has been possible to study the spectrum of spontaneous and induced mutations and to show that mutational "hot spots" are present. It has also been shown with a tRNA gene irradiated *in vitro*, that after *in vivo* processing, chemically different mutations are fixed in bacteria compared to human cells.

The involvement of extracellular protein factors in the regulation of DNA replication, specific RNA synthesis, and cell division, has long been recognized. Several factors have been isolated with the ability to stimulate the growth of cells and the expression of specific genes believed to be involved in the entrance of mammalian cells into, and progression through, the cell cycle. One of the most highly studied among these is EGF, a 6-kDa single polypeptide chain with three internal disulfide bonds, which is known to initiate its action through high-affinity binding to the specific cell-surface EGF receptor. In response to EGF, the receptor undergoes autophosphorylation on tyrosine residues by its intrinsic protein kinase activity besides phosphorylation of exogenous substrates.

Despite the variety of functions elicited in response to EGF, little is known about the biochemical mechanisms by which EGF activates the receptor's tyrosine kinase activity, stimulates the internalization of the EGF-receptor complex, and eventually stimulates DNA replication and specific RNA synthesis and cell division. The major objective of the research is to identify the amino acid residues in EGF that are necessary for (1) its binding to the EGF receptor, (2) stimulation of the EGF receptor protein kinase activity, and (3) stimulation of the growth of quiescent cells.

The gene for human EGF has been cloned into *Escherichia coli* to generate the product as a bacterial secretory protein. The recombinant protein was purified to homogeneity and found to be identical in structure and function to authentic human EGF. Structure-function analysis by site-directed mutagenesis was initiated at several sites of EGF based on its solution structure, the amino acid residues conserved through evolution, and studies with fragments of EGF. The results have shown that tyrosine-37, arginine-41, and leucine-47 are in regions of the molecule that are critical for its binding to the EGF receptor. Several variants have been derived that bind to the receptor but are deficient in stimulating kinase activity. These variants have potential antitumor properties. Studies with double mutants suggest that there are multiple, independent binding sites between EGF and its receptor. NMR studies have been initiated to explore the structures of the variants. In addition, a program has been established to examine both short- and long-term cellular responses to the mutants.

Ongoing work on radon and heavy ion carcinogenesis in whole animals and in the *in vivo–in vitro* model systems will continue. The studies include (1) alpha-particle activation of oncogenes, (2) gene rearrangement involving mobile gene elements, (3) malignant transformation of tracheal cells, (4) determination of the relative biological effectiveness for alpha-particle and neutron-induced cancers, and (5) mutagenic mechanisms in radon exposure.

Work will continue on (1) the tumor surface protein (TSP-180) identified as a member of the family of integrins and found on the surface of both human and murine tumor cells (monoclonal antibodies that are specific for the endothelial cells of the pulmonary vasculature have been

developed, and their potential in imaging and targeting of agents will be exploited), and (2) the determination of the effects of environmental agents on the stability of the genome and the role of transposable genes in carcinogenesis.

KP05–Carbon Dioxide Research

During the next five years, the Carbon Cycle Research Group will continue research in developing operational global carbon cycles that encompass our understanding of complex issues of bidirectional carbon dynamics. The CDIAC will emphasize development of global data bases needed for climate change analyses. The principal purpose of this latter program is to provide assistance to ESD in R&D activities.

In carrying out this task, the Carbon Cycle program is responsible for fulfilling DOE research needs in understanding global energy systems through focused in-house research projects, identifying research needs to support global carbon cycle model development, and recommending methods for fulfilling these needs. The monitoring involves preparing and updating multiyear research plans for DOE. The ORNL staff prepares technical and topical reports to update research progress, to provide responses to specific questions, and to resolve technical issues. The CDIAC continues to broaden its efforts in supporting international CO_2 research.

ORNL Center for Global Environmental Studies

Many of the decisions that will determine our direction in the next millennium hinge on issues that are complex, interwoven, and global in scale: greenhouse gases, climate change, ozone breakdown, deforestation and desertification, resource depletion, and the spread of pollution. These and other global environmental issues must be explored far more seriously, far more comprehensively, than ever before.

ORNL's Center for Global Environmental Studies, established in 1989, provides a unique, inter-disciplinary base for such explorations. The Center has three main goals:

1. Improving the understanding of the global-scale workings of environments in air, on land, and in water.
2. Developing capabilities to anticipate the long-term, large-scale effects that human actions have on the biosphere.
3. Identifying appropriate options for technological and societal responses.

Guiding Principles

Like the U.S. Global Research Program, the crosscutting national initiative to which the ORNL Center corresponds, the Center for Global Environmental Studies takes a new view of the kinds of research needed in this formidable but exciting field. The Center's work is based on several assumptions that set it apart from the Laboratory's traditional approach to research and analyses:

- *The scope of the processes and problems we are exploring is far greater, both in scale and in time, than traditional research projects are equipped to deal with.* Problems such as ozone depletion, the greenhouse effect, and global change are no respecters of national borders; they affect the entire planetary commons. Our understandings and responses, therefore, must be equally broad. Similarly, processes such as climate change and dwindling biodiversity may become clearly evident only when viewed over decades or even centuries. We must, therefore, envision and develop programs that can serve as foundations on which to build for many years.
- *Collaboration, both among traditionally competitive institutions and across disciplinary boundary lines, is absolutely essential for any meaningful understandings to emerge.* The globe's environment responds to the interactions of many different systems, factors, and processes: air circulation, ocean currents, land-use changes, economic incentives for development (or its converse), the migrations of smokestack industries, national energy practices and policies, even political turmoil. Narrow, discipline-bound approaches can give us only detailed analyses of individual aspects of the biosphere, individual trees, so to

speak, when what we need now is an overarching view of the global environmental forest.

- *Policy, economically and politically practical policy, must be one of the prime drivers of global environmental research.* We must consider (1) what is happening in and to the biosphere, (2) what should be done about it, and (3) what can be done, given the economic, technological, and political constraints within which actions must be taken.

These, then, are the principles that guide the Center's organization and work: (1) a large-scale, long-term view; (2) a commitment to collaboration, both among institutions and among disciplines; and (3) a continual eye to realistic policy.

Areas of focus

In keeping with the Center's large-scale view, the central and unifying framework for our work is global systems analysis. This involves developing increasingly sophisticated models that reflect the dynamic interactions of numerous subsystems called global vegetation; human cultures and behaviors; and earth systems such as atmospheric chemistry, ocean composition and circulation, and the links between air, land, and sea. Our long-term goal is to develop models that reflect the interplay of demographics, land-use patterns, economics, ecological relationships, and other factors that influence the globe's environment. Complementing our central focus on global systems are four areas of more specific concentration: (1) measurement science and instrumentation; (2) data systems; (3) large-scale environmental studies; and (4) policy, energy, and human systems analysis. The first three of these are funded by OHER and are described in more detail below:

1. *Measurement science and instrumentation:* better monitoring of the state of the environment and its changes. ORNL has a long history of excellence in instrumentation in high-energy physics, health physics, pollution monitoring, nuclear reactor technology, and nuclear and chemical waste. We are now directing this expertise toward instrumentation for atmospheric, terrestrial, and aquatic research. Areas of strength that can immediately benefit the Center include laser-based instrumentation, which we expect will play an increasingly vital role in global-change research; mass-spectrometry and isotopic analysis; remote sensing and fiber optics, another key technology for climate studies; and automation, miniaturization, and portability. Logical applications of this expertise include laser-based devices to measure trace gases, temperature, and pressure; low-cost, air-droppable packages for reading atmospheric or oceanic conditions; and instruments for studying cloud formation and properties in support of the U.S. ARM Program.

2. *Data systems:* the key to making sense of the global environment, now and for decades to come. The amount of data collected in the course of global environmental research is already staggering, and will grow explosively as newer, more sophisticated instruments and monitoring projects emerge. For example, in a few years, NASA's Earth Observing System will begin transmitting enough data to fill all the books in the Library of Congress, every three weeks. In addition to handling massive quantities of data, information systems must present the data in a user-friendly form–one that will ensure the usability of information over decades, since the import of some data may not become clear for many years.

3. *Large-scale environmental studies:* projects that examine the environment from a longer perspective than the traditional ecological research. Global-scale studies cannot be based on mere extrapolations of traditional detailed studies; many of the subtle ecological processes on which traditional research thrives are less meaningful, for these purposes, than aggregate processes that are invisible at close range. The ORNL Center is developing much needed tools and techniques for understanding how to scale up research to the global scale.

Summary

The range and depth of ORNL's scientific expertise uniquely qualify the Laboratory to

take up the challenges of the Global Change Program. By establishing the Center for Global Environmental Studies, ORNL is drawing on its proven expertise and worldwide scientific connection while also laying the foundation for expanded, focused research into the problems of global change.

The Center for Global Environmental Studies is dedicated to an Earth system-centered, interdisciplinary approach to scientific research. It views human interaction with the environment, through population distribution, land use, technology, energy conversion, and other processes, as one of the driving forces of global environmental change. The Center stands in a unique position to serve the needs of federal agencies and international efforts, and to make a significant contribution to our understanding of the delicately balanced biosphere we call home.

KP06–Nuclear Medicine

A long-term activity has been the development and evaluation of new radiopharmaceuticals for diagnostic and therapeutic applications in nuclear medicine. Major emphasis is on the development of agents for the evaluation of heart disease, cerebral blood flow, and regional evaluation of tissue metabolism. Tissue-specific agents such as our recently labeled fatty acids, have proven to be valuable additions to the field. Clinical evaluations are currently under way using distributions of radiolabeled agents through our Medical Cooperative Program. New emphasis will be placed on protein-labeling activities, development of a ^{188}Re radionuclide generator, and collaborative studies with UT to develop new radiolabeled tissue-specific agents using positron emission tomography technology.

Major Facilities

Planning is underway for the construction of several major facilities at ORNL that are intended to alleviate space and equipment constraints on current and planned research programs. The overall framework for these facilities is the Environmental, Life, and Social Sciences Complex proposed for the west end of ORNL (Fig. 9). In this complex, relevant facilities for the BER Program are three line items: the Center for Biological Sciences, the Earth Systems Facility, and the Advanced Environmental Photonics Laboratory. These are supplemented by four General Plant Projects (GPP) (Life Sciences Data Analysis Facility, Health Effects Information Facility, Environmental Engineering Facility, and Environmental Data and Modeling Facility). These are discussed below. The West End Site Plan, which includes the proposed Environmental, Life, and Social Sciences Complex, was approved by the ORNL Site Development and Design Review Committee in FY 1991.

Center For Biological Sciences

All of the Biology Division's existing facilities are badly aged, inefficient, and increasingly difficult to maintain. As a continuing (and worsening) drain on resources, they pose an urgent threat to ORNL's ability to sustain its high-caliber biological research. The CBS will allow us to take critical steps both toward protecting our research investment, and toward meeting Admiral Watkins' environmental-compliance goals, in a cost-effective way. The new Center will bring our user-oriented research out from "behind the fence" and into the open academic community, where collaboration and interactions with researchers from throughout the world can flourish. The CBS will bring together the following user facilities for collaborative research:

- *Transgenic Mouse Facility.* A world-class center for producing and breeding new mutant mouse strains, giving researchers throughout the world powerful tools for deciphering the structure and function of the human genome.

- *Macromolecular Mapping and Engineering Facility.* A facility, which coupled with the planned Advanced Neutron Source, will allow probing the three-dimensional structure of native and site-directed proteins and reveal a new level of molecular detail inaccessible to X-ray techniques and beyond the reach of today's neutron-scattering equipment.

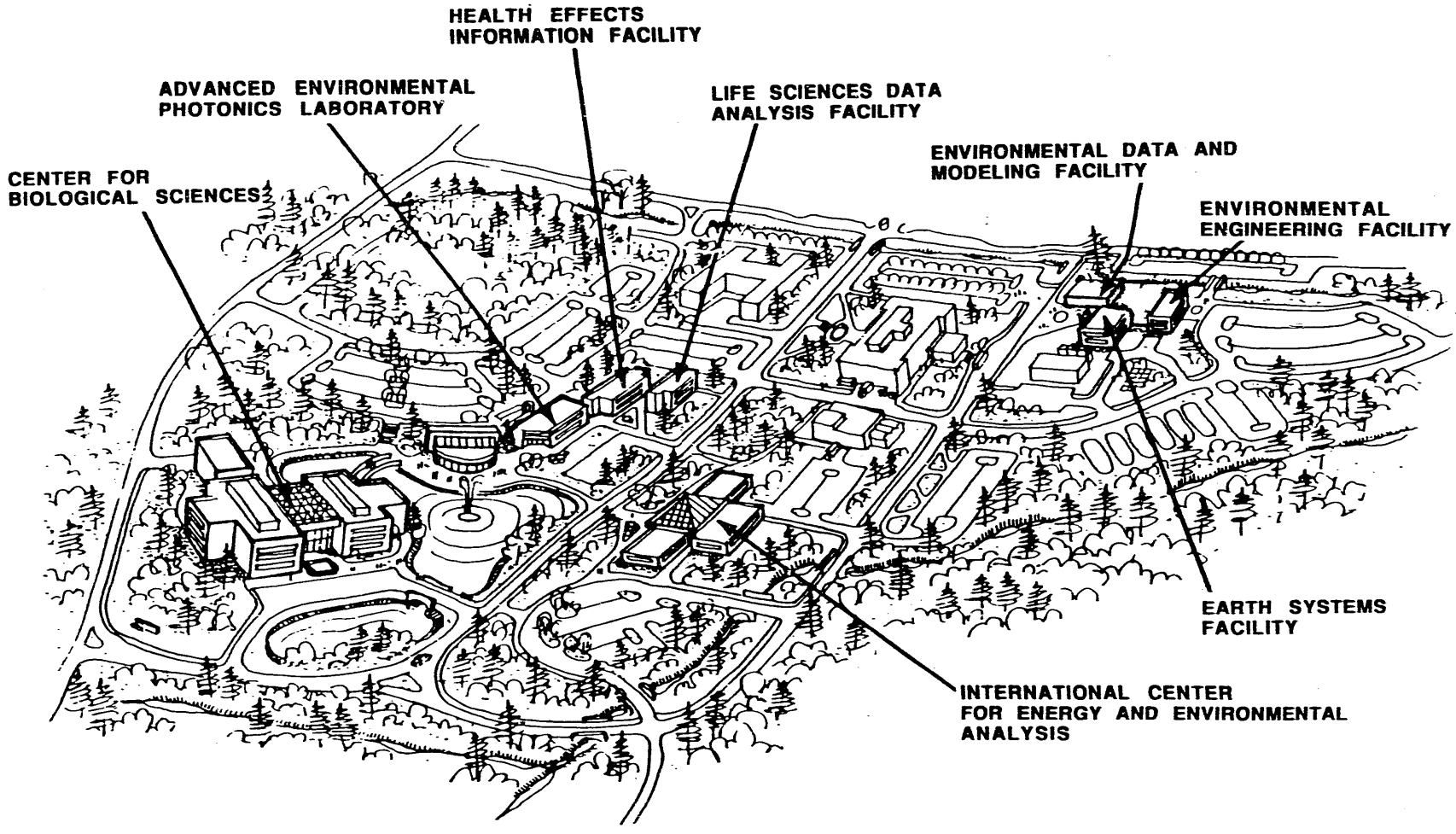

Fig. 9. Conceptual plan for the Environmental, Life and Social Sciences Complex proposed for the West end of Oak Ridge National Laboratory.

- *Bioprocessing Research Facility*. A facility that will bring the Laboratory's biological researchers and analytical equipment into closer contact with the bioprocessing facility already housed at the main site.

- *Mouse Breeding Center for Human-Disease Models*. A facility to house a center for breeding other mutant mouse strains including mutations by radiation and chemicals, to provide animal models for exploring serious human diseases.

- *Expanded Graduate School of Biomedical Sciences*. A new center to improve the accessibility of the Laboratory's research facilities and allow expanded educational opportunities in our collaborative program with the UT.

The CBS will be a two-story steel frame and masonry structure about 250,000 ft.^{2} in size, and is estimated to cost about $90 million. The Conceptual Design Report for the CBS was completed during FY 1991, approved by the DOE Oak Ridge Field Office, and forwarded to DOE Headquarters. The next steps in ORNL's planning for the CBS include preparing major systems acquisition documentation, completing National Environmental Policy Act documentation, conducting a safety analysis and review, preparing a quality assurance plan, and conducting general project planning activities. A field work proposal has been submitted to conduct these and other pre-Title I planning activities in FY 1992 and FY 1993. ORNL needs OHER's active support for the CBS in the FY 1994 planning cycle.

Advanced Environmental Photonics Laboratory

The AEPL is a proposed $8 million facility that will serve as a focal point for integrating currently diverse activities involving photonic devices such as lasers, fiber optics, spectrometers, and detectors. Such devices are increasingly used in characterizing and monitoring during energy production, in defense operations, and in DOE's accelerated program for environmental restoration and waste management and biological research. The laboratory rooms will house lasers, optical benches, instrumental assembly and testing facilities, and facilities for simulating environmental test situations together with attendant environmental chambers and the necessities for validation and intercomparison testing.

Earth Systems Facility

The Earth Systems facility is a proposed $18 million facility designed to consolidate the interdisciplinary talents of ORNL researchers in the environmental and earth sciences. The facility will be structured, physically and organizationally, to promote accessibility, collaborative research, and user interactions. It will be a 50,000 ft.^{2} laboratory facility containing specialized computer capabilities, wet labs, staging areas, and related support space specifically designed to support our global change research program activities. Particular emphasis will be placed on creating work space that supports the interdisciplinary nature of the research including biogeochemical cycling research and modeling, solid earth processes, climatology and hydrology, and assessment capabilities (e.g., stable element laboratories, geographic information system work areas, and data-archiving systems for ARM Program).

General Plant Projects

The four General Plant Projects (GPP) that are proposed for the west end of ORNL and that are of most relevance to BER research are the following: the Life Sciences Data Analysis Facility (approved in FY 1990 and awaiting construction); the Health Effects Information Building, which is on the FY 1992 approved ORNL list that in turn has been approved by the DOE Oak Ridge Field Office and forwarded to DOE HQ for approval; the Environmental Engineering Facility, which is also on the FY 1992 list but is of low priority and is not likely to get funded until FY 1993; and the Environmental Data and Modeling Facility, which is also on the FY 1993 list. Each of these have total estimated costs of $1.1 million. These facilities will support general data analysis and information processing activities in the environmental, life and social sciences, and thus will benefit many programmatic sponsors, including OHER.

Major Foreign Meetings

To maintain and enhance international collaborations and share research results, ORNL researchers will seek OHER approval to attend major society meetings and symposia held in foreign countries. Table 12 includes a list of major foreign meetings scheduled for FY 1992 and FY 1993. Several requests for approval to participate in these meetings are anticipated.

Table 12. Major foreign meetings during FY 1992 and FY 1993

Meeting	Location	Date
International Poplar Council Meeting	Zaragoza, Spain	September-October 1991
International Conference on Virology and Radioimmunodiagnosis in the Tropics	Lucknow, India	December 1991
XXII Annual Conference of Society of Nuclear Medicine, India and International Seminar, Indoamerican Society of Nuclear Medicine	Agra, India	December 1991
Conference on Laser Photoelectron Spectroscopy	Osaka, Japan	March 1992
Biospheric Model Validation Study (BIOMOVS)	Vienna, Austria	March 1992
Validation of Assessment Model Predictions (VAMP)	Vienna, Austria	March 1992
U.S.-Poland Research Exchange	Poland	March-April 1992
International Energy Agency Biofuels Agreement: Effects of Intensive Harvesting	Edinburg, Scotland	April 1992
IXth International Symposium on Radiopharmaceutical Chemistry	Paris, France	April 1992
Second Mediterranean Symposium on Nuclear Medicine and Radiopharmaceuticals	Athens, Greece	April 1992
International Association of Hydrogeologists: International Commission on the Hydrogeology of Hazardous Wastes	Oak Ridge, Tennessee	April 1992
XII ALASMIMN Nuclear Medicine Congress	Madrid, Spain	May 1992
International Energy Agency (IEA) Task AG (Effects of Intensive Harvesting on Site Productivity) Workshop-"Impacts of Harvesting and Site Preparation on Carbon Cycling Processes in Forests"	Edinburg, Scotland	May 1992
International Conference on Quantum Electronics	Vienna, Austria	June 1992
International Conference on Monitoring Toxic Chemicals and Biomarkers	Berlin, Germany	June 1992
United Nations Conference on Environment and Development	Rio de Janerio, Brazil	June 1992
Ecological Economics	Stockholm, Sweden	July 1992
European Association of Nuclear Medicine (EANM) Congress	Lisbon, Portugal	August 1992
International Geological Congress	Kyoto, Japan	August 1992

Table 12. (continued)

Meeting	Location	Date
Ninth European Conference on Dynamics of Molecular Collisions	Prague, Czechoslovakia	September 1992
European Association of Nuclear Medicine Congress	Vienna, Austria	September 1992
International Popular Council Meeting	Zaragoza, Spain	September 1992
IUFRO Centennial Conference: Atmospheric Effects of Energy Crops	Eberswalde, Berlin, Germany	September 1992
Workshop on Effects of Radiation on Aquatic Biota	Obinnisk (formerly U.S.S.R.) and Kyshtym, Ukraine	September 1992
Dahlem Conference, Acid Deposition Effects on Ecosystems	Berlin, Germany	September 1992
Royal Society: Colloid Symposium	London, England	September 1992
Organic Matter Symposium	Lancaster, England	September 1992
International Humic Substance Society	Italy	September 1992
13th Annual CODATA Meeting	Beijing, China	October 1992
United Nations Environmental Program's Scientific Advisory Committee	Nairobi	January 1993

Work for Non-BER Organizations

This section discusses the role that non-BER support has on the facilities, personnel, and program objectives of ORNL's BER Program. Non-BER support includes work funded by other DOE offices, other federal agencies, and non-federal organizations. BER program activities benefit from the non-BER funding in several ways, including (1) enhancement of personnel skills and expertise needed in current and future BER programs; (2) application of non-BER technological advances to BER activities; and (3) improved cost effectiveness through sharing of plant overhead and fixed costs. In addition, applying the Laboratory's BER resources toward work funded by other DOE offices, and by non-DOE organizations, helps DOE in a larger capacity by enhancing the solution of problems of national importance, the capabilities needed for current and future DOE programs, and the transfer of technology to the private sector in order to strengthen the U.S. position in world markets.

Figure 10 presents the distribution of FY 1991 funds (operating BA) for the three ORNL divisions comprising the bulk of the BER funding at ORNL. As can be seen, non-BER support for these three divisions in FY 1991 was about 56% of their combined FY 1991 operating BA. Sources of support include DOE organizations such as the Assistant Secretary for Environment, Safety, and Health, and non-DOE organizations such as the Department of Health and Human Services, as shown. Following is a description of this work, organized by funding source.

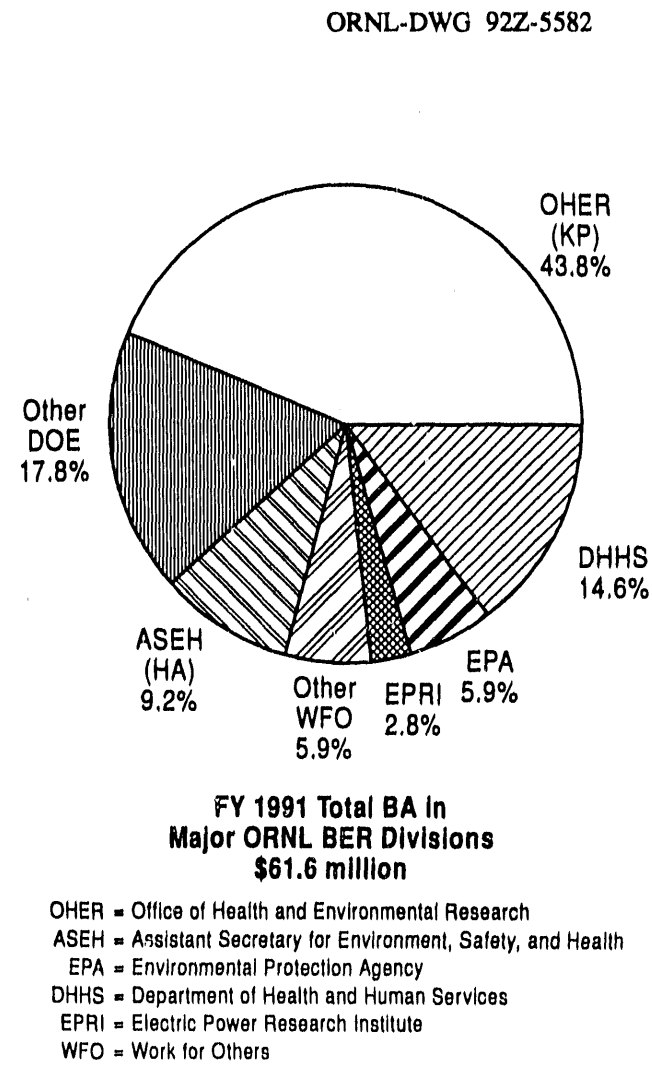

Fig. 10. Distribution of FY 1991 funds (operating BA) for the three ORNL divisions comprising the bulk of the BER funding at ORNL.

Other DOE Organizations

Assistant Secretary for Environment, Safety, and Health (ASEH)

ESD is continuing to provide technical support to ASEH's Offices of Nuclear Safety (ONS), Environmental Guidance (OEG), Environmental Compliance (OEC), NEPA Oversight, and Environmental Audit. ORNL support to the ASEH is an important complement to OHER research. All research is receiving increased regulation oversight and our involvement in this process keeps staff aware of important regulatory developments.

In support of ONS, division staff provide analyses and evaluations of proposed radiation protection orders.

In support of OEG, division staff lead a multidisciplinary team that tracks proposed regulations and prepares analyses of regulatory initiatives related to hazardous waste management and other EPA programs. These analyses evaluate the technical approaches used in proposed rules and the implications of new requirements for DOE facilities and operations. They are also used by OEG in formulating DOE responses to EPA and other regulatory agencies on proposed requirements that might affect the department's activities. ORNL also supports OEG by providing training in environmental laws and regulations to DOE managers. Two-day and four-day training courses are presented at DOE facilities across the United States. During FYs 1991-1992, ESD also provided a staff person on off-site assignment to the Office of the Secretary to provide technical support on environmental regulations. Support also includes preparation of reference books on environmental laws and special studies as required.

In support of the OEG's Air, Water, and Radiation Division, HASRD is preparing an environmental radiological survey procedures manual. This document provides detailed procedures for detecting, characterizing, and evaluating radiological pollutants. Specifications for instrument selection and operation, sample procurement and analysis, quality assurance, and documentation are also included. This manual will serve as the basis for environmental pollutant surveys at DOE, contractor, and subcontractor facilities. Also, HASRD and ESD staff collaborate on the preparation of the Environmental Regulation Update Table, which is a monthly review of the status of pending and proposed environmental legislation.

The Center for Risk Management is participating in OEG's Risk-Based Standards Working Group, which is developing guidelines to ensure that human health and ecological risk assessments are performed in a consistent and scientifically defensible manner at all DOE facilities.

In support of the NEPA Oversight Office, ESD staff developed a protocol for evaluating the status of NEPA compliance at DOE facilities. Throughout FY 1991, staff visited eight additional DOE facilities as part of the Secretary of Energy's Tiger Teams. Support to the Tiger Team assessments will continue in CY 1992.

In support of the DOE EH Safety and Health Working Group, HASRD staff have developed a Risk-Based Priority Model to aid in developing a consistent, DOE-wide Safety and Health (S&H) Five-Year Plan. After undergoing extensive review, the model has been approved by DOE for use in ranking safety and health issues, such as Tiger Team Assessments, at DOE sites. HASRD staff prepared documentation for the model and are currently assisting in the training of field office personnel at DOE sites through February 1992. Once the budget call is received, HASRD staff will also provide assistance in preparing the S&H Five-Year Plan for inclusion in the Congressional budget process.

This year, ESD has continued to participate in a NEPA training program for DOE managers. During FY 1991, training was provided at an additional six DOE locations. Support also includes review and analysis of NEPA documents (e.g., environmental impact statements and environmental assessments among others) prepared for DOE; preparation of background materials for use by DOE staff in developing guidance on NEPA issues; and technical assistance at DOE Headquarters. This support also provides technical assistance in evaluating environmental analyses related to DOE's high-level nuclear waste repository program.

ORNL will continue to assist ASEH's Office of Environmental Analysis (OEA) in developing environmental assessment methodologies and environmental, economic, and energy data bases and in analyzing important energy and environ-

mental issues such as air quality, acid deposition, and water resource impacts. During FY 1991, as part of its support to OEA, ESD provided support to the President's Council on Environmental Quality to develop a National Strategy for Long-Term Environmental Trends Reporting. Assistance is also provided in planning and preparedness for environmental protection and public safety; this includes assisting DOE in implementing its supporting responsibilities to other federal, state, and local agencies in radiological emergencies. One problem being studied is the development of procedures, equipment, and techniques for decontamination and emergency operation in contaminated environments.

ORNL's cooperative work with foreign countries through ASEH is exemplified by the technical advice and equipment that ORNL provides to the Junta de Energia Nuclear in Spain for measuring radionuclides in people and in environmental samples such as food products, soil, and air. ORNL's assistance allows for increased counting capacity by alpha spectrometry of samples containing ^{239}Pu and by rapid, accurate, and inexpensive techniques of samples containing ^{241}Am.

ORNL staff are also supporting ASEH through participation in the Biospheric Model Validation Study (BIOMOVS) and Validation of Assessment Model Predictions (VAMP) program. These programs are assessing the validity of models used to predict the movement of radionuclides and toxic chemicals through the environment.

A program for the DOE Office of Environment Safety and Health for technical and management support of its hazardous materials Packaging and Transportation Safety (PATS) program has been designed and maintained by HASRD Staff. This includes the design of an online PATS database.

Office of Environmental Restoration and Waste Management

An ORNL office operates in Grand Junction, Colorado, to assist DOE in the conduct of the Uranium Mill Tailings Remedial Action Program (UMTRAP). The UMTRAP effort primarily consists of radiological surveys on private property near inactive mill tailings sites. Advancing state-of-the-art equipment and methodologies are an integral component of UMTRAP. New work entails verification of the success of remedial action at those sites where cleanup has been undertaken.

The Measurement Applications and Development Group, HASRD, continues to participate in DOE's Formerly Utilized Sites Remedial Action Project (FUSRAP). The Division identifies areas of potential chemical and radiological contamination and performs assessment sufficient to determine the need and extent of remedial actions. Surveys to verify the success of remedial actions required to clean up a contaminated site are also an integral part of the work performed for this agency. To support field activities, a mobile field laboratory was designed, procured, and equipped with state-of-the-art radiation detection and environmental sampling instruments.

Increased activities related to environmental biotechnology and bioremediation have been undertaken, including support for the Savannah River Demonstration of bioremediation and the initiation of the cometabolic demonstration of trichloroethylene (TCE) at the K-25 Site.

ESD conducts a diverse series of activities for this Office at many DOE facilities. On the Oak Ridge Reservation, efforts are directed toward hydrogeologic and geochemical characterization of the groundwater regime, as well as assessing the interactions of groundwater with an active surface water system. This work provides a fundamental data base upon which the evaluation of site-specific remedial action decisions can be reached. Staff are involved with site characterization at ORNL, K-25, and Y-12; for instance, the occurence and nature of dense non-aqueous phase liquids at Y-12 in the deep subsurface is a specific topic of concern. Biological monitoring in the streams that drain from remediated sites at all five DOE facilities operated by Energy Systems is another vital, innovative, and cost-effective activity conducted by ESD staff; such monitoring allows rapid and continuous evaluation of the effectiveness of clean-up that has been conducted.

In addition, there is an extensive environmental restoration supported effort directed at characterizing the nature and extent of contaminants that have been released from the ORR into the river systems (White Oak Creek, Clinch and

Tennessee Rivers) that drain to the south. Current activities include extensive core sampling and sediment geochemical characterization leading to risk assessments that will guide remedial actions.

Innovative *in situ* treatment technologies designed to prevent the release of contaminants from historical disposal operations have also been developed. *In situ* vitrification, a process by which contaminated soil is melted in place to form a leach-resistant mass was successfully demonstrated at ORNL.

ESD staff are also heavily involved in field demonstrations for technology development. For instance, biological reactors are used for assessing the removal of TCE from groundwaters. Other staff lead a soil remediation demonstration at the Portsmouth Plant, while others are involved with integrated demonstrations at Savannah River, Fernald, and elsewhere.

Assistant Secretary for Conservation and Renewable Energy

ESD is responsible to DOE's Biofuels Systems Division for R&D of biofuels feedstocks. Working with woody and herbaceous species, research focuses on plant genetics, whole-plant physiology, innovative cultural methods, biotechnology, and environmental studies to develop productive cost-effective crops. Environmental research and regional and economic analysis are conducted at ORNL. Most other research is performed through subcontracts and interagency agreements by different universities and other federal research institutions. ORNL maintains a unique database on energy crop research.

Research in the ESD program is closely coordinated with the DOE biofuels conversion research at the National Renewable Energy Laboratory. Increasing concerns about greenhouse effects, plant stress response, and ways of removing carbon dioxide from the atmosphere have recently increased interest in biomass energy at other agencies. Its direct relevance to carbon dioxide studies funded by OHER, the EPA, the U.S. Agency for International Development (AID), and the Electric Power Research Institute (EPRI) has become apparent. The ESD Biofuels Feedstock Development Program supports ESD research in nutrient cycling and plant responses to environmental stresses in managed agroecosystems. Such research complements OHER-sponsored research in natural ecosystems. The program has also recently completed a cooperative effort organized by the American Forestry Association to describe forestry opportunities (including energy crop production) for mitigating the effects of global warming in the United States. A major thrust of the effort is to define the land base available for carbon sequestering and energy crop production. ESD is also working with EPA to define the status of biomass energy technologies and to identify constraints to commercialization.

The ESD also participates in a technical capacity in the International Energy Agency's (IEA) Forest Growth component for DOE. All of DOE's Biofuels Division payments to the IEA are made through the ESD. Technical participation has involved biotechnology, economics, harvesting, and physiology. Exchange of genetic material, productivity data, yield response/economic data, and scientist exchanges, have resulted from ESD's participation.

ESD also provides environmental technical assistance to the Division of Geothermal and Hydropower Development. Current activities in this area include a study of environmental mitigation practices that are associated with the development of hydroelectric projects. The objectives of this new study are to identify, compile, and analyze information on the implementation and monitoring of specific mitigation practices and, to the extent possible, to quantify the costs, benefits, and effectiveness of these practices.

Toxicity studies in HASRD using a unique gas-phase mammalian cell culture exposure system identified S_2F_{10} as the major contributor to toxicity in electrically stressed SF_6. This work is expected to lead to improved worker safety in industries using SF_6 as an insulator.

Dielectrics research is being carried out in HASRD for the Division of Electrical Energy Systems of the Office of Energy Storage and Distribution. Researchers are studying the physical properties of dielectric materials, the mechanisms of breakdown of such materials, and the development of superior dielectric materials. This work has been conducted over several years. Five international symposia on gaseous

dielectrics have been organized and hosted, and the proceedings have been published. Studies of the toxicity and potential environmental effects of products formed during electrical breakdown of dielectric materials are also carried out. Research is also being conducted to delineate and understand the basic physical mechanisms of dielectric breakdown at an electrode/solid insulator interface. The work focuses on the effects of microstructures, defects, impurities, and filament formation.

Assistant Secretary for Fossil Energy

ESD and other divisions provide technical support to DOE in the preparation of NEPA reviews of site-specific projects in the Clean Coal Technology Demonstration Program. These include programmatic as well as site specific assessments.

Office of Civilian Radioactive Waste Management

The Office of Civilian Radioactive Waste Management (OCRWM) has supported review of the study plans for the proposed repository site at Yucca Mountain, Nevada. Continued activity for OCRWM tasks will depend on specific program directions.

Office of Policy, Planning, and Analysis

Work for the Office of Planning and Analysis includes (1) research on transportation, (2) energy efficiency, (3) infrastructure costs associated with alternative fuels, (4) alternative fuels supply issues and effects on energy security, (5) consumer choice and demand issues for alternative fuels, and (6) automobile and light-truck fuel economy standards and analysis.

Non-DOE Organizations

Other federal agencies that provide BER-related funding to ORNL through interagency agreements with DOE include the EPA; the Department of Health and Human Services (DHHS); the National Oceanic and Atmospheric Administration; the National Science Foundation (NSF); and the U.S. Army, Navy, and Air Force. Both DOE and non-DOE sponsors benefit from the work done for other agencies because the work is complementary, and all of it is performed in the same general locations in laboratories where facilities, equipment, and staff are shared.

Air Force

Development and evaluation of the Defense Priority Model for ranking U.S. DOD waste sites continues at a reduced level. Technical support is being provided for environmental assessments and impact statements.

In conjunction with Energy Systems HAZWRAP, ESD and HASRD have collaborated to perform remedial investigations/feasibility studies projects at the more chemically contaminated, complex sites in the Air Force's Installation Restoration Program. This work is currently being conducted through ORNL's Grand Junction office. ORNL staff have also continued to conduct Environmental Compliance and Management Program Audits of Air Force Bases in the Tactical Air Command in FY 1991. ORNL staff have provided support in preparing environmental assessments and impact statements on a number of Air Force projects.

In collaboration with the Center for Environmental Biotechnology, ESD is aiding in the design and testing of new bioreactors and microbial consortia.

Army

Efforts for the Army include (1) studying the feasibility of using Army high-volume hazardous waste streams as supplementary feedstocks in industrial boilers, (2) validating data for the Energy Conservation Investment Program, (3) performing a development study for an Energy Conservation Technical Information and Analysis Center, (4) developing surface-enhanced Raman scattering for chemical detection, (5) developing laser eye protection devices, and (6) assisting in preparing environmental assessments and impact statements for the demilitarization of chemical agents by the Army. Through Energy Systems HAZWRAP, ORNL staff are also participating in environmental compliance audits for the Rocky Mountain Arsenal. Assistance with analysis of environmental matters for the Army Corps of Engineers and the Waterways Experiments Station continues. Possible health and environmental effects of munition wastes have been studied, and munition

production waste disposal methods are being assessed.

With respect to toxic/hazardous wastes cleanup and remedial action, a series of Applicable or Relevant and Appropriate Requirement (ARAR) investigations has been conducted at the contaminated sites throughout the Army installations. Efforts continue to provide a computational framework for inferring radiation dose from bioassay measurements. Studies continue to investigate the toxicity of trinitro toluene (TNT) composting material and to evaluate the utility of a fish model system as a biomarker for environmental carcinogenesis. Research on battlefield goggles that would provide protection from laser beams is proceeding by evaluating various crystals for their absorption properties. Assistance was provided to the Federal Emergency Management Agency in the identification of important issues involved in preparing communities to deal with potential accidents associated with the U.S. Army's chemical warfare agents disposal program. In addition, efforts are denoted to assist the Army's Environmental Hygienic Agency in preparation of Material Safety Data Sheets for ultimate incorporation to DOD's Hazardous Material Information System.

Department of Health and Human Services

DHHS supports research in carcinogenesis, protein engineering, protein crystallography, genetics, and toxicology. DHHS funding is expected to remain relatively constant over the next three years. The main branches of DHHS that provide support are the National Cancer Institute (NCI), the National Heart, Lung, and Blood Institute (NHLBI), the National Institute of Environmental Health Sciences (NIEHS) including the National Toxicology Program (NTP), the National Institute of Child Health and Human Development (NICHHD), the National Institute of General Medical Sciences (NIGMS), the Food and Drug Administration (FDA), the National Library of Medicine (NLM), the National Institute on Aging (NIA), and the recently formed National Center for Human Genome Research (NCHGR). Genetic, reproductive, and general toxicology data bases are being developed, analyzed, and evaluated for the EPA, FDA, NLM, and NTP, which are available nationally as well as in other countries.

NCI supports research on (1) DNA repair (specifically studies of DNA-O^6-methylguanine methyl transferase and N-methylpurine-DNA *N*-glycosylase), (2) the expression of preneoplastic markers in tracheal cells, and (3) variants of EGF derived by site-directed mutagenesis. For NCI, ORNL is studying cell interaction and the expression of preneoplastic markers and the role of transforming growth factor Type b in the control of tracheal cell proliferation. Studies in this system involve the changes in response to growth factors as cells progress from preneoplasia to malignancy.

During the next five years, questions about the responses of ecological systems and how they relate to potential human health effects will be addressed.

NICHHD supports a program on the induction of insertional mutations by means of transgenic-mouse technology. Caused by integration of foreign DNA into the host genome, such mutations are valuable for correlating gene structure with function.

NIGMS supports studies to improve our understanding of hydrogen-bonded biological systems. HASRD scientists are examining the hydrogen-bond structure of macromolecules by means of X-ray and neutron diffraction along with analysis programs running on super computers.

For NIEHS, ORNL is enlarging the data base on the response of germ cells to chemicals. Induction of both gene mutations and chromosome aberrations is being measured, and these genetic lesions are being studied in depth. Multiple dominant endpoints that have special relevance to risk are being investigated. DNA probes are used to characterize the nature of genetic lesions induced by chemical mutagens. ORNL is also developing a computerized transgenic-mouse database, and is mapping transgene integration sites utilizing fluorescence *in situ* hybridization procedures. Mouse endogeneous retrieval LTR elements are also being studied.

For NHLBI and NCI, the Nuclear Medicine Program is developing a basic understanding of the chemistry and physiology of cerebrovascular and cardiovascular imaging agents. Under support of the NCI, the Nuclear Medicine

Program provided their osmium/iridium generators to collaborating researchers who evaluated various applications for cardiovascular imaging.

Saturation mutagenesis of two specific regions of the mouse genome is supported by NCHGR. The mutations recovered following parental exposure to a high-efficiency point-mutation inducer identify functions controlled by genes in multi-megabase-long genomic regions that are currently undergoing physical (DNA-structure) mapping.

Analytical tools were developed for use by ATSDR in evaluating reports of clusters of health effects near hazardous waste sites. A user-friendly microcomputer version will be implemented next year and provided to state health officials for their use. Also for ATSDR, the Risk Analysis Section in HASRD is providing guidance on the performance of health assessment at hazardous waste sites on the Superfund list. Methodologies to predict acute and chronic health effects resulting from exposures to hazardous chemicals are being developed. NIA supports establishment of banks of frozen embryos from several mouse and rat strains developed specifically by NIA for aging studies.

U.S. Nuclear Regulatory Commission

In support of the Office of Nuclear Materials, Safety, and Safeguards, the Measurement Applications and Development Group of the Health and Safety Research Division conducted a review of 30,000 terminated licenses for Parts 30, 40, and 70 of the Code of Federal Regulations.

The Biomedical and Environmental Information Analysis (BEIA) Section of HASRD is collaborating with the Chemical Technology Division on a project to develop a National Profile on Commercially Generated, Low-Level Radioactive Mixed Waste. In addition, HASRD provides technical assistance to NRC/NRR in updating NRC's health physics positions on inspection, enforcement, and licensing issues. The Health Physics Positions Data Base is used both by headquarters and regional staff to ensure uniformity in licensing actions. The data base is maintained on a DBase III+ in-house modified program. BEIA staff will assist the NRR staff in updating the data base, modifying the software to maximize usefulness of the information to the user, and documenting the data base information for users in the form of a NUREG document. ORNL will also assist NRC in subsequent revisions to the data base and to the software used to maintain the information.

Support was provided to the Emergency Operations Center of the NRC to implement dosimetry codes on microcomputers for use in emergency situations. Assistance was also provided to ensure access and maintenance of state-of-the-art dosimetry models. Partial support was provided to assist in the updating of the International Commission on Radiological Protection's Reference Man.

ESD initiated a technical support project to aid NRC in reviewing the states' plans for siting low-level radioactive disposal facilities.

Electric Power Research Institute

Research sponsored by EPRI addresses critical national issues related to electric power generation. Major efforts in this area are directed at understanding the processes by which atmospheric deposition of energy-related pollutants affects ecosystems and the processes by which fish populations may compensate for increased mortalities caused by the operation of electric power generation facilities.

A major six-year project on the effects of acidic deposition on the nutrient status of forest ecosystems, the Integrated Forest Study Program, was completed in CY 1991. ORNL is the lead organization; coinvestigators include the Institute of Ecosystem Studies, the State University of New York at Syracuse and at Albany, the University of Pennsylvania, the University of Washington, Colgate University, Duke University, Emory University, the University of Florida, the University of Maine, the National Park Service, the Forest Service, the Canadian Forest Service, and the Norwegian Forest Research Institute. This program involves atmospheric deposition studies at sites in Florida, Georgia, Maine, New York, Washington, North Carolina, Tennessee, Canada, and Norway. Mechanistic laboratory and field research has been conducted at ORNL, Duke, Washington, the Institute of Ecosystem Studies, and the University of Georgia in support of this field-oriented project. A complete book on the important findings of the research is in press.

The EPRI program on Compensatory Mechanisms in Fish Populations (COMPMECH) has

been renewed for a second three-year period, and a complementary five-year Hydro Project on integration of Physical and Biological Methods for Assessing Instream Flow Requirements has been funded. The overall objective of COMPMECH is to improve predictions of fish population response to disturbance. The focus of the Key Species Project is on quantifying and modeling reproduction, growth, and survival for six fish species that represent a cross section of life-history strategies and that are known to experience mortalities and/or habitat alterations because of the operation of steam and hydroelectric generation facilities. The scope of the Hydro Project includes (1) examination of the effects of water flow reductions in streams on the numbers and size distributions of fish that can live there, and (2) evaluation of the capabilities of models relating fish abundance to flow in order to predict flows needed to maintain fish populations. This EPRI program complements ORNL's responsibilities for the environmental subprogram of DOE's Hydroelectric Program, particularly the feasibility of fish population models for instream flow measurements. It also complements ORNL responsibilities within the KP program of DOE's Office of Energy Research, particularly the charge to increase our understanding of the effects of energy-related activities on the environment. A new project has recently been initiated on bioremediation of near-surface waters. It is focusing on the role of plant roots in stimulating naturally occurring microbes in degradation of organics in energy-related wastes.

EPRI continues to fund research at ORNL in areas related to the efficient use of electric energy. An efficiency research project currently under way is a test of full-size ice-storage systems for cooling commercial buildings.

Environmental Protection Agency

ORNL's work for the EPA addresses numerous health and environmental problems and issues. The research focuses on identifying the effects of pollutants associated with energy-production processes, effluents, and disposal. During the past year, studies have been initiated to relate the effects of contaminant releases to ecological responses using ecosystem simulations. In addition, research also addresses the toxicity of leachates of solid wastes and the human health hazards from incineration of hazardous chemicals.

Major contributions were made to both the terrestrial and aquatic portions of the final integrated Assessment of the National Acid Precipitation Assessment Program (NAPAP).

ESD staff members are playing a major role in support of EPA Headquarters program staff in development of an analysis of ecological indicators suitable for use by the new Environmental Monitoring and Assessment Program (EMAP). ESD staff members have also contributed to this program in the development of landscape indices of disturbance, which are of potential use in interpreting the ecological significance of future change in landscape patterns. Studies have been conducted to aid in development of a biomarkers strategy for monitoring. ESD staff are also assisting EPA in developing integrated assessment approaches for the overall EMAP.

ESD staff co-chaired the EPA-sponsored meetings of the United Nations Economic Commission for Europe Task Force studying the Application of the Principles of Environmental Impact Assessment to Policies, Plans, and Programs. ESD is also responsible for development of the task force report which, once approved, will be published by the United Nations. EPA has also asked staff of ESD to develop an environmental assessment sourcebook for their use in reviewing NEPA documents and conducting training, as well as for distributing to other federal agencies and to developing countries, who request information on the United States environmental assessment process.

EPA is supporting work to combine technologies in geophysics and the Ultrasonic Ranging and Data System (USRADS) to automate the geophysical survey progress. USRADS automatically positions a surveyor on an area of land and pairs the instantaneous measurement from a portable geophysical survey device (i.e., terrain conductivity meter or X-ray fluorescence device for the detection of heavy metals) once each second and stores the information in a field-operated microcomputer. This provides access to a large amount of accurate data in a cost-effective manner prior to the completion of the survey while still in the field. This represents a significant advancement over conventional techniques of manual logging, transcription, and interpretation of data.

Literature reviews and chemical hazard information profiles are prepared for EPA-selected topics and chemicals. Administrative management, coordination, and information support will continue to be provided to the EPA Gene-Tox Program to help evaluate mutagenicity bioassay systems. Interim guidance will be recommended to EPA on the use of genetic bioassays to screen samples of wastewater effluents. In addition, the Chemical Unit Record Estimates (CURE) Database was developed to provide comprehensive summaries of risk assessment parameters and values derived from more than 3000 EPA chemical exposure documents to serve as a research tool for agency scientists. There are currently 1900 chemicals in the database, all of which have been classified according to the structural categories developed by EMIC for the EPA Gene-Tox Program. This feature will now provide a basis for structural activity comparisons to span both genetic toxicology and low dose toxicology and carcinogenicity. A personal computer (PC) version of selected information from the master CURE file has been developed and is currently being tested with the OHEA. Risk Assessment projects performed at ORNL include the development of Reference Doses (i.e., RfD—Oral and Inhalation) and Reportable Quantity (i.e., RQ—carcinogenicity and chronic toxicity) profiles and reduce uncertainty in risk assessment. In addition, a new health risk assessment document [Health and Environmental Effects Document (HEED)] was prepared by BEIA. A HEED is a comprehensive summary and risk assessment of the available health and environmental information on chemicals. The data is critically evaluated and appropriate studies are identified to serve as the basis for the following risk assessments: Water Quality Criteria, Oral Reference Doses, Inhalation Reference Concentrations, Chronic Reportable Quantities (RQ), Cancer Potency Factors, and Cancer RQs. The HEEDS are used by the EPA as a source of information from which advisory or regulatory criteria on chemicals can be made.

The EPA is supporting research at ORNL to evaluate the use of physiologically based pharmacokinetic models in the risk assessment process. The models allow for prediction of the relationships between applied dose and effective dose to target tissue. The chief advantage of physiologically based models is that by simply changing the physiological parameters, the same model can be used to describe the dynamics of chemical transport and metabolism in mice, rats, and humans. These models are being used to investigate interspecies extrapolation and the extrapolation of dose between routes of administration.

A major collaborative research project to investigate radon entry and mitigation effectiveness, sponsored by EPA, TVA, and DOE/OHER, includes seven houses in New Jersey and eight houses in the Tennessee Valley area. Continuous monitoring of radon, temperature, and differential pressures was conducted in basements and main floors of the homes. Detailed measurements are conducted prior to installation of mitigation, such as sub-slab ventilation. Mitigation effectiveness is evaluated after conducting several months of pre-and postmitigation monitoring in both warm and cold weather.

The EPA supports work in mammalian genetics to follow up on our findings that exposure of the zygote to certain chemicals causes high frequencies of congenital anomalies. The project (1) studies the parameters that influence the induction of such anomalies, and (2) develops dose-response curves for specific chemicals that are of interest to some of EPA's Program Offices. The information to be developed is essential to EPA's effort of developing risk-extrapolation procedures. The EPA also supports fundamental studies on the mechanisms of alkylation mutagenesis in human cells in culture.

Navy

Basic studies are being conducted of the fundamental properties of gases and gas mixtures appropriate for use in diffuse discharge switches for assessment purposes. A new optical data storage technique based on the surface enhanced Raman effect is being investigated. ORNL is also involved in studies of the properties of high-energy metastable negative ions and the laser-induced formation of molecular ions from excited atoms. This work complements and supports OHER studies of negative ion reactions relevant to energy deposition by ionizing radiation. ORNL provides technical support to the Navy on compliance with environmental

regulations and on the potential health effects of hazardous materials used by Navy personnel. An assessment of potential health impacts associated with low levels of formaldehyde in drinking water was also conducted for the Navy. Results indicate that minimal impacts are expected. Efforts are also devoted to assist the Navy's Environmental and Health Center to prepare Material Safety Data Sheets for incorporation into DOD's Hazardous Material Information System.

Through the Hazardous Waste Remedial Action Program, HASRD is providing technical assistance to the Navy for its Radon Assessment and Mitigation Program (NAVRAMP). During the screening phase, extensive assistance was provided for both data quality assurance and data management. Consultation with facility engineers facilitated efforts to reduce radon exposures at sites where very high concentrations were discovered. During the assessment phase, additional sampling will be conducted at selected bases to identify all buildings with unacceptable levels of indoor radon.

The National Science Foundation

NSF-sponsored research on the ecological processes and interactions that contribute to ecosystem resilience, the ability of an ecosystem to recover from disturbance, was completed. New NSF-sponsored research was initiated in FY 1991 to examine spatial gradients in nutrient recycling and their effect on stream ecosystem stability. This work utilizes our unique set of experimental streams, our Walker Branch Watershed, and radioisotope tracers to research key factors in the response of streams to nutrient limitation and other disturbances. An improved understanding of ecosystem recovery processes derived from this basic research will benefit the ORNL studies of disturbed aquatic systems near the Oak Ridge facilities that are being conducted in concert with remedial action efforts.

ORNL is continuing to provide technical assistance to the Division of Polar Programs in their effort to evaluate the environmental impacts of the U.S. Antarctic Program. ORNL has prepared a programmatic environmental impact statement and will develop several site- and project-specific environmental impact assessments. Emphasis is being placed on waste and fuel management, sensitive resources, and global concerns for the pristine Antarctic environment.

The NSF supports ORNL research to evaluate the scientific bases for assumptions used in the risk assessment process. The major assumptions arise from the necessity to extrapolate experimental results (1) across species from rats or mice to humans, (2) from the high-dose regions to which animals are exposed in the laboratory to the low-dose regions to which humans are exposed in the environment, and (3) across routes of administration. The work is intended for use by federal agencies responsible for regulating human exposure to chemical carcinogens.

The NSF has also supported a program for developing means to maintain genetic lines of Drosophila in the frozen state. Currently, more than 10,000 such lines are maintained worldwide by standard continuous breeding techniques, which are cumbersome and costly. Successful freezing of embryos requires (1) the means to keep them viable while they are made permeable to water, solutes, and cryoprotectants, and (2) the optimization of conditions for their cryopreservation.

American Petroleum Institute

The American Petroleum Institute supports research at ORNL to evaluate the pharmacokinetics and pharmacodynamics of benzene in humans. The work is intended to provide a better estimate of the risk of developing leukemia following exposure to low doses of benzene.

U.S. Department of Agriculture

Research supported by the U.S. Department of Agriculture (USDA) Forest Service continued in 1991. ESD completed studies of the physiological mechanisms governing red spruce response to acid rain as part of the northern spruce research cooperative. In addition, ORNL continues to provide guidance and research support to the U.S. Forest Service Global Change Program. The USDA also supports research on the characterization of phosphoribulokinase, thereby expanding the scope of OHER's protein engineering program at ORNL's Biology Division.

Department of the Interior, Geological Survey

ORNL's ESD is developing new methods for the collection and analysis of trace metals in

precipitation for the U.S. Geological Survey (USGS). The project is a joint effort among ORNL, the USGS, and the Illinois State Water Survey, and it is designed to lead to a new nationwide network for trace metals in wet deposition.

Agency for International Development

AID is supporting research related to climate change in two areas. Both involve significant collaborative work with ORNL's Energy Division. The first involves assistance to the many bureaus of AID in developing agency-wide recommendations for their role and policy on the climate change strategy. This also involves interaction with DOE, EPA, NASA, USDA, NOAA, the IPCC, and nongovernment organizations.

Other Support

Other agencies that support research related to BER's mission and goals include TVA, the National Aeronautics and Space Administration (NASA), the National Oceanic and Atmospheric Administration (NOAA), the Consumer Product Safety Commission (CPSC), the National Research Council of Canada, the U.S. Park Service, the Federal Energy Regulatory Commission (FERC), and several universities.

Research for the Park Service focuses on regional analyses of environmental perturbations. ORNL is conducting an environmental analysis of a proposed extension of a scenic parkway within the Great Smoky Mountains National Park. ORNL provides input to environmental analyses of hydroelectric projects for the FERC and is preparing assessments of multiple hydro developments on river basins.

Support was provided to the Defense Nuclear Agency in the development of dose-response models to predict equivalent prompt dose from a protracted radiation exposure. A study of measured ^{60}Co levels from steel samples exposed to the Hiroshima A-bomb blast with modeled values using the DS86 system was completed.

Two indoor air quality field studies were completed. Approximately 400 homes were monitored for a broad range of indoor air pollutants including radon, formaldehyde, combustion gases, particulates, organics, and microorganisms. Multiagency support by EPA, CPSC, TVA, EPRI, and other private organizations allowed cost-effective use of limited resources to maximize the information obtained.

Work is being performed for the Oregon Health Sciences University (OHSU) in the study of genetic susceptibility to alcoholism. Strains of mice that diverge in their behavioral responses are being banked by cryopreservation at successive stages of the selection process. The project is supported by a grant to OHSU from the NIH, and the cryopreservation is being performed under a subcontract at ORNL.

A project on the cryobiology of human spermatazoa is proceeding in collaboration with the Methodist Hospital of Indiana (Indianapolis). The work is supported by NICHHD and complements OHER-funded research in cryobiology.

The BEIA Section of HASRD provides technical assistance for the Soap and Detergent Association to assess the health and environmental effects of exposure to two groups of nonionic surfactants, alcohol ethoxylates, and alkylphenol ethoxylates. This compilation of information will assist the member companies of the association in assessing the health and environmental effects of their products and also provide a mechanism of communicating such information with regulatory agencies.

Issues

This section addresses the near and long term issues facing operation of the BER Program at ORNL, and addresses topics such as program planning; funding; work for others; facilities; and environment, safety, and health issues associated with the BER work.

Program Planning

ORNL desires to continue its technical support of OHER's planning and interagency coordination. We continue to recommend joint planning between OHER and its contractor laboratories. For example, the Genome meeting held in early 1991 provided an effective planning forum for all parties involved in DOE Genome work.

The ORNL BER Program was given two opportunities to provide comments on draft OHER planning documents during FY 1991: the Multi-Year Program Plan and the Radiation and Chemical Health Effects Section of the Multi-Year Plan. This is an effective vehicle for communicating research objectives. Specific comments on the plans were provided previously; however, some of the comments were generic and bear repeating in this report.

OHER planning must address the restoration of research facilities necessary to meet modern research and ES&H requirements. In this regard, relocation of the ORNL Biology Division to the new proposed CBS must be a top priority.

In the field of molecular biology and genome research, ORNL recommends that OHER build upon its proven strength in protein engineering; expand the human genome program to include functional mapping; encourage advanced spectrochemical, genetic and analytical technologies for DNA sequencing; infuse major capital equipment monies for current instrumentation needs (particularly x-ray crystallography); encourage the use of cell culture model systems for comparative animal to human studies, but not to the total exclusion of animal experiments required for extrapolation of radiation risks across species; and examine whether electromagnetic field effects should be a legitimate area for further scientific study.

General comments include the importance of risk assessment in establishing priorities for environmental remediation, health protection, and future energy technology programs; the importance of subsurface science and land use ecology in understanding technology impacts; the missing middle ground between molecular biology and global studies (e.g., land use changes as they affect biosphere/atmosphere interactions) in current research; the need to consider global initiatives in risk to the biosphere from climate change and the rate-controlling influence of biological processes on the carbon cycle; and the expansion of environmental processes and stress ecology beyond microbial systems.

The basic environmental sciences, health sciences, and instrumentation development in support of environmental activities have grown too slowly. In addition, biological sciences have been slow to appear in OHER's new initiatives (e.g., terrestrial and aquatic ecology, environmental biotechnology and global carbon cycle/biosphere response).

Because of the static DOE research budget and the uncertainty of programmatic directions, there is a risk of OHER losing leadership in radiation biology, health effects, and ecological research. However, major opportunities exist for both ORNL and OHER in the global sciences,

the mammalian genome, risk analysis, environmental biotechnology, and waste R&D. Issuance of the April 1991 report on *Basic Research Needs for Management and Disposal of DOE Wastes*, (DOE 1991) is a positive step toward describing the fundamental research that can provide the foundation for applied studies that will be needed to manage and dispose of DOE wastes.

In less than two years, ORNL has progressed from zero to nine genome projects, most of which grew from ORNL investment of LDRD funds. ORNL utilized its interests in advanced sequencing technology and functional genetic studies in the mouse to achieve this success. Our near-term goal is to receive recognition as a DOE Human Genome Center.

Funding

During the June 1991 DOE-HQ on-site review of ORNL's draft multi-year Institutional Plan, the BER program commented on the diminishing R&D budget at ORNL. Subsequently, we were asked to summarize our perspective of factors contributing to the decline in basic R&D funding in the OHER budget at ORNL. These are as follows:

- Overhead has increased significantly in recent years, which cuts into the "buying power" of research dollars.
- Direct charges of ES&H costs to divisions has also reduced buying power of research dollars.
- The OHER budget has experienced historic decreases.
- Congressional "earmarking" of the OHER budget has decreased funding for basic R&D.
- Congressional protection of new, more applied initiatives has further constrained basic R&D funding in core scientific areas.
- The "waste chargeback" impact of FY 1990 by nonproportional B&R account charging resulted in a reduction of the FY 1990 funding in KP0302 of more than $800K, which continues to manifest itself in FY 1991 as a reduced base.
- DOE defense laboratories are expanding their base of OHER funding.
- Growth and funding of special purpose laboratories, and mainly universities, has been disproportional to and at the expense of multiprogram laboratories.
- Until recently, OHER has been hesitant to begin new initiatives to prevent erosion of basic R&D funding.

The increased costs for environment, safety, and health compliance have made significant impacts on the R&D program.

A major problem is that in most of ORNL's core scientific areas any budget growth is minimal. Overall the BER Program at ORNL has not kept pace with the cost of living. Notable exceptions have been global change, human genome, and protein engineering.

A more localized funding issue affecting the BER Program was resolved in FY 1991. The issue dealt with the appropriateness of using ORNL overhead funds to pay the standby utility costs of a building formerly occupied by Biology Division (Building 9207). In FY 1991, Building 9207 was classified as excess space for the laboratory, which allowed the standby utility costs to be borne by ORNL overhead.

Work for Others

Work for Others (WFO) [i.e., non-DOE sponsors] is a major and important part of ORNL's integrated biological and environmental research program. It includes work for other federal agencies as well as work for private companies and institutions. ORNL continues to perform high quality, critical research work for other organizations, often times building upon historic KP research, and we feel that DOE should recognize and take pride in these accomplishments. We will submit these WFO accomplishments (as appropriate) with our monthly OHER highlights.

ORNL is continuing to work closely with the private sector in keeping with the goals and aspirations of DOE. Work for Electric Power Research Institute (EPRI) was an example of an important part of the integrated acid deposition program. We anticipate EPRI support of research related to global change. Work for organizations such as EPRI should be considered as a special category of WFO because of the similarities of research interests to those of OHER.

DOE administrative oversight of WFO program has become so stringent as to now be adversely affecting laboratory programs where WFO is intended to augment DOE programmatic R&D. Work for others in the basic areas of biological and environmental research is being increasingly impacted by stringent DOE oversight to prevent abuse in applied WFO programs.

DOE needs to develop reciprocal memoranda of understanding (MOUs) with other organizations to facilitate cost-effective interagency utilization of unique R&D facilities. It has been suggested that OHER explore the possibility of developing arrangements (e.g., MOUs, blanket work orders, or basic ordering agreements) with organizations such as EPRI, DHHS, and perhaps the NSF. This would help to reduce the administrative costs of conducting work for others.

A major accomplishment was the resolution of the issue regarding ORNL's acceptance of grants from NIH. The ORNL BER Program Office worked closely with DOE-HQ and the DOE Field Office, Oak Ridge to resolve whether or not grants may be accepted. ORNL appreciates support from its DOE programmatic sponsors in resolving this problem. It was decided by DOE-HQ that grants may be accepted by ORNL. However, the issue of payment of indirect costs by other federal agencies for work done at DOE laboratories still requires resolution.

Facilities

Research progress in the BER Program is hampered by a lack of facilities. For example, in FY 1991, the ORNL space shortage resulted in the moving of over 30 personnel in non-KP programs off-site to rental office space, thus reducing their interaction with KP-funded researchers at ORNL. Continuing current research practices is difficult given aging and inefficient facilities, particularly in the Biology Division. Expanding BER research into new areas such as global studies and advanced photonics is similarly constrained by a lack of adequate facilities. To address these issues, ORNL is pursuing a combination of programmatic line item facilities and non-programmatic general plant projects (GPP), as described in the section on "Program Orientation."

Members of the Nuclear Medicine Group working in the Health and Safety Research Division (primarily KP06 funding) have been asked to vacate space by June 1992 so that appropriate decontamination and decommissioning activities at adjacent facilities can proceed. It will be necessary to find suitable laboratory space for these research activities. ORNL management is continuing to explore alternatives for locating the KP06 activities. OHER support is needed in ensuring that the timing of these actions maintains the continuity of the research.

Capital Equipment

The reliance on sophisticated equipment in biological and environmental research places a high demand on capital equipment budgets. OHER is encouraged to make its case for an increased capital equipment budget. Capital equipment budgets are generally insufficient to maintain state-of-the-art facilities for existing programs and to attract outstanding young scientists.

A major component of the developing structural biology effort at ORNL centers around macromolecular (protein) X-ray crystallography, which requires dedicated facilities capable of the full spectrum of crystallographic work. In FY 1992 the ORNL Laboratory Directed R&D Program awarded $300,000 in operating funds to Biology Division for revitalizing structural biology at ORNL. The capital supplement provided by OHER in early FY 1992 to Biology Division for this work is much appreciated and will go far in maximizing the research productivity of this activity.

A major component of the Environmental Biotechnology initiative will be to provide relevant information on how energy-related activities affect major ecological processes. In order to advance our understanding in these areas, several current research efforts concerned with ecosystem health, bioremediation and subsurface transport employ techniques and methodologies of molecular biology. To position the laboratory competitively and enable maintaining our role in environmental biotechnology requires increased investment in state-of-the-art equipment and instrumentation.

Resource Quantitation

Staff and Publications

The total BER Program staff at ORNL was approximately 460 at the end of FY 1991 (including students and visiting scientists). Nearly 40% of the BER-supported staff hold Ph.D.s, one individual is an M.D., one individual is a D.V.M., and the remainder have M.S. or B.S./B.A. degrees. In addition, many of the professional staff members hold university appointments.

ORNL's research programs provide opportunities for graduate as well as undergraduate students to work with researchers. The visiting scientists program is highly successful. Emphasis continues to be placed on both the periodic and longer-term appointments of visiting scientists and students to offset any reduction in professional staff that may occur. Table 13 shows the staff composition of the ORNL BER Program.

The professional staff continues to maintain an excellent publication record using a variety of publication media: scientific journals, books and book chapters, and ORNL reports. Table 14 summarizes information transfer for BER-sponsored research for FY 1990, FY1991, and FY 1992, including the numbers and types of publications. Appendix C lists all OHER support publications for FY 1991 by division.

User Facilities

User facility statistics for the BRF and the NERP are given in Table 15. The total FY 1991 number of user days and visitors increased significantly over FY 1990 levels for the BRF and NERP combined.

Meetings

Meetings being organized for FY 1992-1993 are listed in Table 16, and meetings organized during FY 1991, in Table 17. The number of meetings organized in FY 1991 by BER-supported staff was approximately the same as that in FY 1990.

Table 13. Oak Ridge National Laboratory Biological and Environmental Research Program Staff

Full-time equivalents rounded to nearest whole number

	FY 1990[a]		FY 1991		FY 1992 estimated	
	BER	Total	BER[b]	Total	BER	Total
Professional (scientific)	80	392	76	256	77	272
Postdoctorates	17	47	19	50	24	63
Technicians	35	128	31	107	32	112
Animal care	27	34	26	32	28	35
Total direct personnel	160	600	152	445	161	482
Professional (administrative)	8	22	9	20	9	21
Clerical, administrative support	29	136	28	84	30	90
Maintenance[c]	3	4	3	4	3	4
Total indirect personnel	40	162	40	108	42	115
Visiting scientists[d]	38	82	73	144	44	143
Graduate students	73	159	101	233	56	224
Undergraduates	75	156	87	181[e]	79	30
Other Students	3	17	5	6	3	10

[a]Energy Division included in total for 1990, but no BER staff present (not included in 1991 and 1992).

[b]FY 1991: 101 Ph.D., 1 M.D., 1 D.V.M., 41 M.S., 45 B.S./B.A. (excludes maintenance, visitors, and students)

[c]In laboratory overhead.

[d]Includes both resident and periodic.

[e]Includes 59 student participants in the High School Honors Workshop in Environmental Sciences.

Table 14. Information Transfer (BER-Sponsored Research)

	FY 1989	FY 1990	FY 1991
Journal articles (peer reviewed)	186	180	102
Proceedings, Books, Chapters	58	78	27
Reports/Documents	72	46	44
Technical Presentations	380	364	279
Meetings Organized	27	18[b]	19
[a]Total User Facility Visitors	145	150	176
[a]Total User Days	3657	4785	5148

[a]Numbers provided are the combined totals for BRF and NERP. (See Table 14 for breakdown.)

[b]1990 data adjusted to reflect BER-sponsored research

Table 15. User facility data for FY 1991

User affiliation	Bioprocessing Research Facility	Oak Ridge National Environmental Research Park
No. of User Facility Visitors		
University	3	56
Industry	1	0
U.S. government agencies	0	10
DOE laboratories	0	0
ORNL	5	41
Foreign	0	2
Others	0	58
Total	9	167
No. of User days		
University	67	1671
Industry	3	0
U.S. government agencies	0	118
DOE laboratories	0	0
ORNL	87	2219
Foreign	0	20
Others	0	963
Total	157	4991

Table 16. Meetings Being Organized for FY 1992–1993

Title	Organizer	Location	Date
Third Conference on Radiation Protection and Dosimetry	C. S. Sims R. E. Swaja	Orlando, Florida	October 21-24,1991
14th Werner Brandt Workshop on Penetration of Charged Particles in Matter, (international symposium)	R. H. Ritchie	Oak Ridge, Tennessee	Spring 1992
NATO Conference Nondestructive Biomarkers in Vertebrates	M. F. McCarthy	Sienna, Italy	June 1992
11th Symposium on Microdosimetry	R. N. Hamm J. E. Turner	Gatlinburg, Tennessee	September 13-18, 1992
International Conference on Laser Ablation	J. C. Miller	Oak Ridge or Gatlinburg, Tennessee	Spring 1993

Table 17. Meetings Organized During FY 1991

Title	Organizer	Location	Date
	Environmental Sciences Division		
17th Annual Aquatic Toxicity Workshop-Bioindicators	S. M. Adams	Vancouver, British Columbia, Canada	November 1990
Symposium for Annual Meeting of the Ecological Society of America	R. H. Gardner	San Antonio, Texas	August 1991
Remote Sensing and DOE Research Parks	R. L. Graham	Oak Ridge, Tennessee	June 1991

Table 17. (cont.)

Title	Organizer	Location	Date
International Symposium on the Biological Aspects of Chernobyl Accident, U.S.S.R. Academy of Sciences	F. O. Hoffman	Zeleny Mys, Ukraine, USSR	September 1990
Validation of Assessment Model Predictions/Multiple Pathways Analysis	F. O. Hoffman	Vienna, Austria	December 1990
Walker Branch Watershed Research Symposium	M. A. Huston	Oak Ridge, Tennessee	March 1991
ESA Contributed Papers on Remote Sensing, Ecological Society of America	M. A. Huston	San Antonio, Texas	August 1991
Working Group on New Initiatives U.S. National Atmospheric Deposition Program	S. E. Lindberg	San Antonio, Texas Washington, D.C.	October 1990 1991
Session on Deposition to Forests, Conference on Atmosphere/ Surface Exchange Processes	S. E. Lindberg	Richland, Washington	June 1991
Concepts in Manipulations of Groundwater Colloids for Environmental Restoration	J. F. McCarthy	Manteo, North Carolina	October 1990
Transect Workshop II (DOE-OHER)	R. V. O'Neill	Las Cruces, New Mexico	March 1991
Plant Ecology Session, Association of Southeastern Biologists Meeting	P. D. Parr	Boone, North Carolina	April 1991
NATO Advanced Study Institute On Global Carbon Cycle	T. -H. Peng	Il Ciocco, Italy	September 1991

Table 17. (cont.)

Title	Organizer	Location	Date
NATO Advanced Research Workshop on Biomarkers	L. R. Shugart	The Netherlands	May 1991
Symposium for Annual Meetings of the Ecological Society of America	M. G. Turner	San Antonio, Texas	August 1991
Technologies for a Greenhouse-Constrained Society	R. I. Van Hook	Oak Ridge, Tennessee	July 1991
	Health and Safety Research Division		
13th Werner Brandt Workshop on the Interaction of Charged Particles with Matter	R. H. Ritchie	Nara, Japan	November 1990
ORNL Workshop of Laser Ablation: Mechanisms and Applications	J. C. Miller	Oak Ridge, Tennessee	April 1991
Workshop on Advanced Laser Technology for Chemical Measurements	J. C. Miller W. R. Garrett	Oak Ridge, Tennessee	November 1990

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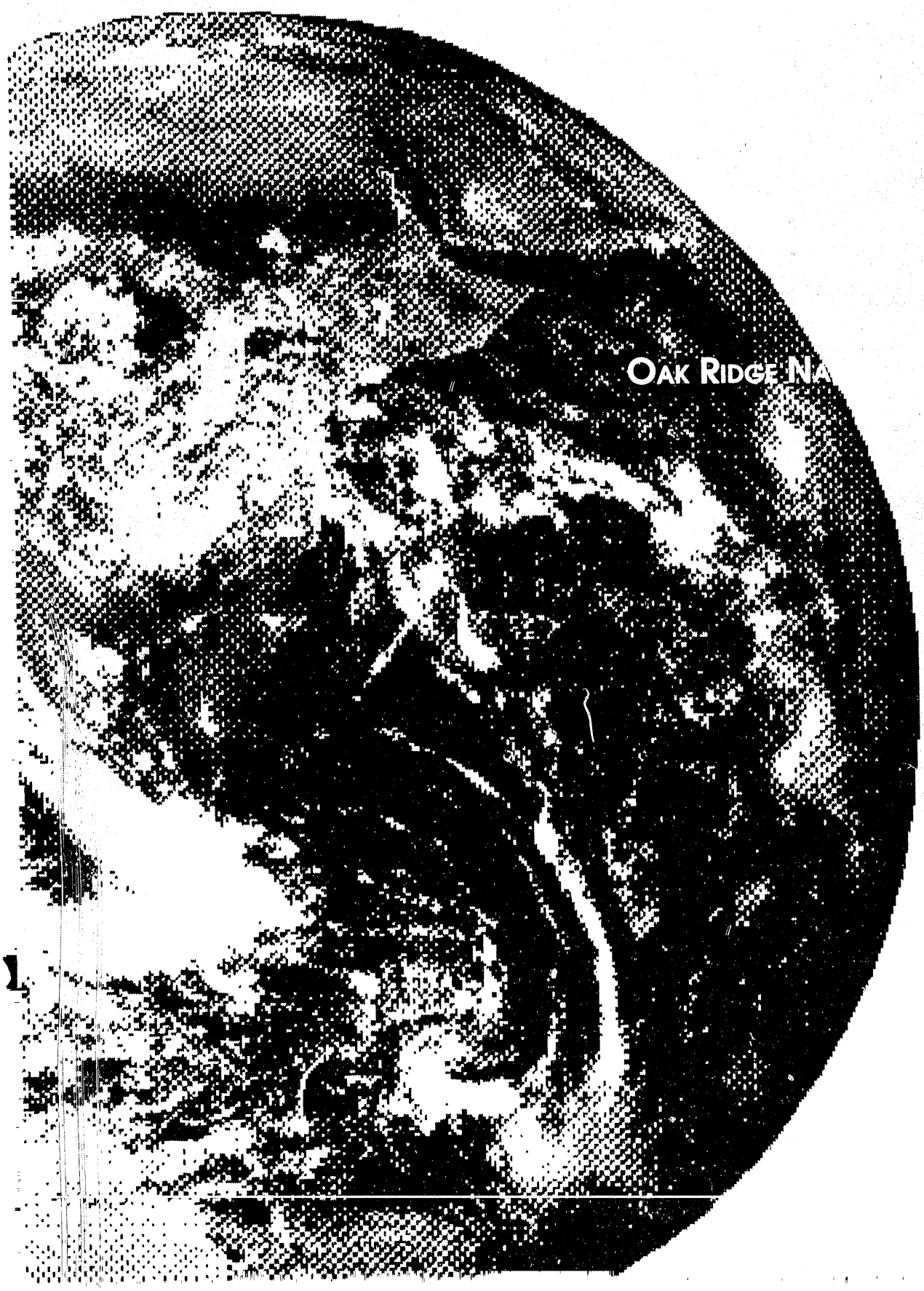
OAK RIDGE NA

Major Initiatives at Oak Ridge National Laboratory for FY1991

- *Advanced Photonics for Environmental Needs.* Highly advanced photonics instrumentation is being developed in response to the needs of both environmental scientists and waste cleanup specialists. Several ongoing instrumentation development programs are listed.

- *The Liquid State of Matter.* The Liquid State of Matter Initiative focuses on the problem of achieving a deeper understanding of fundamental liquid phase behavior with the goal of predicting new phenomena and improving existing technologies. Current research areas are listed.

- *Subsurface Research.* Subsurface research, an essential element in the waste research and development (R&D) plans, focuses on analysis of the movement of energy-related contaminants in humid regions with highly organic natural waters. Current laboratory and field studies are detailed.

- *Environmental Biotechnology.* Environmental biotechnology, a multidisciplinary science, focuses on the development and application of innovative biomarker, biomonitor, and bioremediation techniques for solving environmental disturbances. Current activities and future plans are outlined.

- *Genome Program.* Oak Ridge National Laboratory (ORNL) is committed to an integrated effort of analyzing the structural and functional characteristics of the Mammalian (human) genome by use of experimental molecular genetics (mutations in the mouse). New technologies, current activities, support facilities, and future plans, are detailed.

- *Structural Biology.* An interdivisional approach to build support for structural biology through the Office of Health and Environmental Research (OHER) is utilized. A proposal that provides for biological applications of small-angle neutron and X-ray scattering, neutron and X-ray crystallography, and nuclear magnetic resonance, is currently being reviewed by OHER. Current and proposed activities are provided.

- *ARM Data Archive.* The Atmospheric Radiation Measurement (ARM) Program will measure radiative flux in the atmospheric column for the purpose of improving global climate models. The ARM Data Archive will provide the primary access to ARM data for the science community. Current activities and future plans are outlined.

Advanced Photonics for Environmental Needs

Fueled by the growing global concern over environmental insults, critical needs have developed for the next generation of instrumentation to have a high degree of sensitivity, selectivity, and portability. These needs arise in quantitative studies of waste generation, transport, and remediation, as well as global atmospheric problems such as the world energy balance (greenhouse effect), the ozone depletion problem, and the study of airborne pollutants.

For instance, the DOE's new Atmospheric Radiation Measurement (ARM) Program will require state-of-the-art remote-sensing instrumentation. Photonics instrumentation, particularly instrumentation involving novel lasers and newly discovered physical principles, is capable of providing "single atom sensitivity" and isotopic, atomic, or molecular selectivity. Furthermore, photonics devices are becoming more compact, field-hardened, and in the case of lasers, capable of remote application.

ORNL's Health and Safety Research Division (HASRD) is a leader in developing and using laser technology to study fundamental chemical and physical processes (Figure A.1). Responding to the needs of both environmental scientists and waste clean-up specialists, many of these

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Fig. A.1. Researchers in the Health & Safety Research Division adjust lasers used in Advanced Photonics Instrumentation.

new techniques can be focused on applied measurements. As examples, two ongoing instrumentation development programs are directly linked to needs of ORNL's Environmental Sciences Division (ESD). One has involved a device to measure UV-B penetration in leaves, and the other, a sensitive optical mass spectrometer for measurement of organics in forest canopies. A third proposed device for laser remote sensing of atmospheric species would address the measurement of greenhouse gases.

This initiative is interdisciplinary (chemistry, physics, environmental science) as well as interdivisional in its contribution to solving urgent national problems.

The Liquid State of Matter

In terms of fundamental knowledge, liquid is the least explored and least understood state of matter. Yet liquid state interactions underlie a wide variety of basic research and applied technologies. Such interactions are of crucial importance in fields as diverse as particle detectors, chemical processes, pollutant transport, and radiation effects in biological cells.

Our Liquid State of Matter Initiative will focus on the problem of achieving a deeper understanding of fundamental liquid phase behavior with the goal of predicting new phenomena and improving existing technologies. Research areas will include:

1. studies of the optical and electrical properties of liquids, especially transient phenomena using fast laser and electron probes, with application, for instance, to improvements of liquid particle detectors;

2. elucidation of the relation of liquid properties to those of gases and isolated atoms and molecules via studies of gases under extreme pressures and of atomic and molecular clusters, important for understanding the transport of pollutants and nutrients in the environment; and

3. studies of the transport of radiation and radiogenic products in the structured water around DNA in a cell, relevant to models of radiation damage and to solving the problem of low-dose effects.

Subsurface Research

We will continue our work in the areas of hydrology, geochemistry, modeling, and colloid chemistry in support of DOE programs in site-directed subsurface transport of hazardous substances and subsurface microbiology. Research in subsurface sciences is directed toward defining, understanding, and predicting the movement of energy-related contaminants in humid regions with highly organic natural waters. This work, in direct response to the accelerated efforts on the part of DOE to address the characterization and eventual cleanup of contaminated facilities, is expected to grow significantly, because it is an essential element in the waste R&D plans.

Presently, activities at ORNL consist of laboratory and field studies that are integrated with the development and application of hydrologic and chemical transport models. These studies include:

1. research on the role of colloids and microbial populations in affecting subsurface transformation of energy by-products, including mixed wastes;

2. modeling of the spatial heterogeneity of soils;

3. research on the thermodynamic and kinetic parameters important to contaminant migration at DOE sites; and

4. development of molecular probes for evaluating microbial activity in the subsurface.

These, as well as new initiatives that are responsive to DOE's waste R&D plans, will continue, and will provide a unique and sound foundation for understanding subsurface contaminant migration in a humid environment. Future plans include research on methods for identifying subsurface heterogeneity and its role in microbial transport and on the origin of microbes in the deep subsurface.

Environmental Biotechnology

Environmental biotechnology is a multidisciplinary scientific area that offers the opportunity for combining existing expertise to develop and apply new approaches for characterizing and correcting environmental disturbances (such as waste remediation). The DOE Subsurface Science Program has provided support for basic research related to microbial processes for the past several years, and it serves as an impetus for several components of this initiative. Basic research on contributions from molecular biology will include identification of genetic loci in microbial systems demonstrating biodegradation activity. Research in toxicology is directed towards development and refinement of more cost-effective tests for identifying and prioritizing contaminants requiring removal or treatment. Biological monitoring continues to be a major focus of this area. Studies are ongoing at all three Oak Ridge DOE facilities and at the Paducah and Portsmouth facilities. By comparing data gathered in these studies with results of remediation activities that have already taken place, efficacy of various cleanup activities can be determined.

Utilizing R&D developments in applied waste technology is affected by policy analyses that establish federal guidelines of acceptability of biotechnological advances. These technologies will also be available for transfer to other DOE facilities. ORNL expertise in social sciences and economics will be used in conjunction with R&D advances to contribute to the decision-making process. Methods that enable early detection of environmental health problems are needed. We will continue to work closely with the Environmental Protection Agency (EPA) in the Environmental Monitoring and Assessment Program as we continue to develop our own suite of indicators.

The utility of aquatic biomarkers for assessing environmental health and recovery of receiving systems will continue to be evaluated and expanded. Research evaluating plants as biomarkers has been conducted. Development of microbial markers and gene probes is proceeding with organic and trace metal contaminants at waste sites. Efforts in bioremediation focus on developing an understanding of the environmental processes affecting rates of contaminant degradation and/or mobilization. Research is directed at recalcitrant organics and mixed waste types. Testing of available bioreactors and construction of new reactors will enable rapid application of existing technologies (Figure A.2). Modification of these environments in bioreactors, as well as *in situ*, will enable application of these techniques to DOE field sites. We anticipate that increased efforts in environmental biotechnology will be applied to DOE's immediate problems. Expansion of these activities in the basic research plan supporting environmental restoration will be required to meet this need.

Genome Program

The Laboratory is strongly committed to an integrated effort to analyze the mouse genome and, through that, the human genome. New methods that will increase the rate and accuracy for sequencing, as well as unique informatics for

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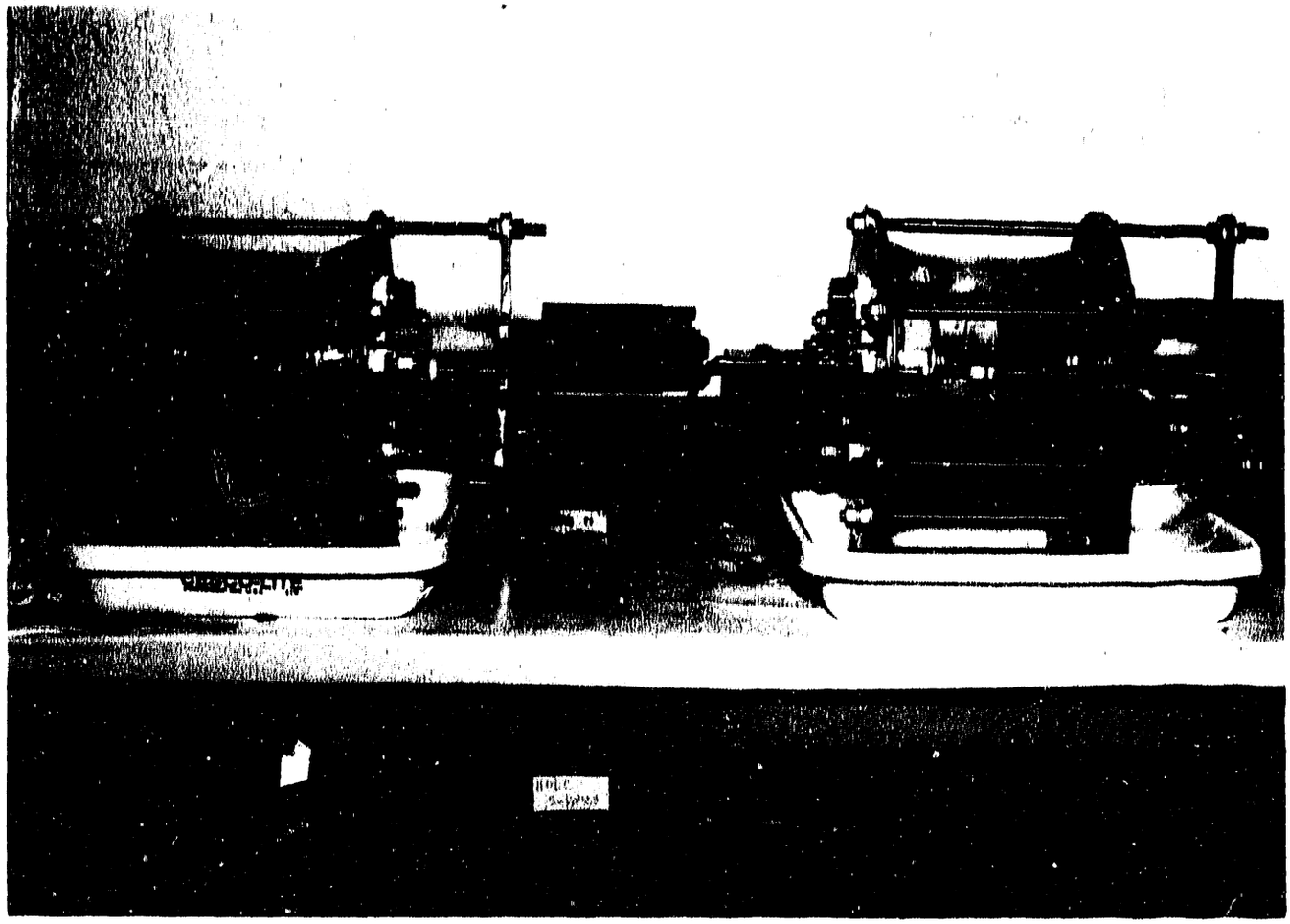


Fig. A.2. Rotating biological contactors used for trichloroethylene (TCE) degradation.

pattern recognition in new sequence data, are being developed in parallel with the generation and molecular analysis of new germline mutations in the mouse. The major objective is to explore the structural and functional characteristics of the mammalian genome by use of experimental molecular genetics. Since there are many parallels between the human and mouse in anatomy and physiology, mutations in the mouse are powerful tools for analysis of the structure and function of the human genome. New deoxyribonucleic acid (DNA) sequencing technologies are needed to provide rapid analyses that will be used in conjunction with analyses of the mammalian genomes. These technologies fall into three categories:

- For conventional gel electrophorosis, methods are being developed to increase the rate of sequence analysis 10- to 100-fold by replacing radioisotopes with stable isotopes and by using resonance ionization spectroscopy to detect DNA labeled with these isotopes. This employs state-of-the-art organometallic chemistry to synthesize the labels and new modification of resonance ionization spectroscopy to detect them.

- To eliminate the gel electrophoresis step, other methods are under development. One is sequencing by hybridization and others involve various mass spectrophotometric

methods of analyzing directly the DNA fragments that are usually subjected to electrophoresis.

- By employing new detection techniques, sensitive and rapid DNA analysis can occur. These include:

  1. single molecule detection of luminescence species;
  2. mass spectrophotometric detection methods; and
  3. synchronous luminescence, phosphorescence and enhanced Raman detection techniques.

Some of these procedures may also be adapted for genome mapping and for analysis of gel blots of DNA. The analysis of the mammalian genomes should be expedited when some of these techniques are available.

This analysis will proceed on several fronts. The analysis of the mouse genome and the interaction with studies on the human genome will proceed as indicated by the following:

- develop complete molecular maps and refined functional maps of several specific regions of the mouse genome as models for the human genome program;
- perform fine structure point mutagenesis and physical mapping of the mouse;
- create molecularly tagged mutations throughout the murine genome by insertional mutagenesis, using both pronuclear injection and embryonic stem cell techniques;
- use efficient mutagens to generate chromosomal rearrangements to expand the genomic regions accessible to fine molecular structure analyses;
- use mutagenesis techniques to create models of important human genetic disorders that can be analyzed molecularly;
- establish a national data base for transgenic mouse mutants that can be accessible by all researchers; and
- employ artificial intelligence and neural network techniques to identify important DNA sequence patterns.

Unique computer-based sequence analysis methods for identification of biologically important regions in newly sequenced DNA are being developed based on neural network, artificial intelligence, and parallel computational techniques. An expert system is under construction for rapid and reliable localization of gene components such as exons, introns, and gene control elements, and the automated assembly of these components to describe whole genes. ORNL is not the only laboratory currently using a portion of this system to localize genes in mouse studies; other laboratories are also beginning to submit sequence data to be searched for important human disease genes (Appendix E).

The Human Genome Management Information System was placed at ORNL to provide the DOE and National Institutes of Health (NIH) Human Genome Programs with a communication network throughout the international community that is engaged in human genome research. *The Human Genome News* and the *DOE Human Genome Program Report* are published at regular intervals from this office.

Facilities which support these main components are found throughout the Laboratory and in local industry and they include:

- a 250,000 mouse colony organized for genetic studies;
- a transgenic mouse facility;
- a NIH-supported data base for transgenic mice;
- the ORNL Advanced Computing Laboratory;
- resonance ionization spectrometry laboratories;
- synthetic chemistry laboratories;
- laboratory equipped with two DNA synthesizers;

- high resolution mass spectrometry laboratories;
- analytical chemistry facilities that include high resolution Fourier transform-mass spectrometry, Fourier transform nuclear magnetic resonance, Fourier transform infrared, and ultra-sensitive laser luminescence capability;
- facilities for sensitive detection of labeled DNA fragments by mass spectrometry;
- facilities for sensitive detection by enhanced Raman, luminescence, and phosphorescence; and
- cryobiology facility to preserve embryos that contain valuable mouse mutations.

Currently, members of a number of ORNL divisions are interacting to develop this multi-faceted program, including Biology; Chemistry; Analytical Chemistry; Health and Safety Research; Instrumentation and Controls; and Engineering, Physics and Mathematics.

Structural Biology

Biology and Solid State divisions are collaborating on an effort intended to develop support for structural biology through OHER. A core proposal that includes biological applications of small-angle neutron scattering, small-angle X-ray scattering, neutron crystallography, X-ray crystallography, and nuclear magnetic resonance, is now under review by OHER. Currently, crystallographic studies of nucleosomes, the building block of chromatin, are partially funded by OHER. Nucleosomes, reconstituted from a cloned DNA restriction fragment, have been crystallized in a form suitable for high-resolution analysis (Figure A.3). Other crystallographic projects would entail three-dimensional structure determination of human epidermal growth factor (EGF) and mutant analogs designed by ORNL's Protein Engineering Program, as well as a human DNA repair protein that removes alkylation lesions.

Biological small-angle neutron and X-ray scattering research was initially funded as a component of the National Science Foundation (NSF)-supported National Center for Small-Angle Scattering Research. Because of the shutdown of the ORNL High Flux Isotope Reactor (HFIR), NSF withdrew its funds and restoration is unlikely. The restart of HFIR compels the establishment of core support from OHER to maintain structural biology research at these national resource facilities, and to continue an ORNL program as the basis for developing structural biology programs at the proposed Advanced Neutron Source (ANS). OHER funding is needed for three online scattering instruments (~$5 million), equipment for a biological sample-preparation laboratory ($1 million), and a multipurpose-(deuterium)-labeling laboratory ($1 million) to ensure world-class facilities to users from the biology community.

ARM Data Archive

As the implications of global climate change are debated, the world becomes more reliant on the accuracy of the mathematical models that describe the global climate. In view of the dependency on these models, the need to increase their accuracy has become critical. The ARM Program is designed to assist in improving the accuracy of global climate models. ARM is a multi-laboratory, ten-year project to measure the radiative flux at a number of climatologically significant sites worldwide. These observations will be used to improve the parameterization of clouds' atmospheric phenomena that are relatively small in physical extent and/or very inhomogeneous (so-called sub-grid phenomena).

ARM will generate massive amounts of data over the course of the ten-year project. Tens to hundreds of terabytes of data will ultimately be archived. These data will include observations taken directly off the sensors, measurements derived by fusing several observations' streams

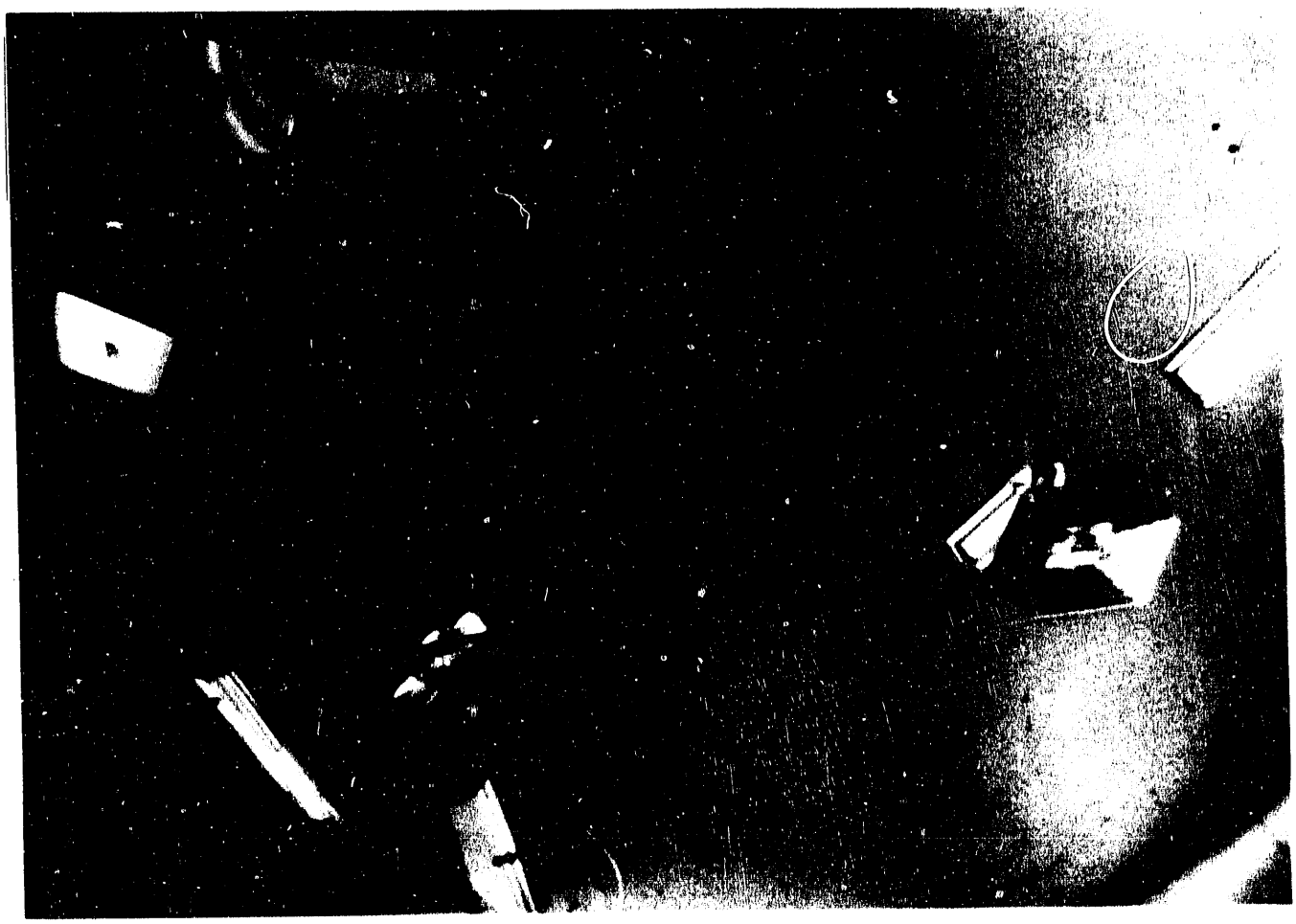


Fig. A.3. Photomicrograph of nucleosome crystals containing human alpha-satellite-defined sequence deoxyribonucleic acid (DNA) and purified histones.

to the quality assurance (QA) data, and other data that describe the quality and context of the observations and measurements. The volume and diversity of data that ARM will generate pose a massive problem in terms of storage; the data easily available will require considerable creativity. ORNL is developing the archive facility and will operate it for ARM.

The ARM Data Archive will store the data generated by the ARM project for the scientific community, and it will also provide the ARM science team with data older than a few months. To succeed in the goal of providing easy, flexible access to the ARM data, the archive will perform many more functions than simply data storage. The following value-added functions are some of the services that the archive will provide:

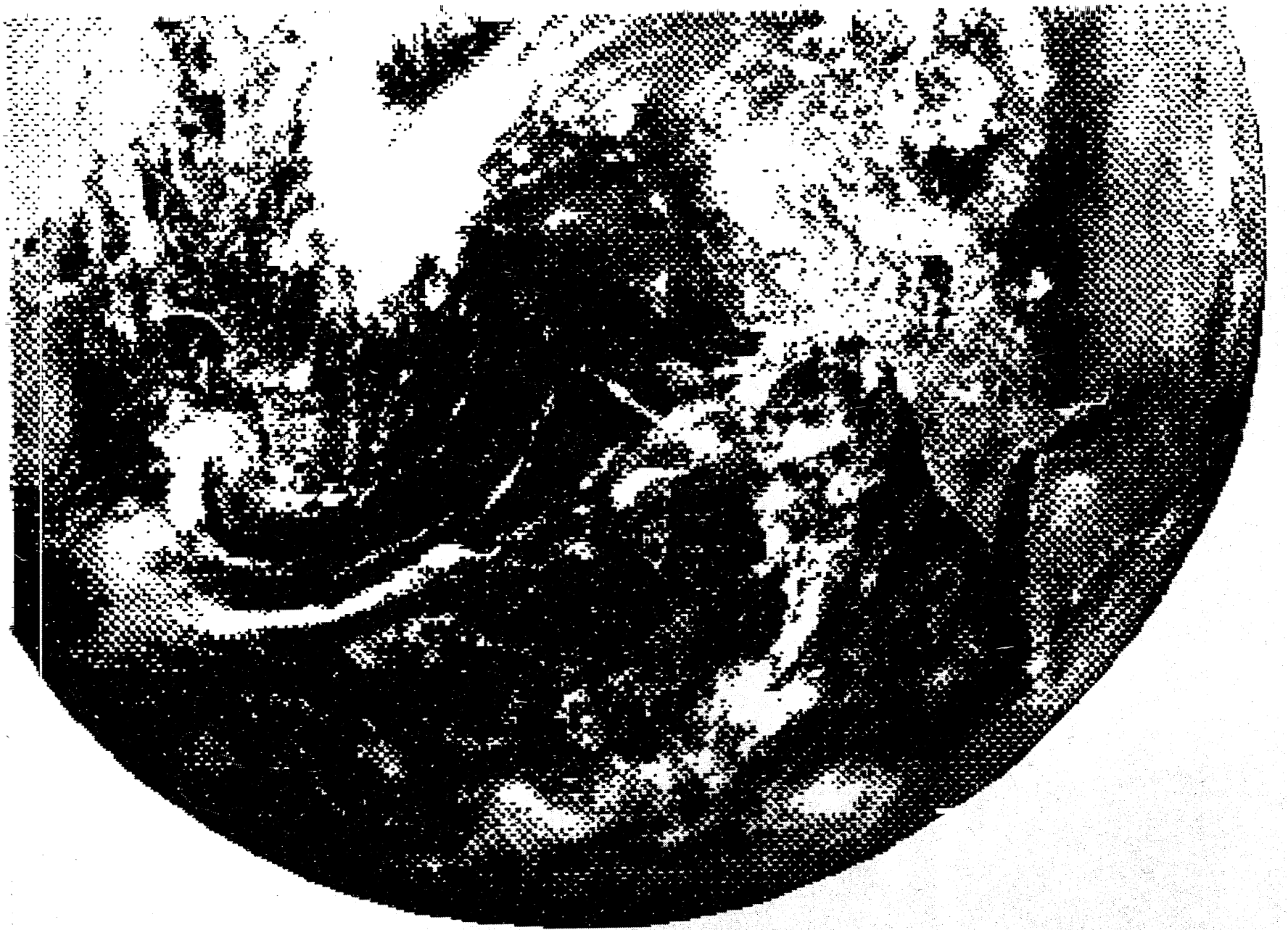
- Perform QA checks on the data to determine long-term trends or drifts that may signal problems with sensors. The data will have had several QA checks performed on them before they reach the archive, but the archive will be the only place in the ARM project where more than a few months of data will be available for performing long-term checks and studies.

- Develop value-added data sets. These can range from simple summary data sets such as daily minimum, maximum, and mean for

different observations, to very complex data associations (e.g., all the data that describe several storm events).

- Provide full documentation of the observations and measurements so that a user can determine the quality and context of any set of observations.

- Finally, the archive will provide the users with a variety of access methods ranging from fully automated workstation-based query systems to the ability to call the archive and have a subject-matter expert help them develop their request.



Research Highlights

- Therapeutic Drug Delivery to Tumors
- Identification of DNA Coding Sequences Using An Artificial Intelligence Approach
- Targeted Mutagenesis at Specific Genes in the Mouse Genome
- Study of Human Genetic Disease Syndromes Through Mouse Molecular Genetic Analyses
- Field Manipulations of Natural Organic Matter and Inorganic Colloids in a Sandy Aquifer
- Evaluation of the Effects of Moisture Gradients on Carbon Storage of Oak-Hickory Forests
- Dynamic Limitations of CO_2 Uptake by An Iron-Fertilized Antarctic Ocean
- Use of Tritium and Helium Isotopes to Define Groundwater Travel Times and Recharge Rates
- Increased Growth Efficiency and Compensatory Responses of Yellow-Poplar Trees to Elevated CO_2 Levels
- Identification of Important Radon Transport Mechanisms in the Southern Appalachians
- Study of Genomic DNA Structure Using Scanning Tunneling Microscopy

Therapeutic Drug Delivery to Tumors

Recently there has been optimism about targeting drugs and radioisotopes specifically to cancer cells with monoclonal antibodies (MoAb) and thus improving the therapeutic gain. While radiolabelled MoAbs have proven useful for localization of tumor sites in humans, both diagnostically and for planning surgical resection, the therapeutic efficacy of these reagents has been limited because of two major problems in the delivery of cytotoxic drugs.

First, the fraction of the total dose that reaches the target site is too small, and second, the distribution of the antibody in the tumor is nonuniform (i.e., most of the antibody stays near the blood cells and doesn't penetrate deep into the tumor mass). To address these problems, S. J. Kennel and J. Wesley of ORNL's Biology Division have shown the following: (1) MoAbs designed to target lung vessels can deliver as much as 90% of the drug administered to the desired target (Fig. B.1) [however, to apply this new finding to tumor therapy, it will be necessary to develop MoAbs that target the tumor blood vessels]. (2) In systems involving the use of MoAbs that bind directly to tumor cells, application of moderately high doses of MoAbs to tumor antigens results in deep penetration and relatively uniform distribution of the cytotoxic agent throughout the tumor, thereby resulting in more efficient therapy (Fig. B.2).

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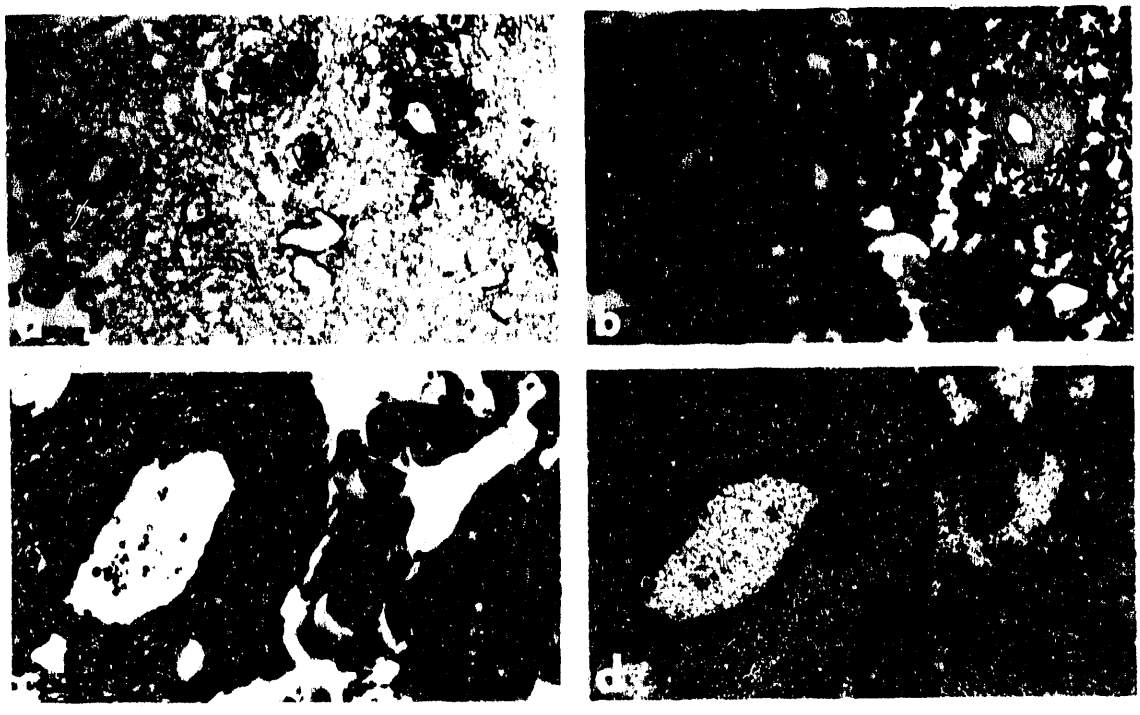

Fig. B.1. **Photomicrograph showing targeting of lung vessels by monoclonal antibodies (MoAb).** Panel "a" represents histology without the MoAb detection system. Panel "b" shows localization of MoAb (indicated by black) in normal lung tissue (no penetration into tumor tissue). Panels "c" and "d" illustrate localization at a higher (400x) magnification.

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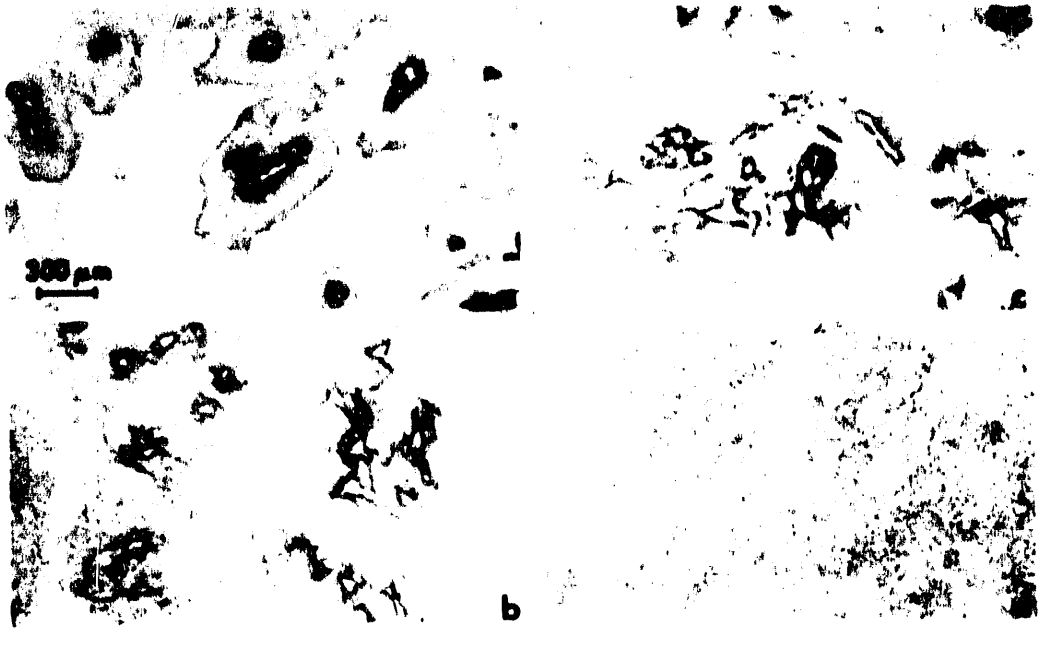

Fig. B.2. **Photomicrograph showing non-uniform distribution of monoclonal antibodies (MoAb) in tumor.** Panels "a" and "b" show that at low MoAb doses, the MoAb (black dots) bind to tumor cells near the supplying blood cells and do not penetrate to more distant tumor cells. Panels "c" and "d" illustrate that at higher MoAb doses, MoAb is more evenly distributed and penetrates to more-distant tumor cells.

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Identification of DNA Coding Sequences Using An Artificial Intelligence Approach

Among the many challenges facing the Human Genome Initiative are locating genes in the long stretches of deoxyribonucleic acid (DNA) sequences that make up the genome and identifying the protein-coding sequences that may be only a few percent of a given gene. Drs. Edward Uberbacher of the Engineering, Physics, & Mathematics Division, and Richard Mural of the Biology Division, Oak Ridge National Laboratory (ORNL), have developed a system, designated GRAIL, that is a significant improvement over current methods for locating coding regions in uncharacterized ("anonymous") DNA. They have analyzed the coding and the non-coding regions of DNA from a number of genes with well-established sequences. Parameters used in the analysis include the frequency of occurrence of the individual bases at each position within codons, frequency of specific hexameric sequences in coding and non-coding regions, fractal analysis of dinucleotide pairs, and other sequence properties.

They have used this information to train computer neural networks to recognize properties of coding and non-coding regions (Fig. B.3). Once trained, the networks are capable of examining a stretch of "unknown" DNA (well-characterized genes that were not used in the training) and localizing with >90% precision the positions of the coding regions, or exons, and the interspersed non-coding regions, or introns. The researchers, together with colleagues in other divisions of ORNL, are refining the approach to deal with shorter segments for more precise analysis and to identify other diagnostic properties of the sequence patterns.

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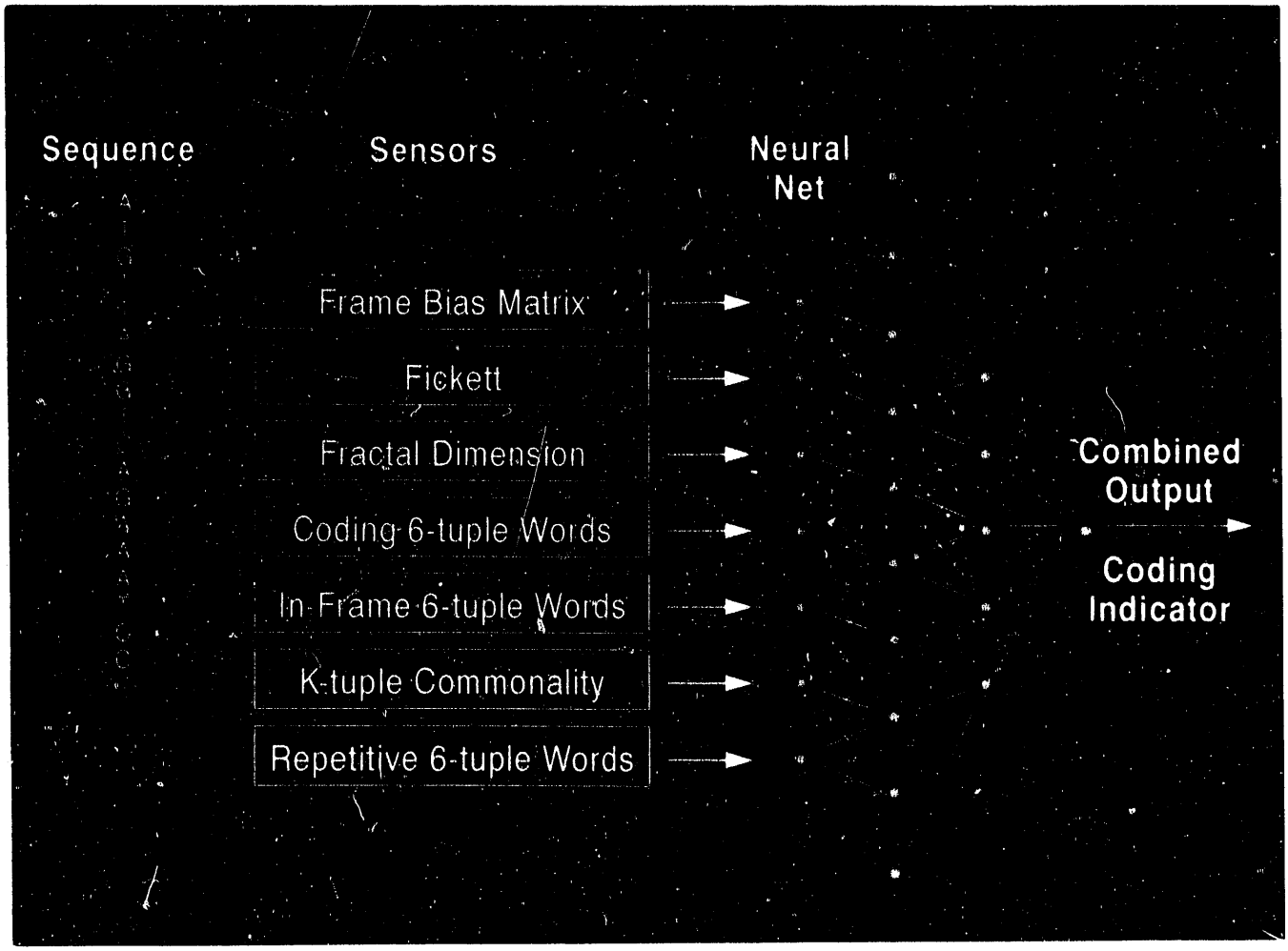

Fig. B.3. Diagram of the GRAIL neural network, used for locating coding regions in uncharacterized ("anonymous") DNA.

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Targeted Mutagenesis at Specific Genes in the Mouse Genome

The generation and molecular analyses of mutations in the mouse are proving to be an effective way of studying the function of genes on the mammalian genome. In an effort to complement its existing mouse mutagenesis programs in the Mammalian Genetics Section, the Biology Division of Oak Ridge National Laboratory has recently undertaken a new initiative to engineer specific molecular alterations into the mouse genome.

As part of this effort, cloned segments of deoxyribonucleic acid (DNA) with distinct sequence alterations are introduced into embryonic stem (ES) cells and are allowed to replace their corresponding sequences on the host chromosomes. The ES cells are then microinjected into an early-stage mouse embryo utilizing a specifically designed microscopic glass capillary (Fig. B.4). As the manipulated embryos mature, the ES cells contribute to the development of all tissue types, including the germ cells in the reproductive tissues, and will result in the generation of a chimeric animal. Offspring from the chimeric animal will then be used to generate individual transgenic mouse lines that contain the sequence alterations that were produced in the ES cells. In this way, mutations engineered at specific sites on the genome can be used to evaluate the functional role of those regions of DNA.

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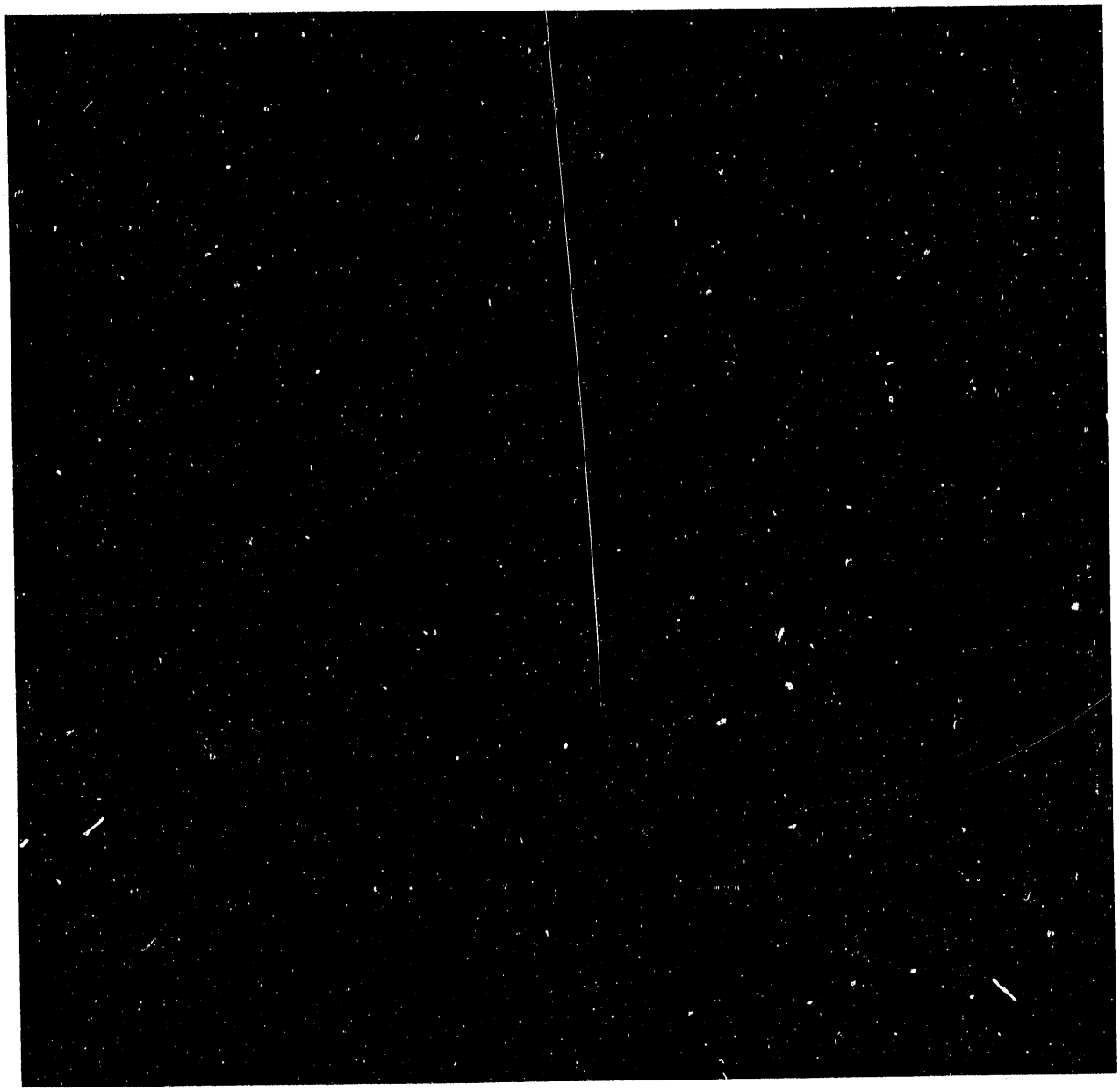

Fig. B.4. Microinjection of cultured mouse stem cells into a host blastocyst for the production of targeted mutations on the mouse genome.

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Study of Human Genetic Disease Syndromes Through Mouse Molecular Genetic Analyses

Several programs at Oak Ridge National Laboratory's (ORNL's) Biology Division emphasize exploiting the genetics of the mouse to study the nature, causes, and effects of human genetic disease. Homologies between regions of the mouse and human genomes, once defined, will permit a type of "surrogate genetics" to be developed for the human genome that is based on analyzing the molecular and organismal consequences of mutations mapping within the corresponding mouse genomic segment. A recent example of such integrated mouse-human genome analysis involves the animals pictured in Fig. B.5.

Mutations at the mouse pink-eyed dilution (*p*) locus are among hundreds of mutations that have been generated over the course of decades in mutagenesis experiments at ORNL.

E. M. Rinchik's group has discovered that deoxyribonucleic acid (DNA) probes mapping to the region associated with two complex human inherited disease syndromes in children–the Prader-Willi and Angelman Syndromes (PWS and AS)–map to the region of the mouse genome affected by these *p* mutations. PWS and AS are often associated with deletions of human chromosome 15 and are multisystem disorders. They often manifest a wide range of effects from individual to individual, in addition to the primary defect that defines the clinical diagnosis. Interestingly, several different classes of *p*-mutant mice manifest phenotypes, such as hypopigmentation shown in (Fig. B.5), facial dysmorphism/cleft palate, hypogonadism, hyperactivity, ataxia, and growth retardation, that are provocatively similar, albeit on a gross level, to those observed in children with PWS or AS. Rinchik's group is using the panel of mouse *p*-locus mutations in both physical-mapping and mutagenesis experiments aimed at trying to dissect, in mice, the individual components of these complex human syndromes.

ORNL-PHOTO 294-92

Fig. B.5. Mice mutant at the pink-eyed dilution (*p*) locus [left (pink-eyed dilute); center (intermediate pink-eyed dilute)] compared to wild-type (right).

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Field Manipulations of Natural Organic Matter and Inorganic Colloids in a Sandy Aquifer

The transport of natural organic matter (NOM) in groundwater is being studied to improve predictions of contaminant mobility in groundwater. John F. McCarthy, Environmental Sciences Division, Oak Ridge National Laboratory (ORNL), and co-workers had shown that NOM can greatly enhance the mobility of polychlorinated biphenyls and cadmium in laboratory soil columns by binding and co-transporting the contaminants; however, field experiments were needed to determine the extent and rate of NOM transport in aquifers, and to elucidate the chemical and hydrological properties of aquifers controlling the transport of NOM and of inorganic colloids. Water containing high levels of NOM was injected into a shallow sandy aquifer. Effects of the injection on inorganic colloids and on the abundance of groundwater bacteria were also monitored (Fig. B.6).

Although significantly retarded compared to the nonreactive tracer, the NOM moved rapidly through the aquifer, with an apparent retardation similar to that predicted from laboratory studies; both laboratory and field results support the hypothesis that NOM migration can be described as a multi-component transport process, with small hydrophilic components having the greatest mobility. NOM also had effects on the transport of metals and of inorganic colloids. The mobile NOM complexed iron on sand particles and increased the levels of the metal transported through the aquifer. The NOM also appeared to contribute to the transport of inorganic colloids by coating and stabilizing iron-oxide colloids formed by the introduction of oxygen into the suboxic aquifer during the NOM injection. The injection of the potential microbial substrate into the aquifer appeared to have little effect on the abundance of bacteria in the groundwater.

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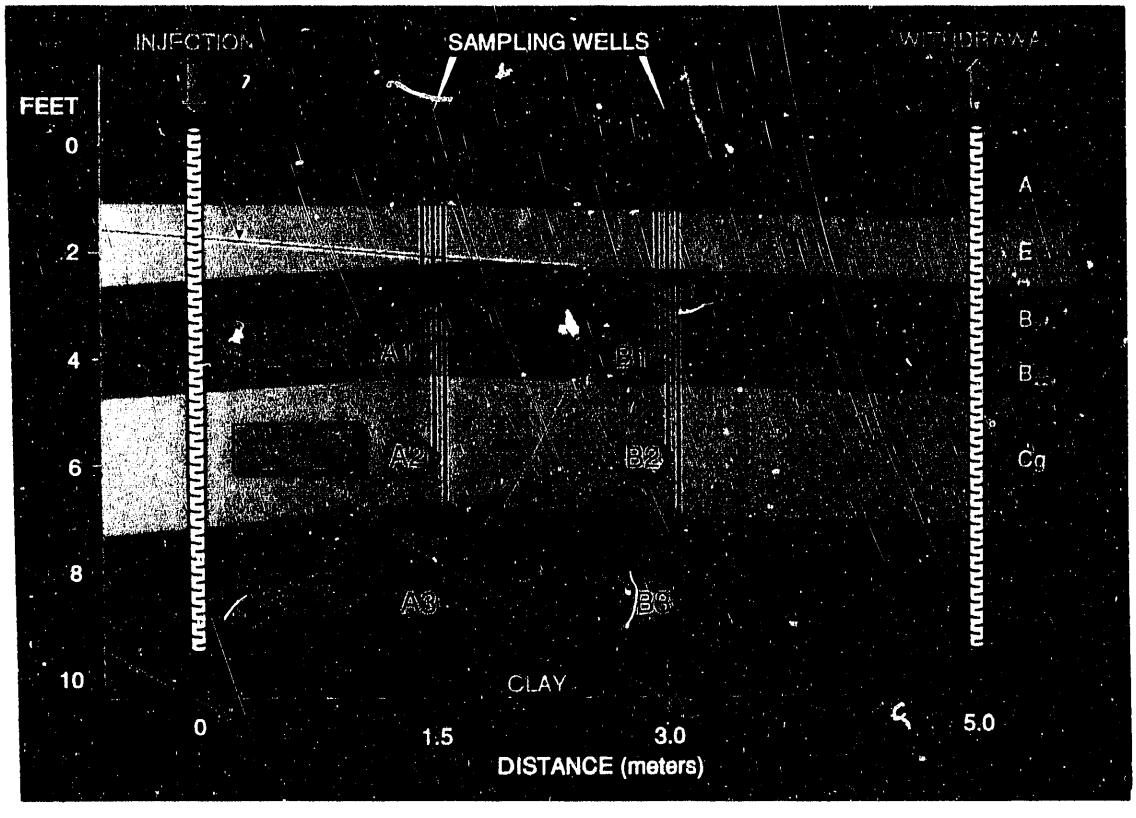

Fig. B.6. The field site is shown with a cross-sectional diagram of the injection, withdrawal and sampling wells. A large volume of NOM solution (80,000 L) was injected under a forced gradient, along with a nonreactive tracer to provide information on the average pore water velocity and dispersion characteristics of the media. The concentration histories of NOM, dissolved and colloidal iron, and bacteria were monitored in water recovered from the six sampling wells.

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Evaluation of the Effects of Moisture Gradients on Carbon Storage of Oak-Hickory Forests

Unresolved sinks in the global carbon cycle have led to renewed interest in long-term carbon storage capabilities of terrestrial ecosystems both as a means of resolving current unknowns and as a means of mitigating increasing levels of carbon dioxide (CO_2). Unfortunately, existing forest carbon storage estimates may not apply under the modified environmental conditions (i.e., warmer temperatures and altered precipitation) projected to result from global warming.

Measurements of tree growth and forest gas exchange are being conducted along topographic moisture gradients to provide information on key processes necessary to modify carbon budgets for future drought scenarios. The research sites are located on the Walker Branch Watershed in the Oak Ridge National Environmental Research Park and include mesic slopes, xeric slopes, ridgetop sites, and riparian zones. Dendrometer bands are used to measure seasonal changes in tree stem diameter to indicate the relative growth of canopy trees. Forest floor and stem respiration measurements are made to quantify biological sources of CO_2 flux to the atmosphere (Fig. B.7). Environmental data are collected, from which process-level models of the component carbon cycling processes are generated. These measurements, together with previous and/or future data on photosynthesis and stand structure, are being used to evaluate net carbon storage within these forest stands.

Seasonal stem growth of deciduous trees is exhibiting uniform phenological patterns of development among species and across topographic locations, indicating that models of carbon storage can be somewhat simplified. Conversely, topographic moisture patterns differentially affect species. Yellow-poplar shows marked reductions in growth on xeric slopes, but oak species seem somewhat insensitive to growth location. These observations agree with long-term growth trends on the Walker Branch Watershed that show little change in oak growth during the dry 1980s but as much as a 50% reduction in yellow-poplar growth during those same drought years. Recent dormant-season observations have also shown that forest floor respiration under photosynthetically active pine canopies is double that of forest floor locations under deciduous trees, indicating that spatial and temporal location can have a dramatic impact on the carbon budgets of forest stands.

The understanding of carbon cycling processes obtained from this research will allow robust estimates of forest carbon gain applicable to a variety of climate scenarios. Accurate estimates of forest ecosystem carbon sequestration are currently needed to resolve questions about the impact of biological systems on global carbon cycling.

ORNL-PHOTO 6989-91

Fig. B.7. Measurement of the efflux of carbon dioxide from the forest floor. Mieke Malmberg and Miguel Marrero, participants in the DOE High School Honors Workshop in Environmental Sciences, measure the efflux of carbon dioxide from the forest floor. Along with other measurements, the data are used in evaluating how much carbon dioxide is sequestered by upland oak forests. Results of the evaluation will help researchers determine whether reforestation would be a viable means of counteracting global warming associated with increased levels of atmospheric carbon dioxide.

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Dynamic Limitations of CO_2 Uptake by An Iron-Fertilized Antarctic Ocean

John Martin and his colleagues have proposed that iron fertilization of the Antarctic Ocean would cause a significant reduction in atmospheric carbon dioxide (CO_2) content. The idea is that plant production in the nutrient-rich surface waters of the Antarctic could be stimulated by the addition of dissolved iron, thereby reducing the CO_2 partial pressure in these waters and allowing CO_2 to flow from the atmosphere into the Antarctic Ocean. However, the rate at which surface waters in the Antarctic Ocean are carried into the interior of the ocean is too slow to effectively carry away CO_2 delivered by the atmosphere. The distribution of tritium and radiocarbon in the Antarctic water column provides the best estimate of the rate at which surface waters in the Antarctic are replaced by upwelling of the underlying water. The distribution of these tracers is used to constrain a box model designed to yield the response of atmospheric CO_2 content to a successful iron fertilization. Model results indicate that after 100 years of totally successful fertilization, the atmosphere's CO_2 content would be lowered by only between 5 to 10% (Fig. B.8). Thus, if a century from now the atmosphere's CO_2 content were 600 ppm without fertilization, with full fertilization over the entire century it would instead be between 570 and 540 ppm. Hence, even if iron fertilization worked to perfection, it would not significantly reduce the atmospheric CO_2 content.

ORNL-DWG 91MC-13918B

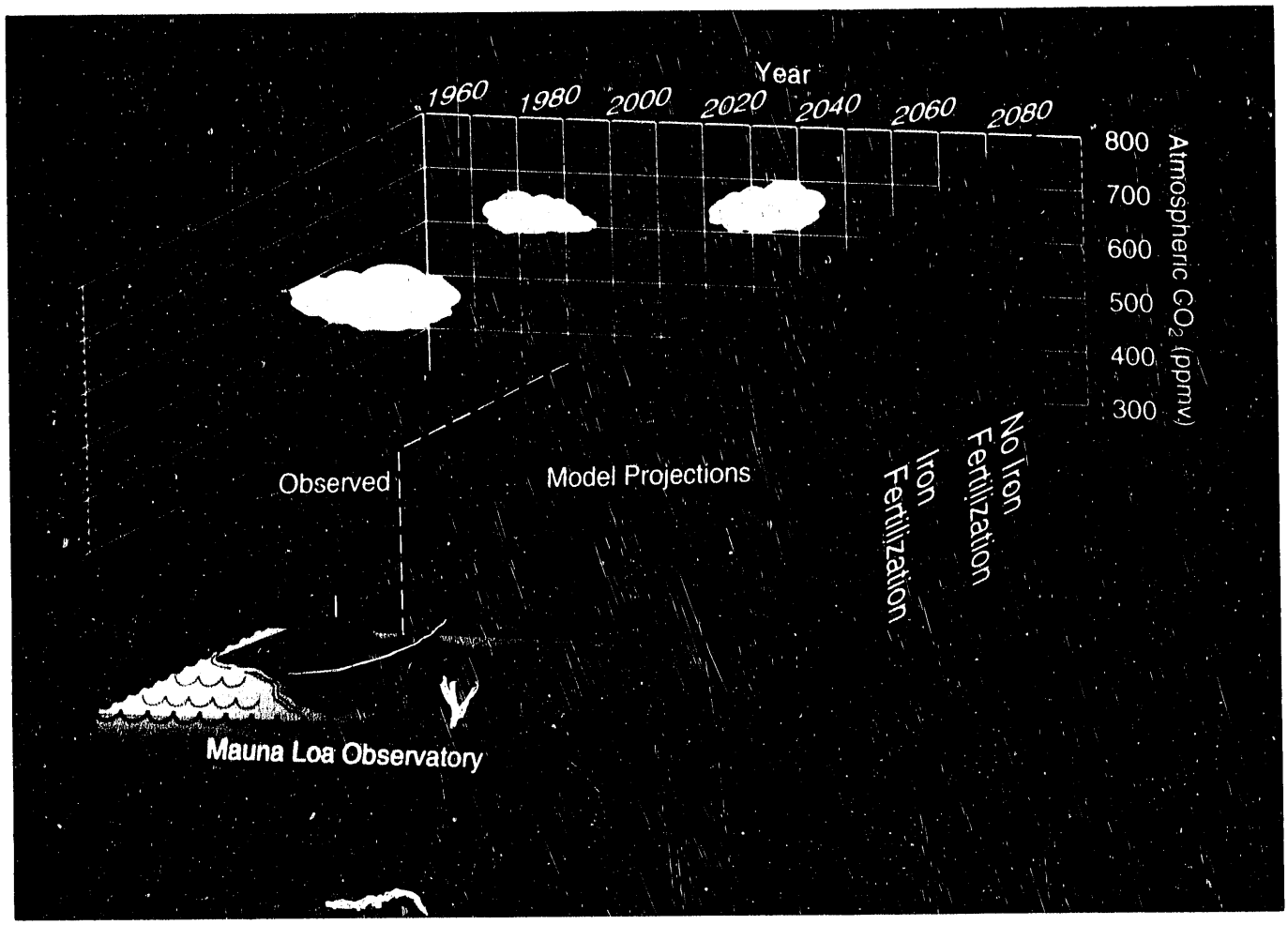

Fig. B.8. Predicted reductions in atmospheric CO_2 concentrations from iron fertilization of Antarctic oceans. ORNL ocean models calibrated to observed CO_2 concentration at the Mauna Loa Observatory in Hawaii indicate that if iron were added to the Antarctic oceans, the subsequent decrease in atmospheric CO_2 would be only about one-third of what was first hypothesized.

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615-576-3434 (FTS: 626-3434)

Use of Tritium and Helium Isotopes to Define Groundwater Travel Times and Recharge Rates

Radioactive tritium (^3H; half-life = 12.4 years) in precipitation (arising primarily from above-ground testing of thermonuclear devices) has been entering groundwater systems since the mid 1950s, with peak values occurring in the mid 1960s. Tritium activities in precipitation are temporally and spatially variable and hence it is difficult to use ^3H alone to determine groundwater ages and recharge rates. However, combined measurement of ^3H and its stable daughter helium-3 (^3He) can be used to determine groundwater ages without knowledge of the ^3H input activity. Vertical profiles of ^3H and He isotope ratios have been measured in groundwater from the well-characterized Borden aquifer located in Ontario. The sum of ^3H and tritiogenic ^3He ($^3He^*$) is used as an equivalent nondecaying tracer, while the ratio of $^3He^*$ to ^3H is used to compute groundwater ages. The sum of ^3H and $^3He^*$ clearly defines the mid-1960s ^3H bomb peak at several locations.

The accuracy of the $^3H/^3He$ dating method depends on the ability of the saturated zone to retain $^3He^*$ against diffusive loss at the water table and on the amount of dispersive mixing that occurs within the saturated zone of shallow unconfined aquifers. Helium-3 confinement is strong while dispersive mixing is weak in the Borden aquifer, resulting in an excellent delineation of groundwater travel times. Computed $^3H/^3He$ age profiles are compared to travel times predicted using a previously calibrated flow model. Although the $^3H/^3He$ age profiles are vertically offset from the modeled travel times, the travel time and $^3H/^3He$ age gradients compare exceptionally well. Recharge rates have been computed using the $^3H/^3He$ age gradients and vary from 62 cm/year beneath the Borden landfill to 14 cm/year north of the landfill. The $^3H/^3He$-computed recharge agrees well with the recharge function used in previous flow modeling (Fig. B.9).

The results of this study indicate that the $^3H/^3He$ dating method is extremely promising for (1) defining baseline recharge values in the context of global climate change, (2) evaluating groundwater flow patterns in complex shallow aquifers (e.g., waste sites), and (3) evaluating the scale dependence of transport processes in the subsurface.

ORNL-DWG 92Z-4989

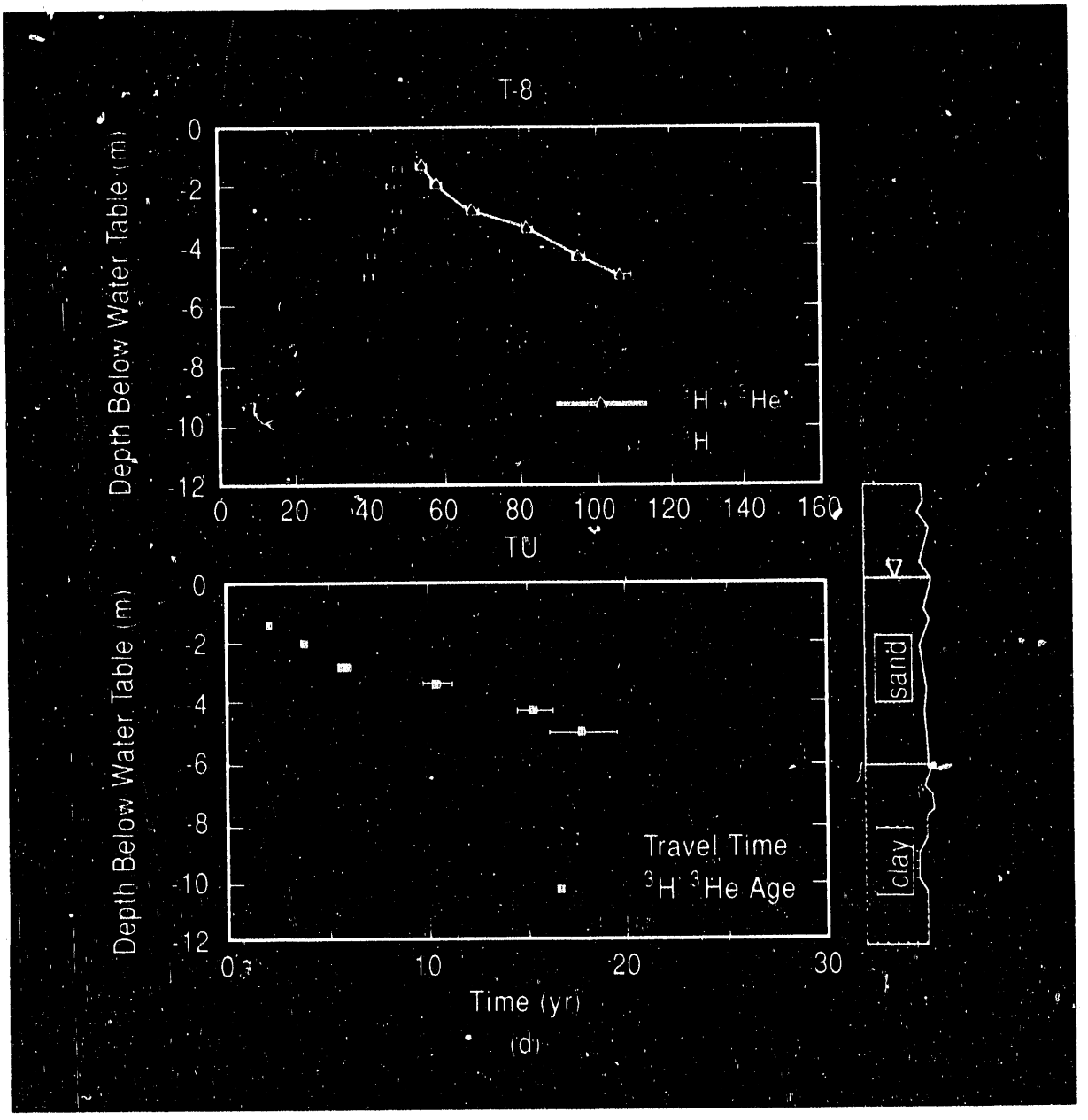

Fig. B.9. Tritium, $^3H + {}^3He^*$, computed $^3H/^3He$ age, and modeled groundwater travel time as a function of depth below the water table at monitoring wells T-8.

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Increased Growth Efficiency and Compensatory Responses of Yellow-Poplar Trees to Elevated CO_2 Levels

Increased forest growth could provide an additional sink for globally rising atmospheric carbon dioxide (CO_2) concentrations. To test whether short-term stimulations of tree growth by elevated CO_2 levels can be sustained without additional inputs of other environmental resources, yellow-poplar (Liriodendron tulipifera) saplings were grown for most of three growing seasons in open-top field chambers with continuous exposure to ambient or elevated concentrations of atmospheric CO_2. Growth efficiency, or the annual increment of stem mass per unit leaf area, increased significantly with rising CO_2 concentrations (Fig. B.10).

The increase in growth efficiency was attributed to a sustained increase in photosynthesis, coupled with a lower rate of foliar respiration in the CO_2-enriched trees. Compensatory responses in leaf and fine root production reduced the potential increase in carbon storage in elevated CO_2 levels, and the effects of CO_2 on tree biomass were modest and not significant. However, these compensatory responses favor efficient use of resources over the longer term. The duration of this experiment is the longest any forest trees have been exposed to elevated concentrations of atmospheric CO_2 levels. The results show that the short-term responses of yellow-poplar seedlings to elevated CO_2 levels can be sustained over several growing seasons under field conditions, but that resource interactions and feedbacks will modify the response of forests to rising CO_2 concentrations.

ORNL-DWG 92Z-4990

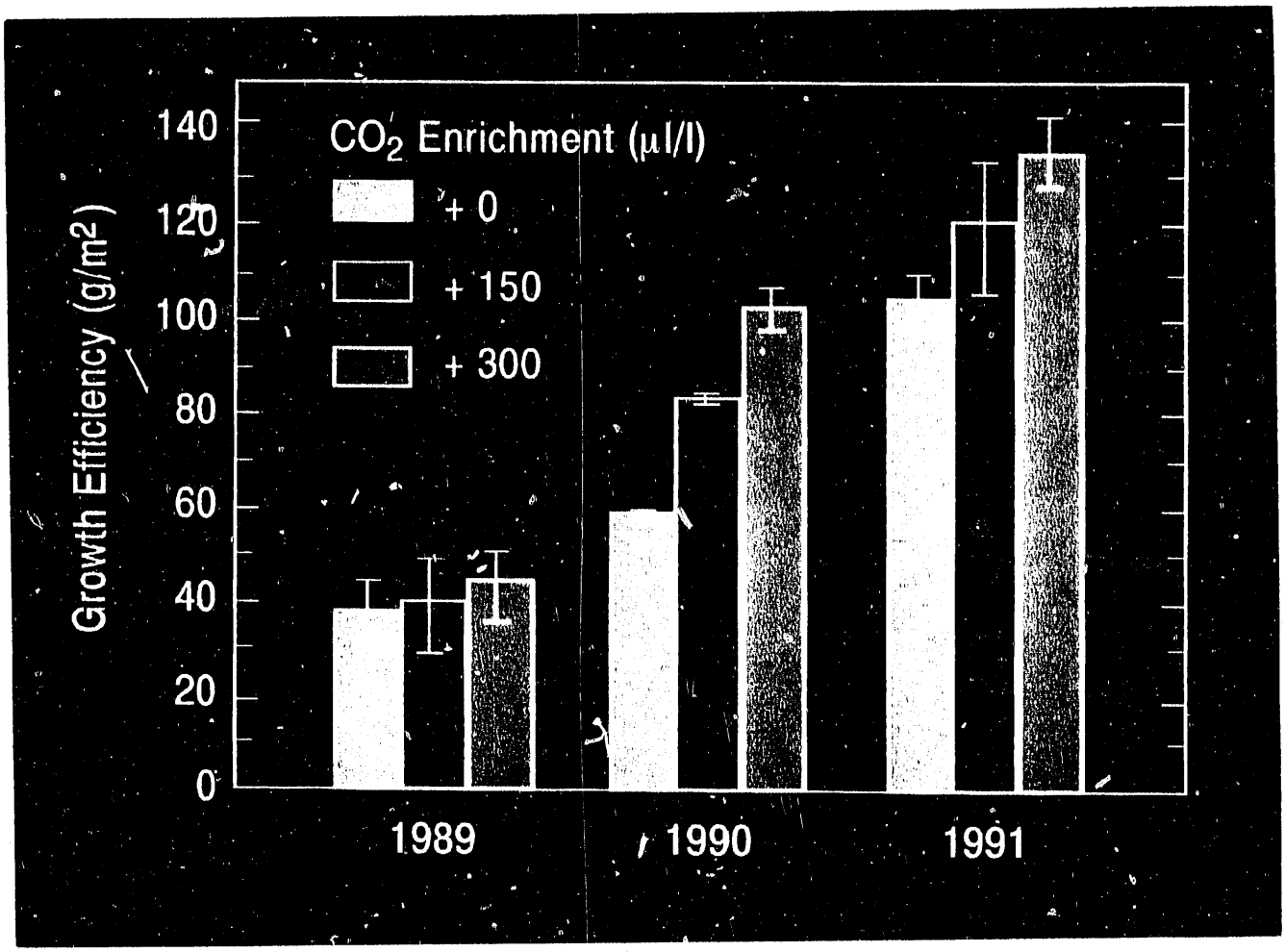

Fig. B.10. Growth efficiency of yellow poplar saplings during the three seasons of exposure to elevated CO_2. The plants were grown in ambient CO_2 (yellow bars), ambient air + 150 µmol CO_2 mol^{-1} (red bars), or ambient air + 300 µmol CO_2 mol^{-1} (blue bars). Growth efficiency was calculated as annual stem mass increment divided by leaf area at the end of the year. Data are the means (± SE) of five plants in each of two replicate chambers. The effect of CO_2 was significant at $P = 0.041$ in 1990 and $P = 0.002$ in 1991.

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Identification of Important Radon Transport Mechanisms in the Southern Appalachians

In hilly limestone regions of the southeastern United States, elevated indoor radon levels are fairly common. A decade of research has revealed that cavities within the karst underlying a house can enlarge the reservoir of radon-rich soil gas that a house can draw on. An enlarged subsurface radon reservoir manifests itself in several ways. If a house can tap into a system of solution cavities, then high indoor radon levels are possible even when the soil gas radon concentrations are not abnormally high. For populations of houses in karst terrains, researchers in the Health and Safety Research Division (HASRD) of Oak Ridge National Laboratory find winter-to-summer ratios of indoor radon to be lognormally distributed, with the highest values apparently belonging to houses able to communicate with large underlying reservoirs.

The topology of the terrain and the disposition of the houses relative to an underground circulatory system of cavities determine the season, winter or summer, of maximum indoor radon concentration. Aerostatic pressure differences created by temperature differences between underground and outside air can develop to produce convective and advective movements of subterranean air. The temperature of air inside caves is fairly constant at about 14°C. HASRD staff members have observed summertime venting of radon-laden air from openings at the lower end of circulatory solution cavities (Fig. B.11). Coincidentally, neighboring houses have increased indoor radon levels. This topographic condition exists in sections of Huntsville, Alabama. In Oak Ridge, Tennessee, ridge houses are often at the upper ends of circulatory systems of solution cavities; underground air movements now amplify indoor radon in wintertime. In areas likely to experience elevated indoor radon during warm weather, radon screening measurements to identify problem houses should be conducted during the summer.

ORNL-PHOTO 6431-90

Fig. B.11. Examination of monitoring devices used to measure indoor and outdoor radon levels. A research team from the Health and Safety Research Division (HASRD) of Oak Ridge National Laboratory made radon measurements in basements and living rooms and in damp and occasionally dripping-wet cavities and caves. Shown is R. B. Gammage.

Principal investigators:
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615-574-6256 (FTS: 624-6256), 576-2712 (FTS: 626-2712), and 576-7607 (626-7607)

Study of Genomic DNA Structure Using Scanning Tunneling Microscopy

The Human Genome Program is seeking to find new technologies to aid in accelerating the reading of sequence of bases for the entire human genome, which has about three billion bases. Researchers in the Health and Safety Research Division (HASRD) of Oak Ridge National Laboratory (ORNL) are developing a novel class of microscopes named as a possible "cost effective, high volume technique" for deoxyribonucleic acid (DNA) sequencing. In fact, these new microscopes are the only techniques where the intact DNA molecule can be visualized, and they have the potential for mapping and sequencing. These microscopes work by scanning a tiny probe very near a surface onto which DNA molecules have been applied.

The atomic force microscope (AFM) mechanically "feels" the surface (Fig. B.12) while the scanning tunneling microscope (STM) electrically "feels" the sample using a small electrical current. Both of these instruments have demonstrated atomic resolution on a number of surfaces. A third type of microscope which was invented at ORNL is the photon scanning tunneling microscope (PSTM), which uses an optical current to a sharpened optical fiber to sense the sample.

These new microscopes have required the development of special sample preparation for properly mounting the DNA strands. Recently we have seen breakthroughs in this area. These came as the result of the combined efforts of personnel from HASRD and the Biology and Chemistry divisions at ORNL.

ORNL-PHOTO 295-92

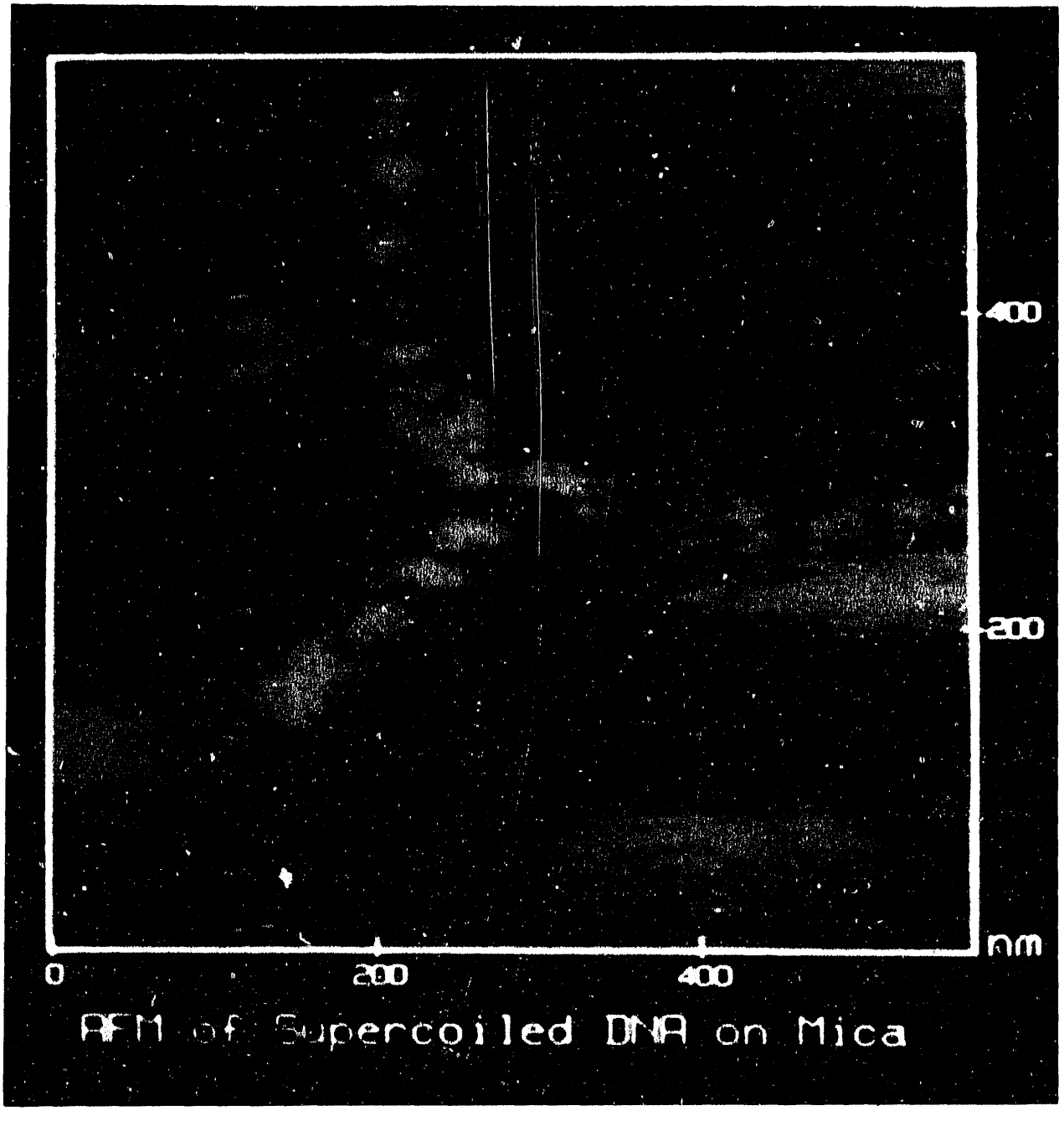

Fig. B-12. An Atomic Force Microscope (AFM) image of a segment of linearized plasmid DNA twisted about itself to form a side branch. This supercoiling of DNA can be routinely imaged with the AFM but the manufactured probe tips available today are not yet sharp enough to image the double helix of DNA.

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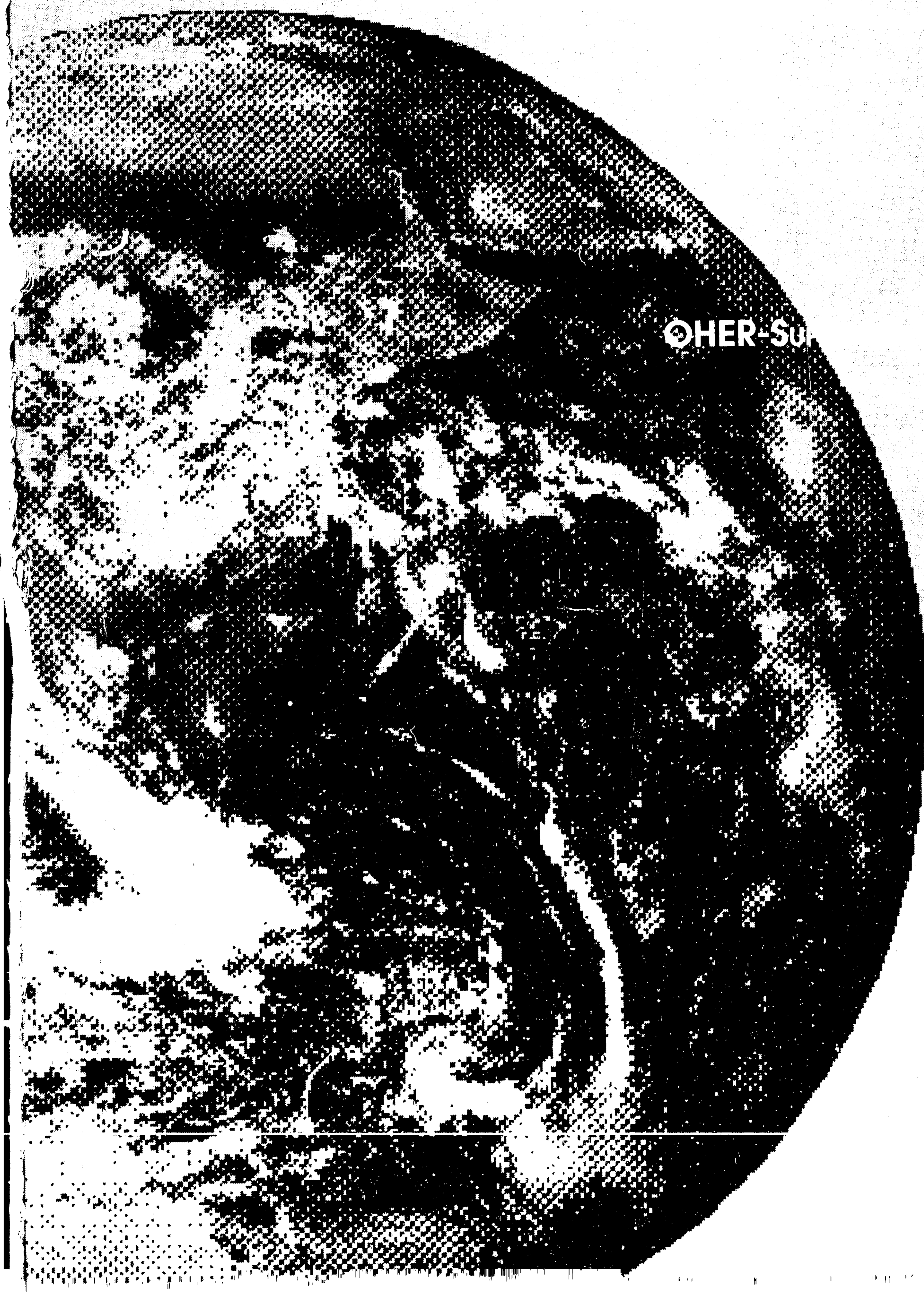
615-574-6215 (FTS: 624-6215) and 574-6214 (FTS: 624-6214)



OHER-Supported Publications

A list of OHER-supported publications from ORNL's BER Program for FY 1991 follows. This list of 269 publications include 109 refereed journal articles, 44 reports and/or documents, and 27 proceedings, books, and chapters.

The list is organized by ORNL division as follows: (1) Analytical Chemistry, (2) Biology, (3) Central Management Offices, (4) Engineering, Physics, and Mathematics, (5) Environmental Sciences, (6) Health and Safety Research, (7) Metals and Ceramics, and (8) Physics.

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