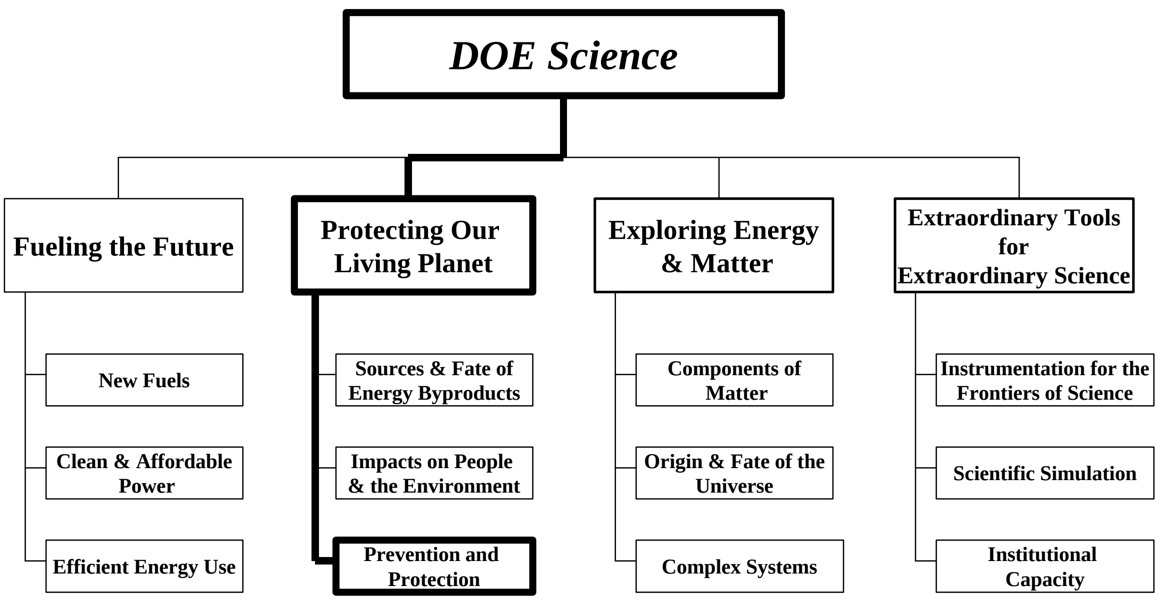
Chapter 7
Prevention and Protection

Scientific Challenge: ***To create new scientific approaches to protect the biosphere from the effects of energy byproducts.***



Chapter 7
Prevention and Protection

Table of Contents

Page

Pollution Minimization ... 71
Description, Objectives, and Research Performers ... 71
Research Challenges and Opportunities ... 71
Research Activities ... 72
Accomplishments ... 72

Cleanup and Remediation ... 73
Description, Objectives, and Research Performers ... 73
Research Challenges and Opportunities ... 73
Research Activities ... 73
Accomplishments ... 74

Carbon Sequestration ... 74
Description, Objectives, and Research Performers ... 74
Research Challenges and Opportunities ... 74
Research Activities ... 75
Accomplishments ... 75

Health Protection—Regulation and Medicine ... 76
Description, Objectives, and Research Performers ... 76
Research Challenges and Opportunities ... 76
Research Activities ... 77
Accomplishments ... 77

Portfolio Summary ... 78

A technological revolution is underway that will impact America's most important industries, including agriculture, chemicals, medicine, and energy production. The Department's research in genetic and biomolecular structure and in computational biology is initiating this revolution. In the future, the nation will have truly remarkable technological capabilities at its command. Energy production from fossil and renewable resources will have higher yields and generate negligible environmental pollution. New varieties of plants will be developed for renewable biomass-based energy production using our knowledge of the genetic code. New biomolecules designed for efficient energy production, environmental cleanup, and management of atmospheric carbon will have been created using design methods similar to those currently used in the manufacture of industrial components.

These advances will all stem from new knowledge of the molecular nature of life and of materials. In particular, they will arise from our increasing knowledge of the relationships between macromolecular structure and function, and from our ability to modify structure to create particular functions or properties in macromolecules.

When the veil of wartime secrecy was lifted from the nuclear reactor at the Clinton Laboratories (now Oak Ridge National Laboratory) in 1946, the Atomic Energy Commission (AEC) inherited a developing field of nuclear medicine full of potential. New radioisotopes—iodine-131, technetium-99m, carbon-14, thallium-201, and gallium-67, to name a few—were produced for the biomedical community. Their impacts on diagnosis and therapy have been enormous. In 1995, nearly one million thallium-201 heart scans were performed in the United States alone. About 13 million patients per year, roughly one-quarter of all U.S. inpatients, receive technetium-99m scans. But the diagnostic value of radioisotopes could only be realized with the simultaneous development of corresponding imaging devices. Simple imaging devices gave way to devices that produced images in three dimensions. AEC research laid the foundation for the development of widely used CT (computed tomography) and PET (positron emission tomography) scanners. Today, imaging technology is central not only to medical diagnosis but also to understanding organ function and dysfunction.

Pollution Minimization

Description, Objectives, and Research Performers

A broad range of pollution minimization research is supported that impacts energy production and use. The DNA sequence and functional capabilities of microbes that produce methane or hydrogen, for example, are characterized. This information, coupled with structural and computational biology research, provides opportunities for the use and redesign of microbes for energy uses. Engineering research is conducted on combustion and fuel bioprocessing for more efficient fuel use and waste minimization. Research on non-automotive battery systems improves battery size, weight, life, and recharge cycles. Research is conducted primarily at national and other government laboratories and universities and, to a lesser extent, industrial firms.

Research Challenges and Opportunities

Microbes make up approximately 60% of the earth’s biomass. They have survived on earth for over 3.7 billion years and are found surviving extremes of heat, cold, radiation, pressure, salt, and acid. An important scientific challenge is to identify microbes and microbial capabilities that already hold solutions to important problems, such as efficient energy production, environmental cleanup, and management of atmospheric carbon.

High throughput structural biology and computational approaches are needed that can better keep pace with advances in DNA sequencing ability, and to determine the structure and function of large numbers of useful proteins. The resultant biological information, coupled with a better understanding of the engineering and use of nanoscale systems can deliver powerful new solutions for producing and using energy with minimal pollution.

In order to achieve higher energy yields and negligible environmental pollution, researchers are challenged to develop and refine combustion models used to predict the efficiency and emission characteristics of combustion devices and to optimize and control combustion processes.

Research Activities

The DNA sequences of energy-related microbes are determined and annotated to identify all the potential genes encoded in their DNA and to get clues about their potential functions. Structural information is determined on selected proteins from these microbes. Research is conducted on combustion-related chemical physics and in the fundamental chemical engineering sciences underpinning energy intensive chemical processes including electrochemical storage and conversion and turbulence in combustion.

Accomplishments

- A paper describing the DOE-funded sequencing of the methane-producing microbe, *Methanococcus jannaschii*, was recognized by *Science* and *Discover* magazines as one of the top discoveries of 1996. The availability of information on the complete DNA sequence of this and many other microbes provides opportunities for the development of new energy sources, tools to clean up the environment, therapeutic and diagnostic resources for medicine, and important industrial products.

- The DNA sequences of several energy-related microbes have been or are being determined to provide information needed to develop new or improved energy sources that minimize pollution. The microbes being characterized include *Archaeoglobus fulgidus* (active in oil well souring), *Thermotoga maritima* (used for energy generation from biomass), *Methanobacterium thermoautotrophicum* (a methane producer), and *Carboxydothermus hydrogenoformans* (a hydrogen producer).

- A simple, elegant experiment demonstrated an error in current models for basic combustion processes. This new knowledge will accelerate our ability to understand and control combustion.

- Basic science research has led to the development of current generation high energy and power lithium and lithium ion batteries, improvements in the safety of rechargeable batteries, and thin film lithium batteries half the thickness of household plastic wrap.

Cleanup and Remediation

Description, Objectives, and Research Performers

Natural and Accelerated Bioremediation Research (NABIR) provides fundamental science that serves as the basis for developing cost-effective bioremediation of radionuclides and metals in the subsurface at DOE sites; understanding intrinsic bioremediation and opportunities for accelerated bioremediation using chemical and microbial amendments; integrating bioremediation with conventional physical-chemical remediation to accelerate site cleanup; and evaluation of bioremediation by regulators, local communities, and other stakeholders. NABIR emphasizes characterization and use of microbes and microbial communities with bioremedial potential. The William R. Wiley Environmental Molecular Sciences Laboratory (EMSL) operates more than 100 leading-edge computational and research systems as part of a national collaboratory user facility for molecular level environmental research. Research is also supported on fundamental molecular level questions underlying the most energy-consuming industrial process, separations, a key component of environmental cleanup. Research is conducted at national laboratories, universities, and industrial firms.

Research Challenges and Opportunities

Former DOE weapons sites contain complex mixtures of chemicals, metals, and radionuclides that need to be cleaned up. It may be possible to supplement or replace current cleanup strategies with new approaches that will be more efficient and cost effective. Developing these new cleanup strategies requires a wide array of scientific information and technological developments. We need to (1) determine the fate of metals and radionuclides in complex, heterogeneous matrices such as subsurface sediments; (2) scale up research from the laboratory to field scale; (3) communicate research findings to a broad audience such as regulators, site managers, tribes and communities; (4) identify, engineer, and exploit microbes with bioremediation potential; (5) develop improved and novel separation technologies, including ceramic membranes, new materials derived from combinatorial chemistry approaches, and novel separations (based on self-assembly systems, combined separation and reactive systems, tailored inorganic systems, and the use of macromolecules such as dendrimers); and (6) develop and implement ultra-sensitive detection capabilities such as single molecule detectors.

Research Activities

Research studies are underway to determine the DNA sequences of microbes with bioremediation potential and to “annotate” the sequences to identify all potential genes and obtain clues about their potential functions. Scientists are seeking to determine structural information on selected microbial proteins. NABIR projects address the biotransformation of contaminants, microbial community dynamics, biomolecular science and engineering to improve and exploit the bioremedial capabilities of microbes, biogeochemistry, assessment of the effectiveness of bioremediation, acceleration of the natural bioremedial capabilities of native microbes, and bioremediation-related societal issues and concerns. Research is supported to improve understanding of methods for separating mixtures of gases, liquids, solids, and their component molecules, cations, and anions.

Accomplishments

- Bioremediation-related microbes that have been or are being sequenced include *Deinococcus radiodurans* (for radiation resistance), *Shewanella putrefaciens* (uses with organics, metals, radionuclides), *Pseudomonas putida* (a metal reducer), *Dehalococcoides ethenogenes* (for solvent metabolism), *Thiobacillus ferroxidans* (a metal reducer), *Caulobacter crescentus* (for metal removal), *Desulfovibrio vulgaris* (a metal reducer), and *Clostridium acetobutylicum* (which has waste remediation potential).

- A set of solvent-degrading genes from one microbe, *Pseudomonas putida*, has been successfully introduced into the radiation- and desiccation-resistant bacterium *Deinococcus radiodurans*. This exciting development indicates the potential of designing microbes that could, potentially, survive in high radiation environments common to many former DOE weapons sites while at the same time degrading or detoxifying other contaminants present at those sites.

- Cutting edge fluorescence microscopy and spectroscopy have been used to study the reaction dynamics of individual enzymes that degrade organic contaminants in real time.

- Over 600 scientists used EMSL to carry out cutting-edge environmental and molecular research in its first year of operation.

- A new technetium extraction process has been developed, for potential use in the Hanford waste tanks. This process will significantly reduce the final volume of waste that will require costly processing and long term storage.

- High-resolution images of metal oxidizing and reducing bacteria have been taken, helping to reveal the role of these organisms as potential agents for bacterial bioremediation. High-resolution spectroscopic measurements have revealed the chemical state of pollutants at extremely low concentrations.

Carbon Sequestration

Description, Objectives, and Research Performers

This new program will provide scientific knowledge on biological processes that drive carbon exchange between the oceans and the atmosphere and between the atmosphere and the terrestrial environment. Genomic DNA sequences will be determined for microbes that play a role in the sequestration of carbon in the oceans or the terrestrial biosphere. Options for storing excess carbon in the deep oceans, in subsurface geologic structures, or using biological solutions will be investigated. Research will be conducted at national laboratories, universities, and industrial firms.

Research Challenges and Opportunities

Implementing carbon management on the scale needed to impact global carbon dioxide levels requires new levels of understanding, from the molecular to ecosystem scale, about geological, chemical, physical and biological interactions between carbon and the environment. Completely new approaches to carbon management will be investigated. These approaches will build on scientific breakthroughs in molecular design or genetic engineering of plants and microorganisms and on advances in understanding of the complex chemical and physical interactions that occur with subsurface geologic structures and aquifers. New techniques to monitor biogeochemical processes and ecosystem impacts of changes in the carbon cycle will be developed to anticipate and assess the environmental impacts associated with various biological and physical approaches to carbon sequestration.

Research Activities

This new research program will issue its first solicitations for research proposals in FY 1999. Biological research will focus on carbon sequestration in soils and the biosphere in both natural and managed ecosystems. Impacts of alterations in the carbon cycle on other elemental cycles, such as nitrogen, will be determined. Microbial genome research will identify and characterize (including genomic DNA sequencing) microbes that play a role in natural carbon cycles to develop novel strategies and tools for manipulating and modeling entire biochemical reaction pathways or regulatory networks that could be used to increase their role in carbon sequestration. Photosynthesis research will focus on understanding and characterizing the genes and regulatory mechanisms involved in photosynthetic fixation of carbon and the subsequent metabolism of fixed carbon. Research may lead to new strategies for replacing fossil fuels with biologically fixed carbon, including fuels and chemical feedstocks, and for altering steady-state levels of atmospheric CO_2. The potential for deep underground sequestration of carbon will lead to research that addresses (1) geometric, structural, and hydrological reservoir descriptions of potential storage sites, (2) changes in reservoir characteristics with drilling and fluid injection, and (3) the physics of multiphase flow in fractured rock systems. Finally, the potential ecological impacts of various carbon sequestration strategies will be evaluated.

Accomplishments

Accomplishments that underpin this new research program include:

- Genomic DNA sequencing of carbon sequestration related microbes, including *Chlorobium tepidum* (a major player in global carbon management) and *Thiobacillus ferroxidans* (for CO_2 fixation), was completed.
- Workshop activities including scientists from government laboratories, universities, and industry led to the publication of *Carbon Management: Assessment of Fundamental Research Needs*.
- The basic biophysics and biochemistry of photosynthetic energy capture and of the photosynthetic apparatus have been characterized.
- Scientists have improved understanding of basic mineral-fluid interactions important for developing strategies to sequester carbon in geologic structures.

- Advances in geophysical imaging needed to understand subsurface structures and properties have been made.
- Methods were developed to evaluate natural and human-perturbed processes in the geologic environment.
- Scientists have directly measured the amount of carbon gained or lost by representative terrestrial ecosystems—a critical first step to being able to enhance an ecosystem's ability to store carbon.

Health Protection—Regulation and Medicine

Description, Objectives, and Research Performers

Human health is protected through better understanding of health risks from low-level radiation and from improvements in medicine. New information is needed by regulatory agencies to decrease uncertainty of determining health risks from low-level radiation exposures, to help determine the shape of the dose-response relationships after low level exposure, and to achieve acceptable levels of human health protection at the lowest possible cost. Radiolabeled molecules are developed for noninvasive studies of metabolic and physiological processes and for the diagnosis and treatment of disease. New, sensitive, high-resolution positron emission tomography (PET) instruments for imaging and magnetoencephalography (MEG) for probing magnetic fields in the brain are being developed. Medical applications of lasers are also emphasized. New imaging technology will be used to “see” genes in action, as a molecular monitor for vital organ function, and to monitor the effects of chemo-, radio- and gene-therapy. Boron neutron capture therapy (BNCT), a cancer treatment based on the interaction of boron-containing compounds with thermal neutrons that can theoretically kill cancer cells without affecting surrounding normal cells, is being investigated. Novel boron-containing compounds and facilities to generate medically useful neutron beams are being developed and phase I/II clinical trials in brain and skin cancer are being conducted to evaluate BNCT toxicity and efficacy. Research is conducted at national laboratories, universities, and government laboratories.

Research Challenges and Opportunities

New radiotracer tools are needed to identify steps in gene expression pathways that may be altered in disease states. New molecular markers for specific biochemical phenotypes are needed as targets for molecular-based treatment of cancer and degenerative brain disorders. Rapid progress in the human genome program and in the development and screening of libraries of new chemical compounds can be used to improve the design and synthesis of new radioisotopes that are directed to specific molecular targets. There are significant opportunities to improve imaging detector technology and algorithms used for information processing that will improve spatial resolution, quantitative accuracy, and detection efficiency of medical imaging. The use of these techniques will be expanded from clinical uses in humans to valuable experimental studies in animals. New classes of boron compounds that selectively accumulate in cancer cells compared to surrounding normal cells are needed for BNCT. Neutron beams enriched for tissue penetrating epithermal neutrons are needed that have minimal contamination with toxic thermal neutrons, fast neutrons, and gamma rays. Phase I/II BNCT clinical trials need to be completed with adequate numbers of patients to unambiguously assess toxicity and effectiveness.

Research Activities

Researchers seek to identify and characterize genes and gene products that determine cellular responses to low doses of radiation and that affect individual susceptibility to low dose exposures. This allows development of methods to incorporate molecular-level information into the estimation of overall health risk. New synthetic organic chemistry techniques are being developed to rapidly radiolabel a wide variety of molecules for targeting many in vivo sites. New radiolabeled compounds are evaluated in vitro and in vivo. Preclinical evaluations are conducted on radiopharmaceuticals for heart and brain disorders, neurodegenerative diseases, cancer, and for development of new molecular targeted therapies.

Ongoing research includes development of a PET scanner capable of <2 mm resolution. miniature radionuclide imagers for small animal and organ specific imaging, a full-head biomagnetometer for the human brain, medical applications of laser technology, and new technologies for merging PET and magnetic resonance imaging (MRI) for anatomically well-defined images of the body's biology. Pre-clinical development of novel boron-containing compounds is underway, and their pharmacokinetics and bio-distribution are being studied. Fission reactors at MIT and McClellan Air Force Base and the accelerator at Lawrence Berkeley National Laboratory are being upgraded to treat patients safely and effectively with enriched epithermal neutron beams. Phase I/II clinical trials of BNCT for the treatment of brain cancer and melanoma are underway at Brookhaven National Laboratory and MIT/ Beth Israel Deaconess Hospital.

Accomplishments

- Technetium-99m generators for bone scanning and other diagnostic studies are now used in 35,000 clinical procedures a day.

- Fluorine-18-fluorodeoxyglucose is now used with PET for imaging and mapping of the normal and diseased human brain.

- Meta-iodobenzylguanidine is a powerful new radiopharmaceutical used to visualize and treat deadly neuroblastomas in children.

- New carbon-11 and fluorine-18 radiotracers are being used to develop new therapies and to study substance abuse, and neurodegeneration.

- New imaging devices include the world's highest resolution and fastest 3D PET instrument, a small animal and breast-specific imager, and laser-based technology for rapid measurements of enzyme activity in single cells.

- PET and magnetic resonance imaging (MRI) were merged, opening new possibilities in diagnostic imaging.

- The most effective boron-containing compound studied to date, boronophenyl alanine (BPA), has been shown to have a preferential uptake in cancer cells versus normal brain of approximately 3-4 to 1 and to not cause unacceptable side effects at present dose levels.
- BNCT phase I/II clinical trials are proceeding with approximately 50 patients to date.

Portfolio Summary

This portfolio area, "Prevention and Protection," encompasses research from many programs and supporting activities that crosscut the research topics covered above. The table below summarizes specific programs that strongly support or moderately support Prevention and Protection, including pollution minimization, cleanup and remediation, carbon sequestration, and health protection. The funding totals for these areas are an analytic tool reflecting the highly crosscutting, leveraged aspects and implications for individual research areas within DOE's science portfolio. **Because research areas may appear in multiple chapters, there will be significant instances of multiple counting, and the chapter totals will not sum to the overall science budget.** Additional details on these research areas are presented in the Research Summary Matrix and the corresponding Research Summary Profiles.

Strongly Supportive RSPs (Combined Budget: $178.76 Million) Advanced Medical Imaging Analytical Chemistry Instrumentation Boron Neutron Capture Therapy Cleanup Research Climate Change Technology Initiative (CCTI) Environmental and Molecular Sciences Laboratory (EMSL) Laboratory Technology Research and Advanced Energy Projects Microbial Genomics Natural and Accelerated Bioremediation Research Program Radiopharmaceutical Development Science Education Support Separations and Analysis
Moderately Supportive RSPs (Combined Budget: $763.55 Million) Chemical Physics Research Energy Biosciences Experimental Program to Stimulate Competitive Research (EPSCoR) Focused Health Research General Purpose Plant & Equipment (GPP/GPE) Geosciences Health Risks from Low Dose Exposures Heavy Element Chemistry Multiprogram Energy Lab Facilities Support (MELFS) Neutron and Light Sources Facilities Small Business Innovation Research (SBIR) Program Small Business Technology Transfer (STTR) Program Structural Biology Research Facilities

Understanding and Predicting Protein Structure Understanding Gene Function
NOTE: Please see Appendix A for more information on the budgets, the research performers, and other related information for each Research Summary.