Workshop Report

Basic Research Needs for Countering Terrorism

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Abstract

This report documents the results of the Office of Basic Energy Sciences (BES) Workshop on Basic Research Needs to Counter Terrorism. This two-day Workshop, held in Gaithersburg, MD, on February 28 and March 1, 2002, brought together BES research participants and experts familiar with counter-terrorism technologies, strategies, and policies. The purpose of the workshop was to: (1) identify direct connections between technology needs for countering terrorism and the critical, underlying science issues that will impact our ability to address those needs and (2) recommend investment strategies that will increase the impact of basic research on our nation's efforts to counter terrorism.

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Executive Summary

This report documents the results of the Department of Energy, Office of Basic Energy Sciences (BES) Workshop on Basic Research Needs to Counter Terrorism. This two-day Workshop, held in Gaithersburg, MD, on February 28 and March 1, 2002, brought together BES research participants and experts familiar with counter-terrorism technologies, strategies, and policies. The purpose of the workshop was to: (1) identify direct connections between technology needs for countering terrorism and the critical, underlying science issues that will impact our ability to address those needs and (2) recommend investment strategies that will increase the impact of basic research on our nation's efforts to counter terrorism.

The workshop focused on science and technology challenges associated with our nation's need to detect, prevent, protect against, and respond to terrorist attacks involving Radiological and Nuclear, Chemical, and Biological threats. While the organizers and participants of this workshop recognize that the threat of terrorism is extremely broad, including food and water safety as well as protection of our public infrastructure, we necessarily limited the scope of our discussions to the principal weapons of mass destruction.

In order to set the stage for the discussions of critical science and technology challenges, the workshop began with keynote and plenary lectures that provided a realistic context for understanding the broad challenges of countering terrorism. The plenary speakers emphasized the socio-political complexity of terrorism problems, reinforced the need for basic research in addressing these problems, and provided critical advice on how basic research can best contribute to our nation's needs. Their advice highlighted the need to:

- Invest Strategically – Focus on ***Cross-Cutting Research*** that has the potential to have an impact on a broad set of technology needs, thereby providing the greatest return on the research investment.

- Build Team Efforts – Countering terrorism will require broad, collaborative teams. The research community should focus on: (1) ***Research Environments and Infrastructures*** that encourage and enable cross-disciplinary science and technology teams to explore and integrate new scientific discoveries and (2) Exploring ***Relationships with Other Programs*** that will strengthen connections between new scientific advances and those groups responsible for technology development and implementation.

- Consider Dual Use – Identify areas of research that present significant ***Dual-Use Opportunities*** for application to countering terrorism and other complementary technology needs.

The during the workshop, participants identified several critical technology needs and the underlying science challenges that, if met, can help to reduce the threat of terrorist attacks in the United States. Some of the key technology needs and limitations that were identified include:

Detection – Nonintrusive, stand-off, and imaging detection systems; sampling from complex backgrounds and environments; inexpensive and field-deployable sensor systems; highly selective and ultra-sensitive detectors; early warning triggers for continuous monitoring

Prevention – Methods and materials to control, track, and reduce the availability of hazardous materials; techniques to rapidly characterize and attribute the source of terrorist threats

Protection – Personal protective equipment; light-weight barrier materials and fabrics; filtration systems; explosive containment structures; methods to protect people, animals, crops, and public spaces

Response – Coupled models and measurements that can predict fate and transport of toxic materials including pre-event background data; pre-symptomatic and point of care medical diagnostics; methods to immobilize and neutralize hazardous materials including self-cleaning and self-decontaminating surfaces

The workshop discussions of these technology needs and the underlying science challenges are fully documented in the major sections of this report. The results of these discussions, combined with the broad perspective and advice from our plenary speakers, were used to develop a set of high-level workshop recommendations. The following recommendations are offered to help guide our nation's basic research investments in order to maximize our ability to reduce the threat of terrorism.

- We recommend continuing or increasing funding for a selected set of research directions that are identified in the Workshop Summary and Recommendations

(Section 5) of this report. These areas of research underpin many of the technologies that have high probability to impact our nation's ability to counter terrorism.

- New programs should be supported to stimulate the formation of, and provide needed resources for, cross-disciplinary and multi-institutional teams of scientists and technologists that are needed to address these critical problems. An important component of this strategy is investment in DOE national laboratories and user facilities because they can provide an ideal environment to carry out this highly collaborative work.

- Governmental organizations and agencies should explore their complementary goals and capabilities and, where appropriate, work to develop agreements that facilitate the formation of multi-organizational teams and the sharing of research and technology capabilities that will improve our nation's ability to counter the threat of terrorism.

- Increased emphasis should be placed on identifying dual-use applications for key counter-terrorism technologies. Efforts should be focused on building partnerships between government, university, and industry to capitalize on these opportunities.

In summary, this workshop made significant progress in identifying the basic research needs and in outlining a strategy to enhance the research community's ability to impact our nation's counter-terrorism needs. We wish to acknowledge the enthusiasm and hard work of all the workshop participants. Their extraordinary contributions were key to the success of this workshop, and their dedication to this endeavor provides strong evidence that the basic research community is firmly committed to supporting our nation's goal of reducing the threat of terrorism in the United States.

1 Introduction

This report documents the presentations, discussions, and recommendations from the Department of Energy / Office of Basic Energy Sciences (BES) Workshop on Basic Research Needs to Counter Terrorism. The workshop, which was held on February 28 and March 1, 2002, in Gaithersburg, Maryland, identified the critical science issues and opportunities in research areas supported by BES that will be important to our nation's ability to detect, prevent, protect against, and respond to terrorist threats in the United States.

While terrorism is not new to the international community, events in recent years such as the 1993 bombing of the World Trade Center and the attack on the Alfred P. Murrah Federal Building in Oklahoma City in 1995 have shown that assets on United States soil have also become targets for terrorist activities. Most recently, the September 11 suicide attacks resulted in the deaths of more than 3,000 civilians. These devastating events have focused the attention of the entire world and caused the United States to launch a War on Terrorism. A major response to these terrorist events has been the formation of the Office of Homeland Security to develop, coordinate, and implement a comprehensive national strategy to detect, prevent, protect against, and respond to terrorist attacks within the United States.

This nation’s strengths in basic science research are expected to play an important role in the initiative to counter the threat of terrorism. In his speech before the American Association for the Advancement of Science in December 2001, Dr. John H. Marburger III, Director of the White House Office of Science and Technology Policy, stated, “Science and engineering have critical roles to play in the war on terrorism.” He went on to indicate, “We need improved tools with which to prevent, detect, protect, and treat victims of chemical biological, radiological, nuclear, and conventional terrorist attacks. Additionally, we will need new and improved tools to recover facilities from those same types of attacks, should they ever occur.”

As a leading supporter of basic science research, the Office of Basic Energy Sciences convened a workshop to understand better how fields of research that it supports can meet our nation’s needs to counter terrorism. This workshop involved participants from the BES research community (including scientists from national laboratories and universities), experts in the technologies, strategies, and policies used to counter terrorism, and representatives from several other governmental agencies and organizations. Appendix I gives a list of participants in the intensive two-day workshop.

There are many examples where basic science research and resulting technology can impact the ability to detect, prevent, protect against, and respond to terrorism. For example, sensors, detectors, chem lab on a chip, and atomic and molecular spectroscopy could all be important to the *Detection* of terrorism. *Prevention* of terrorist acts could be enhanced through improved methods for controlling and tracking radiological materials and the development of new manufacturing methods that minimize the creation of hazardous industrial chemicals. Likewise, *Protection* against terrorism could be increased through improved filters and membranes and the development of new protective fabrics, while improvements in our ability to *Respond* to a terrorist event could be made by developing methods to immobilize and neutralize hazardous materials.

The goal of this workshop was to identify direct connections between technology needs for countering terrorism and the critical, underlying science issues that will impact our ability to address those needs.

To set the stage for the discussions of critical science and technology challenges, the workshop began with keynote and plenary lectures that provided a realistic context for understanding the broad challenges of countering terrorism:

- Dr. Jay Davis, National Security Fellow at the Center for Global Security Research at Lawrence Livermore National Laboratory (LLNL), provided the keynote lecture entitled “The Role of Science and Technology in Countering Terrorism.” Dr. Davis spent three years prior to returning to LLNL as founding director of the Defense Threat Reduction Agency of the Department of Defense. His presentation stressed the overall socio-political complexity of the terrorism problem.

- Dr. Micheal R. Anastasio, Deputy Director for Strategic Operations at LLNL, lectured on “Counter Terrorism and Long-Range R&D Needs.” Dr. Anastasio serves on the National Academy of Sciences Sub-Panel on Radiological and Nuclear Threats and focused on the principal threats associated with radiological and nuclear materials.

- Professor Micheal J. Sailor from the University of California at San Diego focused on “Basic Research Needs to Counter Chemical Threats.” Prof. Sailor stressed the need for science and technology integration to allow new scientific breakthroughs to impact the practical tasks of fighting terrorism.

- The final plenary lecture addressed the biological threat and was presented by Dr. David Franz (Colonel, U.S. Army Retired), Vice President, Chemical and Biological Defense Division of Southern Research Institute. Dr. Franz has served as both Deputy Commander and then Commander of the U.S. Army Medical Research Institute of Infectious Diseases (USARMID).

This panel of experts shared some very important perspectives with the workshop participants concerning the nature of terrorist threats, the complex processes involved in countering these threats, and the important role that basic science can play. Although we could never capture the full impact of these presentations in our written report, the following sections summarize some of the key points associated with basic science's role in countering of terrorism.

1.1 Context for Scientific and Technological Applications for Countering Terrorism

To enhance the nation's ability to counter terrorism, one must first recognize that terrorism is an extremely complex socio-political problem and that there are simply no "Silver Bullets" to easily solve the problem.

- Scientific breakthroughs or new technologies alone will not end terrorism. Any solution must be compatible with existing doctrine, operations, and training. In other words, to be useful, science and technology must be considered as part of an overall system, and the technological piece of that system must be simple and easy to use.

- It is important to note that no one customer exists for new science and technology applications for countering terrorism. In fact, there are many customers, none of which has sole responsibility for countering terrorism in the U.S.

- Finally, the ultimate customers are not familiar with science and technology and are unlikely to understand or appreciate the needs or capabilities of the basic research community, but that does not mean that they will not ultimately benefit from research efforts.

1.2 Opportunities for Basic Research

While the context for understanding terrorism is very complex (and somewhat daunting), there are many important contributions that science and technology can make:

- The strength of basic research is in new knowledge and the associated cost effectiveness. Terrorism presents tough problems, and new approaches can be extremely valuable.

- Basic research can provide assistance across all categories of homeland security; however, the special relationship between *detection* and *response* (forensics and attribution) presents some of the more significant opportunities. Our nation's terrorism policies stress retribution and rapid identification of those responsible.

- The ability to couple physical measurements with modeling tools is very important. Too often, those responding to terrorist acts either have measurements but no models to help in understanding their significance, or they have models with no actual data to guide their application. In addition, tools to help interpret sparse data sets or to analyze large volumes of data will also be extremely useful.

- Dual-use is an extremely important concept and can contribute to the "critical mass" of interest needed to support science and technology investments. A good example might be a scientific goal that contributes to the development of a biohazard detector, but at the same time, it has relevance to human health diagnostics.

1.3 Challenges to the Basic Research Community

The challenges that our plenary speakers addressed were not those associated with the science itself but with the scientist's and technologist's interface with the overall efforts to counter terrorism.

- Scientists and technologists must be honest and straightforward about what is possible and what is not. Those responsible for countering terrorism are looking for solutions, not hype.

- The basic research community must be prepared to work with a team that they will probably not lead. Scientists will set the scientific directions but not the overall approach and strategy for countering terrorism. Thus, scientists and technologists will need to understand enough about the overall approaches to countering terrorism that they can understand the true value of their work to that broader integrated effort.

- The focus on integration, both at a systems level and at a technology level, must be constantly addressed.

With this background and perspective in place, the workshop participants divided into smaller groups to discuss specific technology needs and critical scientific issues. The following sections summarize the workshop discussions and address the Radiological and Nuclear, Chemical, and Biological threat areas. Each section separately addresses (1) the technology needs posed by terrorist threats in that area, (2) specific examples of how basic research supported by the BES Materials and Chemical Sciences programs already plays an important role in the effort to counter terrorism,[1] (3) the fundamental scientific issues and challenges that promise to impact the ability to counter terrorism, and (4) future research needs, including new science thrusts as well as new facilities and infrastructure development.

The participants in this workshop fully recognize that the threat of terrorism extends beyond the topics addressed in this workshop. Of particular interest to the Department of Energy is the potential vulnerability of our nation's critical infrastructure for energy, information, and transportation. The Basic Energy Sciences Advisory Committee is planning a separate comprehensive workshop structured around energy reserves, production, and consumption with break-out sessions for specific energy sources and consumption sectors.

[1] These areas of research include Materials Synthesis and Processing, Biomolecular Materials and Interfaces, Physical & Chemical Properties of Materials, Surfaces, Interfaces and Thin Films, Nanoscale Materials and Structures, Nano- and Micro-scale Diagnostics, Microfabrication, Atomic and Molecular Spectroscopy, Catalysis and Chemical Transformations, Separations and Analysis, Radiation Effects, Heavy Element Chemistry, and Biochemistry.

2 Radiological/Nuclear Threats

2.1 Terrorism Threats and Technology Needs

The nuclear threats facing the U.S. are constantly evolving and have grown more complex since the end of the Cold War. However, the events of this past year have proved the necessity to reevaluate these threats on a scale never before considered.

In the past, potential adversary states were easily identified, and nuclear weapons program development was monitored through treaties, intelligence agencies, nuclear reactor monitoring, and scientific advancements. With the dissolution of the Soviet Union, the possibility of diversion of complete weapon systems or nuclear material to rogue nations and terrorist organizations has increased. In addition, new nuclear powers (e.g., Pakistan and India) have further complicated global proliferation issues. While the operability of nuclear weapons has always been important to national security, their role has been more as a strategic deterrent rather than as an offensive/defensive weapon. In the current climate, complex and highly organized domestic and state-sponsored foreign terrorist units have multiple mechanisms at their disposal to engage in nuclear threats. In addition, the potential threat scenarios have now been expanded to consider the use of all radiological materials as potential “weapons,” introducing the need to monitor, track, and respond to a greatly broadened suite of materials.[1]

The most potentially catastrophic terrorist threat involving radioactive materials is the possibility of a self-sustained fission chain reaction detonated in an urban area. This scenario is credible and is taken very seriously by the federal authorities. Such an event could result in a significant number of deaths and massive devastation. The resulting fallout, containing highly radioactive fission and activation products, would contaminate many square miles. Such a device need only contain several kilograms to a few tens of kilograms of a fissile isotope, could be transported in a small truck, and would be difficult to detect because of the relatively small amount of external radiation that it would produce, especially if shielded, before detonation.

Prevention of such a devastating terrorist attack requires that terrorists do not obtain the essential ingredient for building an atomic bomb, namely, fissile actinide isotopes such as U-235 or Pu-239. If they have obtained such isotopes, the fissile material must be detected before introduction into the U.S., or during transport and before assembly into a functional device. Other credible threat scenarios include the use of radiological materials as potential weapons. A noninclusive list of potential threats includes the use of so-called "alternate nuclear materials" or the generation of "dirty" bombs, which use a combination of conventional explosives and nuclear material. Radionuclide release may occur from the sabotage of nuclear facilities or repositories, from raids/attacks on nuclear materials in transport, or from hospitals where radionuclides are used for diagnostics and therapy.

To realize how work supported by the Office of Basic Energy Science can impact homeland defense and counter terrorism, an understanding of the threats and the mechanism of a nuclear-based terrorist attack is required. The threats discussed above have common features. The three basic objectives for a terrorist are to obtain radiological or nuclear materials, to develop or utilize known technology for "weaponization," and to deploy the weapon/material in a desirable area. Within each of these objectives are inherent weaknesses that a counter-terrorism effort can exploit.

2.1.1 Detection

The primary goal of any counter-terrorism effort is to prevent an attack as early in the development stages as possible. Many current approaches employed to prevent a nuclear/radiological attack rely upon detection of materials. Access to nuclear or radiological materials as well as weapon production capabilities and facilities has been considered of primary importance.[2]

Many technologies have been proposed for monitoring production, from radiation detection methods employed in on-site inspection governed by treaties to stand-off detection of chemical effluents resulting from the processing of nuclear materials.[3] Several factors complicate the application of such methods, however. First, the list of fissionable isotopes that merit monitoring has been expanded to include potential "alternate nuclear materials," including Np-237 and certain isotopes of Am. Furthermore, the possible use of a "dirty" nuclear device, or a combination of a conventional and a nuclear explosive device, brings any radioactive material into the realm of a potential threat.

The need to detect both traditional and alternate nuclear materials leads to many requirements that are not met by current scientific technologies (e.g., simple, inexpensive, low-level detection of nuclear material in the field, differentiation of nuclear fuel versus weapon production, etc.). Further, there is a growing need to develop a broader and more thorough system to monitor transportation and commerce corridors for the transport of radiological materials. Any systems employed must address the requirements of rapid throughput, elemental/isotopic discrimination, and low system cost. Also, for the first responders to any terrorist incident, there must be a reliable, cheap, "yes or no answer" approach to the detection of nuclear material.

The nuclear emission (alpha, beta, gamma) of constituent isotopes is one of the more sensitive clues for detection of radioactive materials. Active interrogation with neutron, electron, proton, and gamma sources also can be used to activate some elements that are then detected by the nuclear emission of the activated isotope. The development of more compact, higher flux sources could enable this technology to be more widely utilized. The field of nuclear detection has further growth potential with the development of new sources and better (more sensitivity, higher energy, greater spatial resolution, and room temperature compatibility) nuclear detectors.

Another technique widely used for isotope analysis is mass spectrometry. This technique, which depends on the method used to ionize or vaporize the material, has extremely high resolution and can determine isotope ratios. Mass spectrometry-based techniques can provide sensitivities down to tens of atoms with nanometer spatial resolution by combining the selectivity obtained via tunable laser excitation of one or more electronic transitions with high-spatial-resolution sputtering techniques such as ion bombardment. Such information, along with the identification of elements and molecular speciation in particulates down to the nanometer scale and below, should be invaluable in tracing the origin of the material for forensic purposes. High sample throughput for identification purposes can be achieved using high brightness x-ray sources, such as third-generation synchrotrons, which soon are expected to provide 50-nm spatial resolution for x-ray techniques such as diffraction and absorption that, respectively, identify physical structure and quantify the presence of a wide range of elements and their local environments.

Other methods of detection for radioactive materials based on ionic and/or molecular recognition need to be more fully developed. Although nuclear methods indicate that an element is present, they do not provide information about its form or oxidation state. Moreover, the sensitivity of nuclear methods for long-lived radionuclides might not be adequate for some applications.

Alternative detection methods could be based on the visible fluorescence emitted under visible or ultra-violet excitation (e.g., the UO_2^{2+} and the Cm^{3+} ion) or the infrared fluorescence emitted by the neptunyl and plutonyl ions. The design of specific ligands that undergo a spectral change upon binding of particular actinide ions is another promising avenue of exploration. If color changes accompany the binding, it is possible that specific colorimetric reagents might be designed to indicate the presence of a particular ion. Advances in rapid element separation using high-speed ion exchange or capillary electrophoresis methods and new solid-state ultraviolet light sources may serve as the basis for physically small, rapid, highly sensitive instruments for quantifying a broad range of lanthanide and actinide elements in a few seconds in sample solutions.

2.1.2 Preparedness

Preparedness refers to the ability to respond to terrorist threats and attacks within the U.S. If an attack cannot be prevented, efforts would turn to response: protection of people and assets, emergency response, and event mitigation/recovery. Measures must be in place to rapidly identify the elements/isotopes of concern, to deal with immediate concerns, and, ultimately, to remove these materials. Dose exposure information must be rapidly collected and evaluated, and the appropriate response initiated. If radioactive material is dispersed in reservoirs, it must be identified, and emergency responders must be ready and able to provide instructions. Methods must be available to deal with individuals contaminated with radioactive material. Promising new reagents are being studied for the removal of actinides from humans, but much more work is necessary before these reagents can be utilized. Cleanup methods and materials must be available for the removal of radionuclides from surfaces, soils, water, and air. Agents for removal of contaminants from soils and surfaces as well as methods for the separation of radionuclides from air and water are necessary. Available reagents must be evaluated and new ones developed if necessary. Modeling of the effects of radioactive contamination in air, water, and soils must be performed, based on reliable kinetic and thermodynamic data so that the consequences of this type of disaster can be determined and its effects mitigated. Finally, the question of the storage and disposal of the radioactive material under emergency conditions needs to be addressed.

Research related to the effect of ionizing radiation on matrix materials may serve a dual purpose, identifying both radiation damage and also shedding light on the utility of radiation as a decontamination measure. Radioactive sources or accelerators that produce ionizing radiation are used to decontaminate biological or toxicological agents from materials by decomposing such agents into harmless products. At the same time, the material being cleansed may also be degraded. Understanding the fundamental processes that occur in both condensed and aqueous phases and, most importantly, at interfaces following the passage of ionizing radiation is necessary. In the case of a nuclear incident, the chemical changes induced by the radiation may result in unexpected products that make remediation difficult and dangerous. Similarly, the effects of radiation on biological materials, although an active area of investigation, need to be explored at the molecular level. Low-dose thresholds (or low-dose linear responses) need to be explored at the single molecule/single cell level.

It should be noted that as the sole agency in the federal government with a spectrum of research activities involving nuclear and radiological materials, the Department of Energy bears a unique responsibility for providing the underpinning science. Preparedness includes, in the context of the science base, maintenance of the infrastructure (laboratories, instrumentation, computers, etc.), and expertise (technical personnel, databases, etc.) for devising technical solutions to the problems that might be encountered with radiological/nuclear materials. Owing to the hazards in working with these materials, the aging infrastructure at DOE's national laboratories represents a particular problem for this area of research. This, coupled with the decline in university programs designed to train actinide and radiochemists is a particular challenge in preparing to address threats associated with nuclear and radiological materials.

2.1.3 Prevention

Another general category of threat reduction involves preventing acquisition or utilization of the materials. Physical protection is the first line of defense. Advanced materials could aid in the containment of hazardous materials to prevent their dispersal upon insult (e.g., explosion scenarios). Physical protection of nuclear materials could be augmented by the application of technology designed to stabilize nuclear/radiological materials to prevent their use or dispersal. These could include implementing advanced proliferation-resistant nuclear fuel cycles, devising more efficient/rapid methods for the recovery and stabilization of existing radioactive sources, and identifying improved material forms for the storage of nuclear materials (this latter point is increasingly important as the U.S. and Russia further reduce their active nuclear weapon stockpiles). A related technology need is identification of possible unconventional methods of material processing to better anticipate possible scenarios and monitoring methods.

Prevention of a nuclear incident also depends on the interdiction of the material or suspicious persons before entry into the U.S. This involves inspection and detection of nuclear materials entering the country. More sophisticated detection, as discussed previously, is clearly pertinent. Advances in detector materials would be particularly valuable in detecting the illicit transport of fissile or other radioactive materials.

2.1.4 Protection/Response and Recovery

If an attack cannot be prevented, efforts would turn to protection of people and assets, emergency response, and event mitigation/recovery. Protection against such attacks may well rely upon rapid identification of material dispersal pathways. Strategies could be envisioned in which critical facilities are equipped with response systems that employ detection systems (with technology gaps similar to those discussed above) to control building ventilation systems, or where broad-area monitors are employed to aid in formulating evacuation routes. In some instances, technology needs may include means of hardening infrastructure to operate in harsh environments.

Rapid identification of the nature of the weapon by emergency responders would be of primary concern, since the initial response would be significantly different, depending on whether a chemical, biological, or radiological/nuclear weapon is used. Careful post-attack analysis of materials can also be invaluable to the identification of the perpetrators. Attribution and the fear of a devastating response are also powerful deterrents to attack. For a nuclear attack, determining the specific radiological agents present in the weapon, (e.g., long-lived isotopes, such as U, Pu, etc., versus short-lived fission products, such as Cs, Sr, etc.) will also dictate treatment. Current approaches for distinguishing these characteristics often rely upon laboratory analysis, requiring sample collection and transport. Technology is needed to provide portable equipment for economical chemical and radiochemical analyses of radiological materials. Finally, technology needs exist in the design of appropriate mitigation/recovery strategies, from prediction of migration of radiological materials (identifying the scope of required treatment) to devising new incident-specific solutions for broad area decontamination. Knowledge of the interaction of nuclear materials with biological systems is also important to develop enhanced remediation schemes and medical therapies.

2.2 BES Research Accomplishments and Implications for Counter Terrorism

The Department of Energy (DOE) programs in radiological/nuclear chemistry had their genesis in the Atomic Energy Commission's chemistry research program that was built on the wartime Manhattan Project. That program was primarily directed at the needs of the plutonium project, and investigated chemical processes for separating uranium, plutonium, and fission products. After the production facilities for producing and processing plutonium were operational and successful, longer range studies were undertaken, such as the discovery of new transplutonium elements and chemical studies of their properties, the development of new analytical methods, systematic spectroscopic studies of the actinide elements, and studies of radiation chemistry. Current BES activities have evolved from this beginning.

Short descriptions of the relevant activities in the areas of Heavy Element Chemistry, Separations and Analysis, and Radiation Chemistry are given below, followed by an abbreviated list of the research topics currently studied within these activities. Other BES activities that provide support for some radiological/nuclear issues are mentioned. A few of the notable accomplishments of the BES activities are described.

2.2.1 Heavy Element Chemistry

The BES Heavy Element Chemistry activity is the sole source of federal support in the U.S. for fundamental research on the chemistry of the actinides and their fission products, both of which are potential "signatures" of activities related to proliferation and nuclear or radiological terrorism. Relevant information developed under this activity includes spectroscopic identification; better understanding of the environmental chemistry (fate and transport) of actinides and fission products; and enhanced chemical characterization methods such as advanced x-ray spectroscopies. The supported research provides the basis for innovative sampling and analysis technologies needed to improve the detection and tracking of special nuclear materials; the timely detection of a clandestine national or subnational nuclear weapons program or noncompliance with international treaties and agreements; advanced field and laboratory nuclear materials analysis methods; and micro technologies for detection and analysis.

Actinide Chemistry topics include the following:

- Fundamental research into the chemistry of f-elements, including thermodynamic and kinetic measurements, for improved chemical syntheses, characterization, and separations.

- Fundamental research that advances the understanding and utilization of photon, neutron, electron, and magnetic interaction-based spectroscopies for chemical studies on actinide and important fission product species, and explores the electronic structure of the 5f elements.

- Fundamental research on the coordination chemistry, reduction/oxidation state behavior, interfacial science, and bonding of the actinides, to improve understanding of their fate and transport, such as that mediated by sorption or partitioning at the mineral/water interface.

- Research on the chemistry of f-elements in gaseous and solid states. Chemistry of transuranium elements on the microgram and larger scale.

- Computational modeling of the molecular structure, bonding, and spectra of 5f element compounds.

- Development of soft and hard x-ray synchrotron methods for element and species identification and characterization of local and extended structure.

Chemical Analysis of Radionuclides

Structural and chemical speciation information is needed to develop predictive models for the fate and transport of radionuclides and to guide the selection of cleanup technologies. While nuclear counting techniques can detect and identify the isotopic make-up of radionuclides, they provide no chemical information. BES-supported fundamental research has contributed to the development of methods to characterize the speciation of actinide contaminants under a variety of conditions.[1]

Spectroscopic and x-ray absorption methods were used to identify the oxidation state and speciation of plutonium in wastes, structural debris, and soils at the Rocky Flats Environmental Technology Site (RFETS). Identification of plutonium oxide in soils added to a growing body of evidence that colloid and particulate transport is a dominant migration pathway for plutonium in soils at RFETS. These results guided the development of new models for protecting surface water quality. As a result of this research, technologies are available to guide our response to in radiological decontamination should it become necessary.

[Los Alamos National Laboratory]

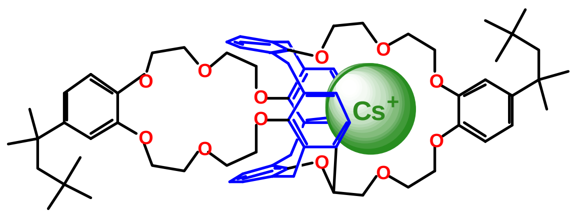
[1] S. D. Conradson, I. AlMahamid, D. L. Clark, N. J. Hess, E. A. Hudson, M. P. Neu, P. D. Palmer, W. H. Runde, C. D. Tait, "Oxidation state determination of plutonium aquo ions using x-ray absorption spectroscopy," *Polyhedron* (1998) 17, 599-602.

2.2.2 Separations and Analysis

The BES Separations and Analysis program supports research on fundamental issues in chemical detection and associated processes for chemical separations needed for reliable detection. Research on methods such as particle mass spectrometry may lead to new means for identifying elements, compounds, and particles relevant to the detection and attribution of clandestine nuclear explosions. This research can lead to innovative sampling and analysis technologies to improve the detection and tracking of nuclear materials, advanced field and laboratory radiological materials analysis methods, and micro technologies for detection and analysis. Some of the relevant topics supported by the activity are listed below.

- Fundamental research on ionic liquids and supercritical liquid systems used for the separation of radionuclides.
- Fundamental research on ligand systems used for the separation/concentration of radionuclides, a necessary first step in the analysis of trace amounts of elements of interest.
- Fundamental research into atomic spectroscopy, with application to multi-photon and other advanced laser ionization techniques for ultra-sensitive elemental analysis/detection.
- Research on the laser ablation of particulates and solids for quantitative chemical and isotopic analysis. (Laser-ablation analysis of particles on air filters is a promising method for determining if clandestine nuclear activities are under way.)
- Research on the size, shape, and chemical characterization (using laser spectroscopic and time-of-flight mass spectrometry) of individual airborne particles.
- Research on single-molecule/particle detection, micro- and nano-fluidic devices for chemical analysis (lab-on-a-chip).
- Fundamental research in the use of mass spectrometry for analysis.

Chemical Recognition and Extraction of Radionuclides



Calix[4]arene-bis(*tert*-octylbenzo-crown-6)
"BOBCalixC6"
(As complexed with Cs^+ ion)

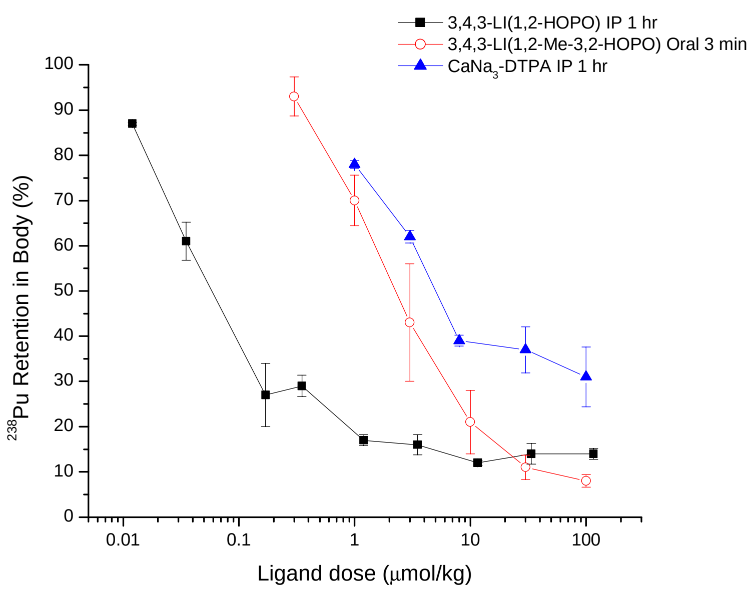
Environmental cleanup of radionuclides, whether because of legacy processing or in response to a terrorist event, will require the design of chemical “tweezers” that can pluck a single ion out of a host of millions or even billions of competing ions. Developing chemical-recognition principles is a critical first step in addressing this challenge. Solvent-extraction technology was recently selected at the Savannah River Site for cleanup of some 31 million gallons of highly radioactive salt waste.[1] The selected technology met the difficult processing requirements, including the ability to remove 99.9975% of the cesium from waste containing an average of only 15 ppm of cesium. The process employs the molecule shown above, known as BOBCalixC6, which had its early roots in BES-supported fundamental research in the 1970s and included the contributions of Prof. Donald Cram (University of California at Los Angles), who won a Nobel Prize in 1988 for his pioneering work in the field.

[1] P. V. Bonnesen, L. H. Delmau, B. A. Moyer, R. A. Leonard, *Solvent Extr. Ion Exch.* 2000, *18*, 1079-1108.

[Oak Ridge National Laboratory]

Actinide Sequestering Agents

The syntheses and characterization of actinide-specific ligands patterned after natural iron-sequestering agents called siderophores have received long-term support from BES.[1] This work is based on the recognition of the chemical similarities between Fe^{3+} and the somewhat larger Pu^{4+}ion. Expanding the coordination sphere of these synthetic ligands and incorporation of the HOPO metal binding group have resulted in a series of new ligands. These new compounds have been evaluated for their efficacy in removing actinides from mice (in studies supported by NIH). (See Figure.) Two of the newly synthesized actinide-specific HOPO chelating agents have shown exceptional promise during the preliminary evaluation of their efficacy for actinide decorporation (removal from the body) and toxicity in mice. These compounds decorporate injected or inhaled Pu and trivalent actinides much more effectively than DTPA (the approved therapeutic drug) in all tests in mice and rats, and they have remarkable oral efficacy.[2]



Dose effectiveness of 3,4,3-LI(1,2-HOPO) injected intraperitoneal (IP) at one hour or 3,4,3-LI(1,2-Me-3,2-HOPO) given orally at three minutes after an intravenous (IV) injection of ^{238}Pu compared with $CaNa_3$-DTPA injected IP at one hour. The figure shows that the HOPO ligands are much more effective than DTPA for removing Pu.

[1] P. W. Durbin, B. Kullgren, J. Xu and K. N. Raymond. "Development of Decorporation Agents for the Actinides," *Radiation Protection Dosimetry* (1998) 79, 433-443.

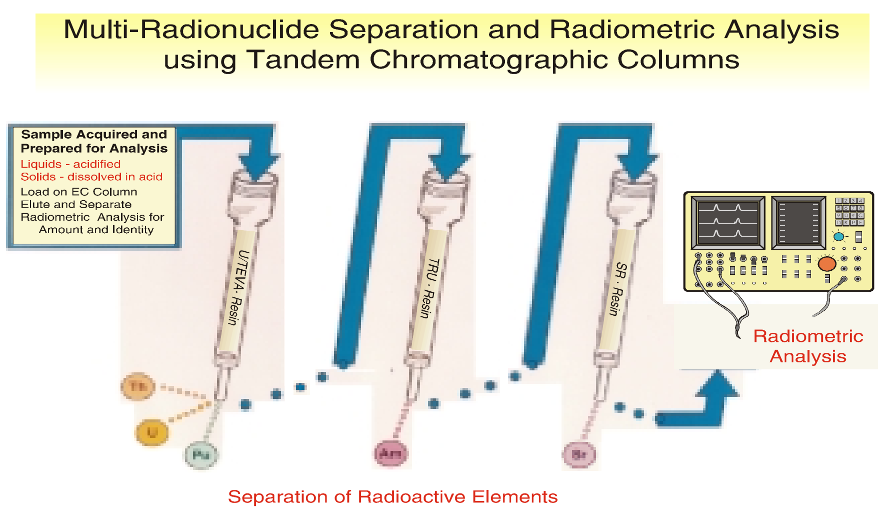
[2] P. W. Durbin, B. Kullgren, Jide Xu, and K. N. Raymond. "Multidentate Hydroxypyridinonate Ligands for Pu(IV) Chelation in vivo: Comparative Efficacy and Toxicity in Mice of Ligands Containing 1,2-HOPO or Me-3,2,-HOPO," *Int. J. Radiat. Biol.* (2000) 76, 113-117.

Detecting Nuclear/Radiological Contamination of Water Supplies

Research supported by BES has led to the development of a series of novel extraction chromatographic (EXC) resins that can selectively remove one or more radionuclides from aqueous solution.[1] The resins combine a highly selective metal ion extractant in an inert polymeric support. Sample solutions, adjusted to the proper acidity, are passed through a series of columns packed with the appropriate resin for a particular radionuclide. The selected ions are retained on the columns, while others pass through (see Figure), and retained ions are washed from the columns for analysis. Columns with different extractants can be coupled so that multiple ions can be detected in a single sample.

These resins can address widespread problems in radiochemical analysis and are well suited to either defining the scope and isotopic signature of contamination resulting from an incident of nuclear/radiological terrorism.

[Argonne National Laboratory]



[1] M. L. Dietz, E. P. Horwitz, R. Chiarizia, "Recent Advances in the Development of Extraction Chromatographic Materials for the Isolation of Radionuclides from Biological and Environmental Samples," in *Solvent Extraction for the 21st Century , Volume 1*, M. Cox, M. Hidalgo, and M. Valiente, Eds., Society of Chemical Industry: London, 2001, pp. 53-58.

2.2.3 Radiation Chemistry

BES is the sole supporter of radiation chemistry in condensed systems (nonbiological) in the U.S. It funds specialized electron radiolysis facilities that serve the academic research community, industrial users, and other national laboratories. Radiation chemistry investigates the fundamental chemical effects produced by the absorption of energy from ionizing radiation. Although not specifically aimed at solving problems in counter-terrorism, the fundamental knowledge developed by this activity underlies the use of radiation sources for decontaminating materials (e.g., mail) that harbor pathogenic organisms. This same knowledge is applicable to the use of radiation sources for deactivating chemical toxins by means of irradiation. Analysis in bones and teeth of free radicals generated by radiation can reveal exposure to radiation and determine the dose of exposure to irradiation. In the event of nuclear terrorism or a nuclear accident, radiation effects on contaminated materials and at contaminated sites must be taken into account to undertake the proper mitigation measures. Some of the relevant topics supported are listed below.

- Radiolytic and photolytic oxidation of multifunctional compounds
- Radiation effects in homogeneous media and multiphase systems
- Structure and chemical properties of radiation-produced intermediates
- Radiation-induced chemistry in supercritical fluids and other solvents
- Radiation effects in solids

2.2.4 Experimental Condensed Matter Physics

This activity supports generic research on semiconductors, magnetic materials, and systems that provide a science base for the development of advanced, highly sensitive sensors and detectors, some of which may have application for the remote detection of nuclear detonations.

2.2.5 Mechanical Behavior of Materials and Radiation Effects

This activity supports studies of the effects of irradiation on the chemical and physical properties of materials, including a number of ceramics that have been suggested as potential immobilization “hosts” for surplus fissile materials in both the U.S. and Russia.

2.2.6 Synchrotron and Neutron User Facilities

The synchrotron and neutron facilities provide a unique set of analytical tools for characterization of materials at the atomic and molecular level. These tools determine the atomic constituents of materials, the positions of the atoms in materials, and the behavior of materials under the influence of external perturbations such as radiation or chemical attack. Various experimental and theoretical tools are available for the nondestructive detection and identification of radiochemical species that might occur after a terrorist event.

2.2.7 Geosciences

Geophysics research focuses on improving subsurface imaging, which includes a large component involved with understanding how seismic waves are generated and then propagate through anisotropic, heterogeneous earth materials. This work can improve capabilities to account for the environment’s effects on seismic observables. This is important for the interpretation of both teleseismic and near-field seismic data in terms of the source mechanics. Indirectly, this work has an impact on the ability to use regionally based seismic monitoring methods to detect very low yield events that might arise from a clandestine testing of nuclear devices.

Geochemistry research focuses on studies of the interaction of minerals and mineral surfaces with water. This knowledge is relevant to the determination of the fate and transport of radionuclides in the environment as well as the long-term stability of nuclear wasteforms with respect to aqueous corrosion/dissolution after they have been emplaced in a geologic repository. The Geosciences program also supports research in analytical methods that can be used for trace measurements of isotopes for geological dating. These same methods may be used for determining isotopic ratios in forensic analyses.

Scientific Analysis Alleviates Public Concern over the Three Mile Island Reactor Vessel

On March 30, 1979, two days after the accident in the Three Mile Island Reactor, press reported the existence of a noncondensable bubble in the reactor vessel. This bubble was said to consist mainly of hydrogen, and the danger of explosion was reported to be imminent. BES scientists analyzed[1] all possible sources of noncondensable gases including radiolysis, and it was determined that a continuing growth of the bubble during several days after the accident was not possible. In addition, they were able to show that the bubble did not contain a combustible mixture. The tools and capabilities of basic research will also play an important role in guiding our response and public education surrounding future possible acts of radiological/nuclear terrorism.

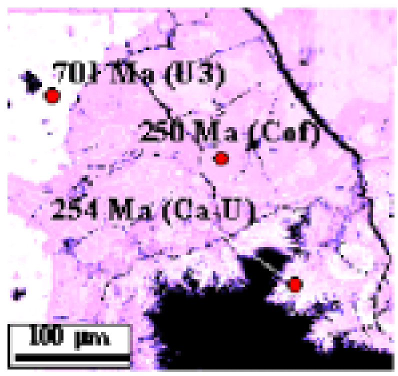
[1] S. Gordon, K. H. Schmitt, and J. R. Honekamp, *Radiat. Phys. Chem.* 21, 247-258 (1983).

Forensic Analysis of Radiological Materials

BES-funded research into the fundamental chemistry of mass spectrometry has helped lay the foundation for ultra-sensitive isotope analysis techniques. Investigations into ionization and gas phase ion processes have led to the development of ultra-sensitive thermal ionization mass spectrometry for isotope analysis and high-precision, high-accuracy secondary ionization mass spectrometry for the analysis of isotope ratios in situ with high spatial resolution (see photo). Finally, improvements in chemical separation and analysis of radionuclides (U, Pu) using electrochemically modulated separation combined with MS show potential for rapid screening of physiological media, such as urine, with a minimum of sample preparation. The isotopic data, as well as elemental proportions, could be used to detect nuclear activity and to fingerprint the source of nuclear materials that may be part of a terrorism event.

[Oak Ridge National Laboratory]

Color-enhanced image of uraninite showing variations across sample (at red dots) in ages (millions of years) determined by SIMS based on variations in U and Pb isotope variations. Note 20-micrometer spatial resolution



2.3 Scientific Issues and Research Opportunities

Fundamental scientific challenges must be overcome to achieve new and improved technologies that effectively counter radiological and nuclear threats. Here some of the problems with current capabilities and techniques are defined more precisely. The underlying issues that must be addressed to resolve homeland security deficiencies are identified, and the opportunities for innovation in solving these problems are cited.

2.3.1 Detection

Technology Need	Present Problem
Rapid, reliable, simple, cheap radiation detectors for first responders.	Current detectors are expensive and moderately complicated.
Field deployable, moderate to high resolution, radiation measurement instrumentation.	Current detectors are delicate and require cryogenic temperatures to obtain energy-resolved spectra.

Radiation measurements are hampered by the limitations of available materials. There are different problems with the two main classes of materials.

Scintillators

The first major class of radiation-detecting materials provides rather limited energy resolution such as scintillators or ambient-temperature semiconductor gamma detectors, such as cadmium zinc telluride (CdZnTe). These materials are likely to be most useful for a first responder, large-area detector system, or ultraminature instrument applications. A scintillator converts ionizing radiation or absorbed neutrons into light that is then measured with a photosensor.

Many types of scintillators are available. Their principal limitations are poor energy resolution and lower than desired quantum efficiency. This provides a significant research opportunity because improved energy resolution or better conversion of the energy carried by a high-energy photon or neutron into multiple lower energy scintillator photons offers the possibility of large gains in overall detector efficiency. Currently, CdZnTe is comparatively expensive, and its cadmium content presents environmental hazards upon disposal. Lower cost synthesis of similar but less hazardous materials is desired. Development of large-area, multiple-detector “blanket” systems for contact use in rapid assessment of low-level surface contamination during environmental cleanup following a radiological or nuclear incident is a concept worth assessing if the cost of needed sensors and signal electronics can be lowered sufficiently.

Semiconductor-Based Materials

The second class of materials used for radiation measurement provides high energy resolution. These are typically semiconductor-based, such as lithium-drifted germanium (Ge(Li)). These detectors efficiently convert incident ionizing radiation into electron-hole pairs that are then detected using conventional electronics.

The principal limitations of these materials are their cost, availability, and, in the case of Ge(Li) commonly used for high-resolution gamma detection, the cryogenic temperature essential for optimum performance. Large-volume detectors of this class are quite expensive because of the difficulty in synthesis and fabrication. Development of improved pixel-based detectors, better surface-passivation techniques to increase the reliability of materials, and lower cost synthesis methods present significant opportunities for achieving cost-effective improvements in detection systems. High-resolution gamma detectors that operate at temperatures significantly higher than 77 K are desirable for field detection or portable instrument applications. High-energy x-ray and gamma lenses offer a means of significantly enhancing detection of radionuclides at a distance for a given detector volume and are useful in imaging of radionuclide sources. However, such lenses are currently handcrafted and are expensive.

Technology Need	Present Problem
Combined sensors to determine nature of threat (e.g., high explosives and radioactive material or radioactive material alone).	Such integrated systems do not exist, and both types of detection systems currently have sensitivity limitations.
Improved methods for remote imaging of radioactive sources contained within large objects such as cargo containers, ships, or trucks.	Current methods for large-object tomography are not suitable for routine surveillance.
Stand-off detection of shielded nuclear materials.	Current active interrogation systems are incompatible with some cargo, and are not portable.

Radionuclide sensing via active methods involves irradiation of the suspect material with photons or subatomic particles, such as neutrons, and assessing the response of that material, such as absorption of an incident photon or emission of neutrons because of induced nuclear fission, to the irradiation field. Some of these active interrogation methods have the potential to detect the presence of light-element–based high explosives as well as most actinide elements. However, absent improved detectors, the intensity of irradiation field needed may damage or destroy plants, animals, and materials. In addition, some suitable irradiation sources are not readily portable (e.g., proton accelerators). Methods for low-cost fabrication of high-power mm RF components would be enable creation of portable (“table top”) accelerators. Similarly, advances in femtosecond laser technology would advance “table top” electron accelerator technology. Further development of electrically powered, portable neutron generators would advance detection of fissile materials in transit at border checkpoints and transportation hubs.

Technology Need	Present Problem
Rapid characterization of aerosol plumes that might contain radionuclides.	Remote interrogation of a suspect plume to obtain elemental composition and particle size distribution for most radionuclide species has not been assessed.

Remote laser sensing offers controlled illumination over distances from meters to kilometers, high spectral selectivity, and high-speed operability. Of particular importance is the issue of detection of signatures from specific radioactive materials. Some other subatomic particles, such as neutrinos, provide very high penetration but are difficult to detect by simple means. Obtaining significant improvement in the generation, collimation, and high-sensitivity detection of such particles is distinctly challenging and could represent the desired breakthrough for safe application of large-object tomography. In addition, improved broadband (femtosecond pulse) sources may have significant utility in longer range aerosol remote sensing.

Technology Need	Present Problem
Ultratrace to single-atom detection of a broad range of elements and isotopes together with chemical, physical, and structural characterization of sample materials for attribution and intelligence-gathering purposes.	Current methods are relatively slow and generally have sensitivities measured in many thousands of atoms and poor spatial resolution. Typically, extensive sample pretreatment is required prior to analysis.

Samples of plant, animal, or mineral materials or manufactured articles differ as to their trace element and isotope content, depending on their origin. Detection of trace constituents indicative of the production of fissile isotopes or having unusual relative isotope abundances of hydrogen or lithium isotopes, for example, can provide an early warning indicator of proliferation activities and, if associated with additional trace indicators, the location of those activities.

Further development of ultratrace analysis techniques is essential to achieve high sample throughput and spatial resolution with broad elemental applicability, high isotopic discrimination, and minimal sample pretreatment. High-spatial-resolution chemical, physical, and structural characterization of samples provides additional bases for differentiating materials and determining their probable origins. Development of existing surface enhanced vibrational spectroscopies (e.g., surface enhanced Raman) combined with high-efficiency, solid-state laser microscopies may provide both the needed chemical speciation and imaging capabilities down to the single molecule level. Further development of electron and ion microscopies and analysis techniques based on x-ray beams focused to nanometer dimension may also provide these required characterization capabilities.

2.3.2 Preparedness

Technology Need	Present Problem
Containment of widespread radioactive contamination caused by a terrorist event.	First responders and others need training in this area and supplies for detecting, containing, immobilizing, and removing contamination.
Maintain critical infrastructure and appropriately trained personnel.	Decaying infrastructure and limited education and training opportunities.

Containment and prevention of isotope migration will be of immediate concern following a terrorist release of radionuclides. Effort is needed to develop rapidly deployable immobilizing agents that can be applied to contaminated soils, buildings, vehicles, etc. Whereas these could be comprised of nonreactive materials (i.e., urethane foams or other rapid forming plastics), such immobilizing agents would ideally facilitate cleanup and removal of the radionuclides following the initial response to a terrorist event. This may be facilitated by inclusion of sorbents within a permeable coating. Finally, one might choose a foam composition that would induce the reduction of high-valent actinides to less soluble lower oxidation states or a foam composition that leads to a significant increase in soil pH, resulting in the precipitation of radionuclides as hydroxides or oxides. To date, none of these selective immobilizing agents exists. Fundamental work is needed in the areas of polymer chemistry and separations chemistry to realize the potential of this approach. Furthermore, it is imperative that personnel be trained to detect radioactive materials and to react appropriately in the case of nuclear terrorism.

Technology Need	Present Problem
Effective therapies needed for decontaminating victims of radioactive contamination, especially for actinide contamination.	The current treatment method for actinide removal is limited in its efficacy

Actinide, especially plutonium, contamination is a significant danger because of its high toxicity. The currently accepted method for reducing and removing Pu in the body consists of intravenous or inhalation administration of the chelating agent DTPA, diethylenetriaminepentaacetic acid. This protocol has significant therapeutic limitations and is inadequate for treatment of the general public. Possible new compounds for actinide removal have shown great efficacy for actinide ions at physiological pH. They are based on the syntheses and characterization of a number of actinide-specific ligands, patterned after natural iron-sequestering agents called siderophores. These compounds have been evaluated for their efficacy in removing actinides from mice (in studies supported by NIH). However, many additional studies are necessary before these new materials can be certified for drug use. A more effective treatment for the decorporation of actinides in case of human contamination is clearly a highly desirable goal for the mitigation of a possible terrorist act.

2.3.3 Prevention

Technology Need	Present Problem
Stabilization of nuclear materials against dispersal.	Radioactive material inventories are increasing, and safe and secure storage of these isotopes is required.

Much research has been devoted to the materials science of the actinide elements, especially plutonium, over the last fifty years. Many types of complexes have been investigated for use in the nuclear fuel cycle as well as for use for safe and secure storage of special nuclear materials. The oxides of uranium and plutonium have received the most study and are the materials commonly found in nuclear fuels, including the mixed oxide fuels (MOX). MOX fuels are being seriously considered for disposal of excess weapons plutonium in both Russia and the U.S.[4] Plutonium is commonly stored as PuO_2, since in this form it is highly insoluble.

In the future, the synthesis of highly refractory actinide materials that are stable to moisture, are highly dense, can be produced at moderate temperatures, and have a number of desirable physical characteristics for nonproliferation such as the presence of neutron poisons will increase the safety and reliability of storage systems. A major obstacle to the widespread production of these types of actinide materials relates to the reaction temperatures, which range as high as 3000 °C to achieve high purity.

Research in this area should emphasize the development and implementation of unique reaction conditions and novel precursors that enable the preparation of materials at lower temperatures (500–750 °C) and pressures. Such research could also be of value to the development of advanced nuclear fuels that could be easily reprocessed but are difficult to convert to weapons-grade materials. The combination of solid-state, homogenous molecular, and/or vapor-phase deposition synthetic chemistry with multidisciplinary analytical and spectroscopic characterization is needed to produce such new materials. Their production could be a major factor in decreasing the likelihood of diversion for terrorist activities because of the difficulty to use such materials for terrorist purposes.

Technology Need	Present Problem
Understanding of alternative process chemistry, proliferation-resistant fuel cycles.	Unconventional nuclear materials processing may not be detected by current methods.

Awareness of chemical agents that could be used in the purification of Pu and U for use in terrorist activities either from nuclear weapons or from irradiated fuel could be an important signature to prevent their use in terrorist attacks. Universally, the standard purification method for U and Pu has been the Purex process, which uses tributyl phosphate as a solvent extractant. Large-scale purchases of this material would immediately be a source of concern. However, it is likely that terrorist groups who might attempt to use these materials would use alternate processes with different materials. Knowledge of these alternate materials and processes would enhance intelligence activities.

There is significant activity internationally on alternate processing systems for irradiated nuclear fuel. These include aqueous systems as well as nonaqueous separation systems, volatility methods, and other advanced concepts. The technological requirements for further advancements in this field include synthesis, and testing and characterization of new separation methods with particular emphasis on the isolation and purification of the actinide elements.

An example of the potential basis for new actinide separations systems is neoteric solvents, such as ionic liquids, supercritical carbon dioxide, or fluorous phases, that can be considered new classes of solvents for targeted dissolution and separation of transuranic elements. Such new processing conditions represent several fundamental unknowns. Use of these solvents may lead to unique signatures that are valuable in identifying and locating process sources; the solvents may lead to cheaper, better, cleaner processing and/or separations; or there may be unique chemistries not possible through traditional solvent routes.

Actinide speciation and coordination in many neoteric solvents are unknown, but knowledge of speciation and coordination is essential in optimizing separation schemes. Solvent characteristics such as thermal stability, radiolytic stability, and heat capacity are for the most part unknown. These characteristics need to be determined for fundamental chemistry and separations purposes. Understanding neoteric solvent-based separations may result in improved methods for separating and purifying actinide elements. It also will aid in identification of unique signatures of reprocessing via this method, if such signatures exist.

The knowledge base that results from basic research studies on separations and heavy element chemistry is an important component in the identification and tracking of new methods for reprocessing of nuclear fuel and the early discovery of such reprocessing should it be attempted clandestinely for terrorism purposes.

2.3.4 Protection/Response and Recovery

Technology Need	Present Problem
Identification of the chemical and physical form of a contaminant.	Insufficient knowledge of chemical signatures, low signal for widely dispersed material, needed information for predicting fate and transport not available.

Environmental sampling and analysis of elements and isotopes diagnostic of the isotope enrichment processes needed for production of nuclear materials are a key means of detecting nuclear threats. River water samples, atmospheric aerosol samples, and other water source sampling may all contain elemental and isotopic signatures diagnostic of nuclear proliferation. Either the radionuclides themselves (e.g., U-235, Np-237, Pu-239, etc.) or byproducts of the enrichment process (e.g., fission products) can be detected in the environment with ultra-low detection limits using chemical or geochemical sampling protocols and analytical instrumentation.

Sampling protocols have been developed for sediments and waters to support environmental restoration efforts, and the general analytical framework to analyze samples is understood.[5] Limitations exist, however, that are principally associated with sensitivity, speed and throughput, fieldability for on-site response, and integration of existing archived data with analytical tools to assist calibration and interpretation. Research objectives associated with these technology gaps include development of new instrumental approaches. Research into the processes that control the fundamental signatures in environmental substrates, governing the correlation between agents and sources, would be one of the prerequisites to developing new methods.

Technology Need	Present Problem
Develop clean-up strategies for deployment after a terrorist event involving radioactive materials.	Initial sorption processes resulting from a terrorist event are kinetically driven. Better knowledge of fundamental equilibrium chemistry, radiation chemistry, and kinetics of chemical reactions involving radionuclides (for improved predictions for during response and cleanup) are needed.

If nuclear materials are dispersed through a terrorist act, large areas at or near the site will become contaminated. Research efforts on fundamental science relevant to the cleanup of radionuclides have been supported by BES. Additional research is being conducted in DOE's EMSP program. However, these research efforts have been focused on development of information for the cleanup of historical, or "aged," contamination problems, which are not likely relevant to the cleanup of recently contaminated sites.

The recent development of new molecular-level spectroscopic methods is providing unprecedented opportunities to explore interfacial processes, in many cases in real time. These techniques enable study of the dynamics of highly specific interactions at surfaces. They include scanning probe microscopy (SPM), x-ray absorption spectroscopies (XAS) with microscale spatial resolution, laser microscopy, scanning electron microscopy (SEM), high-resolution transmission electron microscopy (HRTEM), and electron microprobe (EM) methods. An ever-increasing body of evidence from these methods demonstrates that radionuclide sorption at the mineral-water interface begins with specific molecular-level interactions. These are the chemical reactions that scale up to yield the macroscopic interfacial phenomena observed in the environment and, ideally, can be predicted with geochemical models. Confidence in such predictions can be improved by a mechanistic understanding of these molecular reactions and their representation as equilibrium thermodynamic or kinetic expressions in such models.

Aged contamination represents an established steady state that has developed over time following the initial sorption. The sorption processes that are relevant following a terrorist event are more likely kinetically driven. To address these science needs, research should focus on defining the initial kinetic processes and the mechanisms whereby radionuclides are sorbed to environmental matrices. The tools described above should make this possible. This information will be essential in developing clean-up strategies for deployment after a terrorist event involving nuclear materials.

Beyond identification of the mechanisms of sorption and transport, research is required on treatment methods appropriate to immobilize or mobilize contaminants in a controlled fashion with minimal disruption to the host matrix. Understanding of interfacial redox and complexation chemistry is distinct from traditional solution process chemistry, but will be key to successful development of new clean-up protocols.

To the extent that the application of separation science to counter terrorism involves the isolation, separation, or preconcentration of radioactive metal ions, the general research needs identified are the following:

- Development of highly specific ligands, allowing separations to be performed in fewer steps, with smaller equipment, or with lesser volumes of reagents, and cost-effective methods for their synthesis.
- Development and application of improved computational methods for ligand design.
- Application of parallel synthesis technologies and combinatorial methods to the preparation and evaluation of new ligands.
- Improved understanding of the thermodynamics and kinetics of solute-solvent interactions, permitting selection of the most appropriate separation medium (solvent, ion-exchange resin, membrane) and offering additional opportunities to increase process efficiency.
- Greater consideration of complexation and mass transfer kinetics in the design of extractants and complexing agents.
- Application of modern experimental (e.g., synchrotron radiation sources) and theoretical (molecular dynamics calculations) methodology to the development of an improved understanding of the properties of liquid-liquid and liquid-solid

interfaces, thus providing new perspectives on the nature of separations-relevant processes occurring at these interfaces.

- Development of environmentally benign separation processes, which produce no secondary wastes and consume no chemicals.

Technology Need	Present Problem
Better understanding of radiation effects on environmental materials.	Insufficient knowledge of chemical consequences of irradiation of environmentally exposed materials.

To mitigate the chemical consequences of radioactive contamination in the environment, predictive models are required. Much is known about the fundamental radiation effects in homogeneous systems of common materials. However, the chemical effects of ionizing radiation on complex, heterogeneous environments are largely unknown.

Fundamental information on the time evolution of events following the absorption of radiation by complex materials and at interfaces is, therefore, needed. The absorption of radiation in complex materials changes the chemical and physical properties of the material. This is particularly important in systems that are common in the natural environment. Oxidation state, surface potential, lattice parameters, reactive site density, solubility, particle size and size distribution of soil particles, humic substances, minerals, metal ions, etc., will all change as a result of the radiolytic processes and affect the mobility and migration of radionuclides in the environment. In a terrorist attack involving nuclear incidents, components of sensors (optical materials, semiconductors, plastics, etc.), which are sensitive to radiolytic effects, will suffer significant performance deterioration. These can be modeled, and remedies may be offered if fundamental information on the effects of radiation is available. Studies should include not only electron and gamma irradiation, but also the effects of alpha particles and neutrons. Ionizing radiation is one of the available methods for preventing the spread of lethal bioagents via sterilization. Improving the efficiency of the sterilization process and minimizing adverse side products are significant challenges. Existing machines use electron beams whose penetration depth is relatively limited. Scenarios should be developed to enhance penetration depth, and thereby the efficiency of the sterilization process. At the high doses required for sterilization, the object itself may be damaged. This not only destroys the object, but may also release noxious gases, which may harm the personnel handling the materials. Fundamental studies, experimental and computational, will identify and quantify the risks from using ionizing radiation and develop strategies to minimize them.

2.4 Research Needs

The preceding sections have identified a number of scientific issues and research needs than can have significant impact in addressing critical problems associated with countering radiological and nuclear threats. The following are some of the most critical issues that were identified

2.4.1 Scientific Issues

Chemical Separations

Chemical separations will play an important role in delineating the scope of contamination, mitigating the damage, and facilitating recovery from a terrorist event. Continued research is required on critical issues including the isolation, separation, or preconcentration of radioactive metal ions. In addition, resources should be directed toward the development of environmentally benign separation processes that produce no secondary wastes and consume no chemicals.

Ion/Molecular Recognition

Selective ligands for actinides and fission products will play a key role in technologies associated with detection, prevention, and response and recovery. Combinatorial chemistry approaches should be used to aid in the design of new receptors. In addition, new approaches for modeling and characterizing the thermodynamics and kinetics of radionuclide-ligand interaction will help to accelerate the development of more effective ligands.

Interfacial Science

There is a significant need to describe the behavior of actinides in more complex media, often involving nonequilibrium conditions, and chemical speciation/distribution at interfaces (solid/solution, aqueous phase/biological membrane, etc.). Research should seek to establish the nature of chemical processes, including those between actinides and fission products and reactive surfaces. This will require the development of new probes to characterize kinetic, thermodynamic, and structural elements at surfaces.

Computing, Modeling, and Simulation

It will be critical to develop improved algorithms and computing platforms to provide accurate predictions for nuclear, atomic, molecular, and macromolecular properties and interactions. Important areas for such calculations are as diverse as determining the influence of hyperfine, electrostatic, and magnetic interactions on atomic and ionic spectra of actinide isotopes to improving the design of novel scintillator materials. Insight gained from theoretical calculations must be integrated into the planning, execution, and analysis of experiments, particularly those designed to assess new approaches to countering terrorism.

Advanced Instrumentation/ Laser and Mass Spectroscopy

Many of the advanced instrumentation needs that were identified, such as large-area tomography, will have to be addressed by multidisciplinary research teams of scientists and engineers. The continued development of high-sensitivity spectroscopic tools will underpin research efforts in chemical speciation of actinide and fission products under a variety of conditions. Advances in laser-based techniques are needed for improved stand-off detection, while improvements in the performance of conventional mass spectrometry instruments are needed to address the broad range of isotopes and elements that need to be quantified.

Novel Materials

Combinatorial chemistry or other rapid synthesis and assessment techniques along with insight gained from theoretical calculations should be employed to improve scintillator performance. The same methods can also be applied to ligand design for specific ion separations. Research in actinide materials is required to address technology needs in material stabilization.

Alternative Processing Chemistry

Fundamental research in physical and chemical separation methods, chemistry in alternative media (including nonaqueous), and methods for isotopic enrichment, is needed to understand the possibilities for alternative processing of nuclear materials and their potential for affecting nuclear proliferation. This research might also lead to the development of new processes that have significant advantages over our current technologies.

2.4.1 Research Environment and Infrastructure

The DOE is the only source of funding for fundamental and applied research studies involving radiation effects and nuclear and radiological materials. The Office of Science has the stewardship role for fundamental research in these areas. However, the resources allocated to these areas have, in general, been decreasing over the last three decades. This has resulted in a net loss of personnel and aging infrastructure, including a lack of modern equipment. These problems are not only acute at the national laboratories, but are also reflected at universities where faculty positions and studies in radiochemistry and nuclear chemistry have been rapidly declining.

Most of the buildings and facilities at the national laboratories used for fundamental research with radioactive materials were built more than thirty years ago. Upgrading and modernizing these facilities is necessary to bring them to modern day standards and also to implement new research tools to advance fundamental research in heavy element chemistry and physics and the effects of radiation. This is an essential first step necessary to re-invigorate the national laboratories. Collaborative efforts or virtual conferencing should be encouraged to facilitate productive interaction among geographically diverse team members.

Education and Training

The key need for all areas of Homeland Security is trained personnel. For the Radiological / Nuclear Threats area, this means that personnel trends in both university and national laboratory programs must be reversed for DOE to maintain a cadre of qualified scientists and personnel that can address radiological technical issues and threats now and into the future. With the realization that nuclear power represents, at least at present, the only major source of energy without the production of carbon dioxide, it is even more critical to attack the personnel and infrastructure problems that can greatly handicap future programs. In addition, the further development of nuclear power, although it brings the risk of terrorist attacks, reduces the dependence of the U.S. on foreign sources of oil and the risk of the U.S. being held “hostage” by foreign oil-producing nations.

Although radio and nuclear chemistry was an active research area at many universities, the facilities to conduct radiochemical research and education at universities are either disappearing or have aged beyond a useful stage. Furthermore, whereas aspects of nuclear science and nuclear engineering were once considered an important part of the general science and engineering curricula, others, perceived to be of more general interest, have replaced these subjects. Without the infrastructure to educate science and engineering undergraduates in nuclear science and engineering, the general population becomes increasingly ignorant of the risks associated with a radiological or nuclear attack and will not understand response efforts.

The supply of trained radiochemists is seriously impeded by the lack of facilities at universities to conduct research and teaching in this area. University radiochemistry programs also provide an additional source of novel ideas and research agendas to complement those at the national laboratories. Without an incentive for adequate infrastructure within the educational system, the universities will continue to close the few remaining programs in nuclear science and engineering, and the knowledge base in radiochemistry and actinide science, and the ability to respond to threats will be eroded. Applications of radiochemistry and, to some extent, actinide chemistry extend not only to defense programs, nuclear energy, and counter terrorism, but also to areas more attractive to the general public such as environmental cleanup and nuclear medicine (e.g., advances in cancer treatment and diagnosis).

One attractive concept is to augment the national laboratory programs and facilities that deal with radiation chemistry and heavy element chemistry and physics by creating regional centers (with national coordination) that can act as user facilities for university programs. The model for this type of center is the user facilities and programs at DOE's synchrotron sources. In this scenario, the national laboratories will provide materials, training, facilities, and instrumentation for visiting researchers to be able to come to the center and perform experiments with materials or equipment not available at their institutions. Part of the staff at the national laboratory will be responsible for training these visitors and facilitating their experiments. At the same time, universities should extend their training and research in these areas with courses taught by national laboratory personnel in their specialty science areas to supplement the traditional university radiochemistry programs.

To help universities initiate and/or continue their programs in nuclear and radiochemistry, DOE should consider the award of start-up funds for newly appointed and established faculty in research areas that are determined to be in the national interest. Such grants might be for five years and renewable based upon peer review. These faculty and their students could collaborate with the national laboratory regional centers to avoid duplication of resources and to strengthen the ties between academia and the national laboratories. Clearly, such programs would benefit DOE and the U.S. by providing qualified scientists and personnel to pursue future radiological/nuclear issues.

BES-Supported User Facilities

Over the last several years, both national laboratory and university researchers have successfully capitalized on the ability to perform experiments with radioactive materials at many of the BES-supported user facilities. This is particularly true at the synchrotron radiation light sources, where significant experiments contributing to the understanding of both fundamental and applied aspects of radiological materials relevant to issues of homeland security have been performed.

Many of the user facilities are situated at national laboratories or at DOE centers that have sufficient infrastructure and experience handling radioactive materials in accordance with DOE standards to permit and support a reasonable number of such activities. However, to facilitate more efficient and productive scientific investigations of radioactive materials, as well as to engage a larger community of users, additional operational support for these studies is necessary, especially since the safety aspects are an integral and time-consuming component of the experiments. Furthermore, having the ability to capably handle materials close to the user facilities is also important, and the need for support of these "satellite" user facility laboratories should be recognized. An increased level of operational support for the use of radioactive materials, at least in the case of synchrotron radiation sources, will also allow utilization of a larger number of synchrotron radiation techniques.

2.4.3 Relationships with Other Programs

DOE is the only source of funding for fundamental radiological and radiation chemistry because of its role in nuclear weapons design, manufacturing, and stewardship, as well as in managing the environmental legacy of weapons production. Strong scientific ties exist between core BES programs and the Environmental Management Science Program (EMSP), particularly in areas relating to the development of chemistry for waste treatment or diagnostics of chemical behavior. It is important to note that these specific areas have been cited as research needs in the context of counter terrorism. Technologies derived from BES-funded research are now beginning to find interest in appropriate NNSA programs. Certainly research investment in analytical tools (e.g., mass spectrometry) has been and will continue to be a vital contribution to programs in radiochemical analysis sponsored by DOE – National Nuclear Security Administration (NNSA) and a variety of other federal agencies.

Strong interests exists between research in heavy element and radiation chemistry and Defense Programs activities within the NNSA. Historically, BES-sponsored programs have been integral to the development of process chemistry for the chemical and isotopic separation of actinides. More recently, these programs are playing a significant role in the development of tools to investigate chemical and structural properties of materials related to weapons components, including the effects of aging and radiolysis. This has led to the development of new partnerships between NNSA laboratories and user facilities supported by BES.

New relationships are likely to develop as a function of increased emphasis on relevant research areas within BES. For example, as research is expanded to include a greater role for fission product research, overlap will be strengthened with technical interests in BER and DOE-NE (e.g., NE-70, the Office of Isotopes for Medicine and Science). These include mutual interest in the biological chemistry and coordination chemistry of radionuclides, as well as the development of novel separations methods for purification and isolation. It is significant to note that interactions are increasing between DOE laboratory programs in heavy element chemistry and university-based programs in radiochemistry. These collaborations are encouraged in principle through the Office of Nuclear Energy through programs such as the Advanced Nuclear Medicine Initiative (ANMI) and the Innovations in Nuclear Infrastructure and Education (INIE) initiative. While these do not specifically fund work in counter terrorism, they may support the infrastructure and training needs (as cited above).

2.4.4 Dual-Use Opportunities

The knowledge to be gained from these and associated research programs will not only hold value in countering terrorism, but can make contributions to many other technology areas. For example, improvements in radiation detection schemes or materials for radiation detection would be beneficial in a range of applications from medical diagnostics to astrophysics research. Improved understanding of chemistry in complex matrices has already been highlighted as a research topic that can bring great benefit to the DOE complex in meeting its responsibilities for long-term stewardship at a number of contaminated facilities and at waste repository sites. Improved knowledge of process and materials chemistry will be integral to the implementation of advanced nuclear fuel cycles, and will equally contribute to solving problems in materials stabilization or disposition. Through examination of interfacial and materials chemistry, this research will also devise new scientific tools suited to addressing technical questions in one of the primary missions of the DOE: stewardship of the nation's nuclear stockpile (in particular, examination of the effects of aging on key materials). Finally, it has long been recognized that the scientific infrastructure associated with actinide and fission product research within the DOE is very similar to that required for further development of nuclear medicine. This is recognized directly in the DOE-funded summer nuclear chemistry schools, as well as in the curricula of a number of university departments emphasizing nuclear and radiochemistry. This overlap will become even more significant in the event that BES-sponsored research can be expanded to include more research on fission products.

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[1] See for example J. Warrick, "Making of a 'Dirty Bomb'," *Washington Post*, March 18, 2002, page 1; J. Glanz, "Despite New Tools, Detecting Nuclear Materials Is Doubtful," *New York Times*, March 18, 2002, page 13.

[2] "Proliferation concerns: assessing U.S. efforts to help contain nuclear and other dangerous materials and technologies in the former Soviet Union," National Research Council (U.S.), Office of International Affairs, Washington, D.C., National Academy Press, 1997.

[3] "Technology R&D for Arms Control," Arms Control and Nonproliferation Technologies, Office of Nonproliferation Research and Engineering, National Nuclear Security Agency, Defense Nuclear Nonproliferation Program, Spring 2001, http://www.llnl.gov/nai/communication.html.

[4] "Mixed Oxide Fuel (MOX) Exploitation and Destruction in Power Reactors," Proceedings of the NATO Advanced Research Workshop, Obninsk, Russia, October 16–19, 1994, Eds., Erich R. Merz , Carl E. Walter, Gennady M. Pshakin, Kluwer Academic Publishers, Dordrecht, 1995.

[5] "Groundwater & soil cleanup: improving management of persistent contaminants," National Research Council. Committee on Technologies for Cleanup of Subsurface Contaminants in the DOE Weapons Complex: Board on Radioactive Waste Management.; National Research Council, Commission on Geosciences, Environment, and Resources, Washington, D.C.: National Academy Press, 1999.

3 Chemical Threats

3.1 Terrorism Threats and Technology Needs

Potential chemical threats from terrorist attacks include chemical weapons, toxic industrial chemicals and materials (referred to in this report as TIMs), and explosives. Chemical warfare agents, or simply chemical agents (i.e., nerve, choke, blister agents, etc.), are well known and therefore possibly perceived by the general public to be the greatest threat. However, TIMs are far more readily available and constitute a significant threat. TIMs are defined as those chemicals with an LCt50 value (lethal concentration for 50% of the population multiplied by exposure time) of less than 100,000 mg-min/m^3 in any mammalian species and produced in quantities exceeding 30 tons per year. [1] Explosives, on the other hand, are undoubtedly the chemical threat agent that has historically been most highly utilized by terrorists.

This section deals only with the challenges associated with conventional (e.g., non-nuclear) explosives. Nuclear and radiological threats are discussed in Section 2 of this report. Each of these specific threats has unique characteristic and associated technology needs to facilitate detection, preparedness, prevention, protection, and response and recovery. This section describes these threats and associated technology needs in more detail, gives examples of how current and previous research within Basic Energy Sciences (BES) is helping to counter these threats, and defines future research directions for improving homeland defense capabilities with respect to chemical threats.

3.1.1 Chemical Warfare Agents

Chemical warfare agents were designed to have devastating effects on their target and to achieve those effects in a short period of time. Chemical weapons are commonly grouped according to their major physiological activity as blister, nerve, choking, and blood agents. The nerve agent Sarin, for example, was used by the Aum Shinrikio terrorist organization in an attack on the Tokyo subway in 1995. The attack exposed 5,000–6,000 people to the agent, hospitalizing nearly 500 people and killing 11. Some of those requiring medical attention because of exposure to the nerve agent were first responders and medical personnel.

Detection

Rapid and specific detection of chemical weapons is an important technological need. The first responders in future terrorist incidents within the U.S. will be local law enforcement, fire, and medical personnel, and the budgets of many localities will not accommodate expensive detection equipment. Thus, cost restrictions are imposed on future detectors intended for widespread use and field deployment.

The Institute of Medicine, National Research Council, published a survey of detectors for chemical agents in 1999.[2] Of the 100 detectors identified, funding for their development came from the Department of Defense (DoD) (28%), commercial companies (56%), and the remainder from other agencies, including the Department of Energy (DOE), Environmental Protection Agency (EPA), National Aeronautics and Space Administration (NASA), and the Technical Support Working Group (TSWG). These figures reflect what was previously considered to be a military need, as opposed to a homeland defense need; however, the figures do not necessarily reflect the source of basic research funding that led to the discovery of fundamental principles on which these instruments are based.

All detectors surveyed had sufficient sensitivity to detect chemical agents at high enough concentrations to present an immediate health hazard, but only the most expensive systems had sensitivities sufficient to ensure the complete health and safety of victims and responders.[2] Further, false-positive responses were a problem in some chemical agent detectors, which is a highly undesirable characteristic for detectors used in a civilian environment. The future of chemical weapons detectors relies on new fundamental developments in the areas of separation and analysis, materials chemistry, chemical transformations, and atomic and molecular spectroscopy.

Protection/Response and Recovery

An integral part of incident response and recovery is the decontamination of chemical agents to remove any residual source of slowly vaporizing material. Chemical-agent simulants have been shown to penetrate porous building materials, thereby providing a continuously emitting source and complicating the decontamination process.[3] An understanding of the movement of chemical agents and decontaminating reagents through porous building materials constitutes a technological need for efficient and complete decontamination. This need is emphasized by a general lack of knowledge regarding health effects from long-term exposure to low concentrations of chemical agents. The potential for low-level exposure also points to the need for finding biological markers of low-level exposure to chemical agents, as well as other chemical threats, to facilitate early detection and treatment for exposure. Decontamination of victims and nonporous surfaces exposed to many chemical agents can be achieved with dilute bleach and through adsorption onto dry decontamination materials. Supporting fundamental knowledge from BES-funded studies of chemical reactions in complex media, materials synthesis and processing, and catalysis and chemical transformations will guide developments in this important area.

Personal protection equipment (PPE) for chemical agents consists of protective clothing and masks for respiratory protection. PPE suitable for use against chemical weapons is commercially available, but the items are bulky and physically demanding to wear. Technological needs exist for lighter weight protective and reactive barrier materials for PPE. Future technologies for catalytic decomposition and adsorptive binding of chemical agents will be founded on basic research advances in areas such as physical and chemical properties of materials, surface and interface science, catalysis and chemical transformations, and materials synthesis and processing.

3.1.2 TIMs

In 1999, the General Accounting Office reported to Congress (Subcommittee on National Security, Veterans Affairs and International Relations, Committee on Government Reform, U.S. House of Representatives) its finding from a survey conducted among law enforcement and intelligence agencies regarding the threat of chemical and biological terrorism in the U.S. The report concluded that "in most cases terrorists would have to overcome significant technical and operational challenges to successfully make and release chemical or biological agents of sufficient quantity to kill or injure large numbers of people without substantial assistance from a state sponsor." [4] In the GAO report, a "large number of people" was defined to be greater than one thousand.

A likely alternative chemical weapon for terrorists is often considered to be TIMs. Unlike chemical weapons, TIMs are not designed to kill people; however, many TIMs are highly toxic and are produced in very large quantities by chemical manufacturers throughout the world. A list of approximately 100 TIMs and their respective toxicity ratings has been published elsewhere.[1] The onset of symptoms from TIMs exposure may be delayed for up to several days in some cases. A powerful example of the deadly nature of some TIMs is the accidental release of methylisocyanate in Bhopal, India, on December 2, 1984. In the Bhopal accident, 40 tons of methylisocyanate were released over 90 minutes, exposing 200,000 people and killing 8,000. This single incident claimed almost three times as many lives as the September 11, 2001, attacks on New York and Washington, D.C.

Detection

Many technological needs for homeland defense from terrorist attacks utilizing TIMs are very similar to those for chemical weapons. However, detection devices designed for use with one class of chemical threat (i.e., chemical weapons) may not properly identify or respond to the other (i.e., TIMs). The Department of Justice recently published the results of a survey of 148 detectors capable of detecting chemical weapons and TIMs.[1] Of 69 handheld-portable instruments surveyed, 12 had chemical weapons detection capabilities, 52 had TIMs detection capabilities, and only 5 would respond to both chemical weapons and TIMs. None of the vehicle-mounted, fixed-site detection systems or fixed-site analytical or stand-off detectors had TIMs detection capability. Technological barriers to generalized multi-threat detectors will require basic research in separations and analysis, atomic and molecular spectroscopy, and materials synthesis and processing.

Protection/Response and Recovery

Many of the decontamination and personal protective equipment issues associated with chemical agents also apply to TIMs. However, in the case of TIMS, material safety data sheets and first-aid information are readily available for these industrial products. In addition, risk assessment studies have already been performed for most common industrial materials. Biological markers and long-term health effects of low-level exposure are also important for TIMs.

3.1.3 Explosives

As a chemical threat, explosives are dramatically different from chemical agents and TIMs. A terrorist action utilizing a conventional explosive may result in a catastrophic event that takes many lives, but the event is not likely to result in post-event decontamination and mitigation problems associated with the explosives compounds themselves. Like TIMs, explosives are produced in large quantities throughout the world for military and commercial applications. Some explosives can be prepared from materials available at virtually any pharmacy. The availability of explosives and the widespread recipes for their use in publicly available books and on the internet contribute to the large number of terrorist events involving explosives.

Explosives have been used in many terrorist attacks within the U.S. and abroad. The most notable terrorist attack within the U.S. that utilized explosives was undoubtedly the bombing of Oklahoma City's Alfred P. Murrah Federal Building in 1995. In that event, the detonation of several tons of ammonium nitrate fertilizer mixed with nitromethane-based racing fuel took the lives of 168 people, including 19 children. In 1993, the World Trade Center withstood an attack by a bomb containing in excess of 1,000 pounds of nitrourea and hydrogen gas cylinders. Six people died and more than 1,000 people were injured in the attack. More recently, a mixture of pentaerythritiol tetranitrate (PETN) and triacetone triperoxide (TATP) packed into the soles of a terrorist's shoes failed to detonate aboard an American Airlines flight in December 2001.

Detection

Commercial detectors for explosives are deployed throughout the world to safeguard against terrorist attacks. Lower limits of detection and higher specificity are ever-present technological needs in the area of explosives detection. Chemically specific standoff detection can be especially important for safe detection of explosives. The low vapor pressures of most explosives impose technological challenges in sample collection and transport that are unique to the detection of this chemical threat.

Protection/Response and Recovery

In some instances, the severity of a terrorist event involving an explosive device could be mitigated by containing the primary blast or through shielding from the blast. The fundamental technological barriers involved in containing a blast are embodied in materials science and structural engineering. Fundamental advances in the areas of separations and analysis, atomic and molecular spectroscopy, and surface and interface science will lead to better detectors, sampling methodologies, and incident containment technologies in the future.

3.2 BES Research Accomplishments and Implications for Countering Terrorism

Fundamental research within the DOE's Office of Basic Energy Sciences has contributed significantly to existing and emerging technologies that can be applied to countering terrorist chemical threats. Fundamental research will continue to have an impact on all areas of homeland defense, including detection, preparedness, prevention, protection, and response and recovery. Examples of some of this research are outlined below.

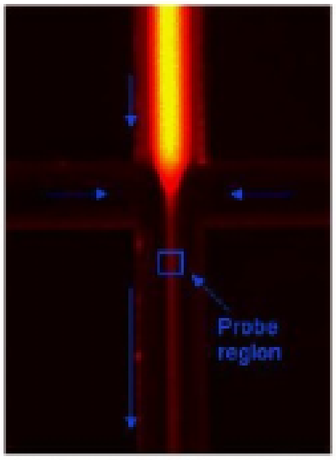
3.2.1 Detection

Optical Spectroscopy

Interfering background components are a ubiquitous barrier to real-world deployment of sensors and detectors. BES-supported research programs in separations and analysis are assisting in breaking down these barriers and enhancing the ability to confidently detect trace compounds. Several research programs are devoted to the development and utilization of laser-based ultra-sensitive detection schemes for monitoring molecular species. Fluorescence, absorption, and laser/mass spectrometric techniques are employed to push the detection limits toward the ultimate goal of single molecule detection. Research in advanced laser-based chemical measurement problems has led to advances in high-sensitivity and high-resolution measurements in gas and condensed-phase chemical systems. This research has evolved to investigate molecules in micro- and nano-domains and at interfaces, including molecules adsorbed on individual particles, contained in microdroplets, and within microfluidic "lab-on-a-chip" devices.

Specialized light sources at BES Scientific User Facilities provide researchers with the ability to scan the electromagnetic spectrum from x-rays up to the infrared. These powerful light sources provide a tool for gaining fundamental insight into molecular spectroscopy and properties that may form the basis for future detection techniques. Resonant laser photoionization of sputtered atoms from surfaces can measure as few as 10 atoms and can measure target analytes in concentrations as low as parts per trillion. Fundamental laser-based studies, coupled with advances in microfabricated separation and analysis systems such as lab-on-a-chip devices, hold much promise for future technologies to counter terrorism. BES-supported fundamental studies in energy transfer and optical spectroscopy have led to the discovery of detectors for nitroaromatic explosives and structurally related compounds at the ppb level.

Microfluidics for Chip-Based Detection



A 5 s integrated CCD image of Jurkat cells labeled with Calcein undergoing hydrodynamic focusing for high sensitivity detection.

Many of the detection and identification approaches for countering terrorism will benefit from microfabricated chemical and biochemical measurement devices. To meet these needs, lab-on-a-chip technology must be able to identify chemical and biological materials in liquids with low false signatures. In these devices, typical analysis volumes will be in the range of one nanoliter where a concentration of one femtomolar would represent only one to several molecules for analysis.

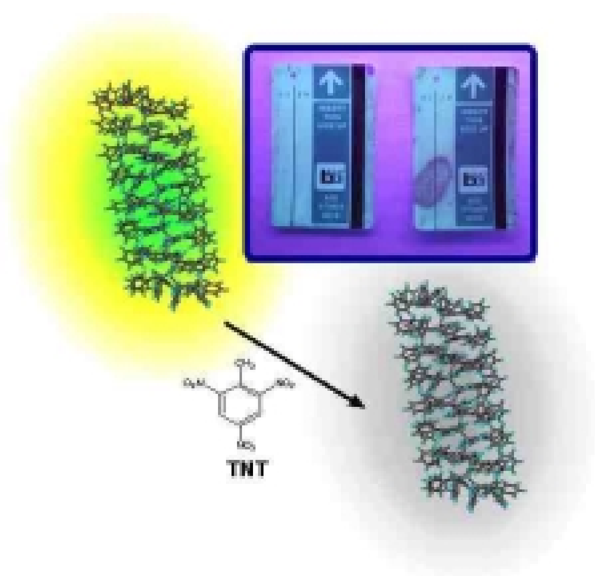
Measurement at the single molecule limit discussed above requires fundamental under-standing of the transfer of target species through the measurement system. Investigations supported by BES have advanced our understanding of the requirements for low-level (single molecule) detection in the liquid phase. Statistical principles developed and experimentally confirmed in these studies allow molecular detection efficiencies to be estimated for a given experimental condition.

[Oak Ridge National Laboratories]

Photochemical Nanomaterials for Explosives Detection

Rapid detection of chemical, biological, or explosives threats has emerged as a major need in countering terrorism. In this area, low-power, portable, and inexpensive devices are key to widespread deployment. BES-funded research on the photochemistry of materials has focused on understanding photosynthesis. In photosynthesis, a large assembly of molecules in a green plant each collects a photon of light, and the energy is then funneled into a small spot, where the chemical conversion of carbon dioxide into fuel can occur. The concept of building an antenna to harvest energy over a large area can also be used to amplify the detection of chemicals. Studies of luminescent silicon nanoparticles, sponsored by DOE BES, led to the development of quantum dots and nanowires of silicon that collect light over a large area and then funnel the energy to the vicinity of a molecule of an explosive, which amplifies the optical signature of the target molecule. Similar light harvesting/amplification detection concepts are being developed in other university laboratories and in private industry.

[University of California, San Diego]

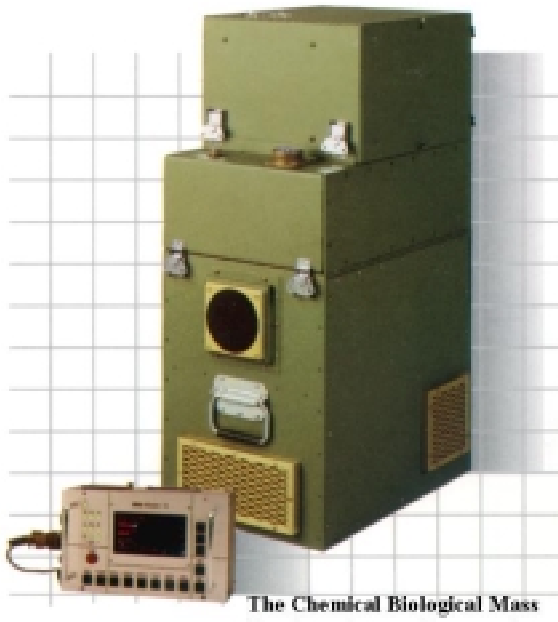


A fingerprint from a person who had recently handled TNT shows up as a dark spot on a subway ticket after treatment with the imaging agent (right ticket).

Mass Spectrometry for Airport Screening

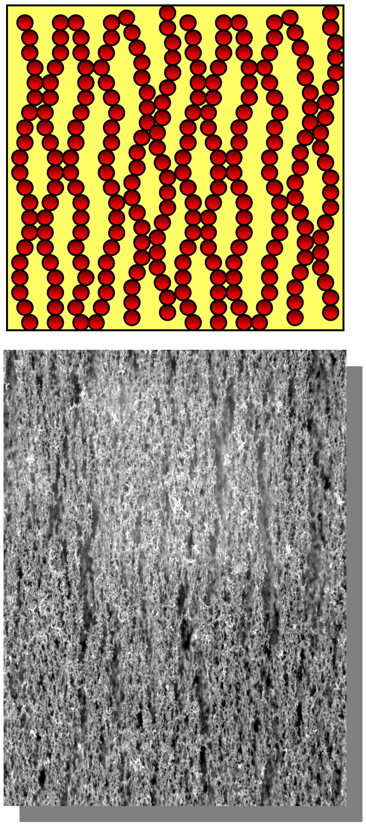
Mass spectrometry has proven to be one of the more effective tools for the rapid trace detection of threat compounds, such as explosives, toxic chemicals, and biological materials. BES-funded research has led to the development of quadrupole ion trap mass spectroscopy, many features of which are incorporated in commercial ion trap instruments that may be found at airport screening stations. Ion traps greatly improve our ability to miniaturize high-performance MS. These basic research developments are also incorporated into the U.S. Army Soldier and Biological Chemical Command that is developing the Block II Chemical Biological Mass Spectrometer (CBMS). This program is developing, demonstrating, and delivering to the Army the first integrated instrument capable of real-time detection and identification of both chemical and biological warfare agents on the battlefield.

[Oak Ridge National Laboratory]



The Chemical Biological Mass Spectrometer employs novel fundamental gas phase processes for highly sensitive and selective detection of threat agents.

Nanocomposite Materials for Chemical Sensing



Field-Structured Composites – showing simulated (top) and actual (bottom) structures.

An important class of chemical sensors is based on metal/polymer composites materials whose ability to conduct electricity changes in a dramatic fashion when exposed to target chemicals. The secret of this behavior is in controlling the spacing between the electrically conductive metal particles. As chemicals are absorbed, the polymer expands, creating more space between the particles and making it harder for electrons to pass from one particle to the next. While extremely sensitive, the practical application of these sensors is limited by previous ability to build composites with precise and uniform spacing between the metal particles.

BES supported research has led to a new approach for building extremely uniform and controlled composite structures. These composites are members of a new class of Field-Structured Composites.[1] They consist of 1–5 micron sized magnetic metallic particles suspended in an uncured polymer solution. The suspension is then exposed to an axial magnetic field, causing the magnetic particles to form chains with highly uniform particle spacing. Upon final curing, these composites demonstrate high sensitivity and extremely reproducible sensing performance. *[Sandia National Laboratories]*

[1] J. E. Martin, R. C. Hughes, and R. A. Anderson, *Science*, Dec. 21 news brief.

Magnetic Resonance Imaging and Spectroscopy

The emerging technique of Magnetic Resonance Force Microscopy (MRFM) is being utilized to study problems where high-resolution 3D imaging is important. Scientists are combining the resolution of atomic force microscopy and the imaging capabilities of magnetic resonance to produce a new method of nondestructive and chemical-specific analysis. Ex situ magnetic resonance imaging is a fundamental breakthrough that may provide a future detection technology. Nuclear magnetic resonance, which places the sample "outside" the magnet, has potential for detecting bulk quantities of enclosed materials.

Mass Spectrometry

The specificity required by many analytical problems benefits from the high information content of mass spectral analysis. Fundamental research has led to many advances in our understanding of the chemical processes comprising the framework of mass spectrometry, ion formation, manipulation, and detection and exploiting its multidimensional capabilities for chemical analysis and characterization. Electron-transfer chemistry, correlation of gas- and condensed-phase chemistry, ion-molecule and ion-ion chemistry, surface chemistry, and mechanisms and energetics of ion processes are among the wide array fundamental issues addressed in this research. Many of the advances from these studies aid in enhanced analysis capabilities and for the future miniaturization of mass spectrometers for field detection devices and have already demonstrated capabilities for detection of chemical agents and explosives. Precise methods have also been developed for analyzing the distribution of stable light isotopes (e.g., D/H, $^{13}C/^{12}C$, and $^{18}O/^{16}O$) to better than 1 part in 10^5 for samples with masses less than one nanogram. Precise isotopic ratio measurement may play a significant role in future forensic and attribution efforts to counter terrorism by helping to identify the geographical and manufacturing origin of terrorist tools.

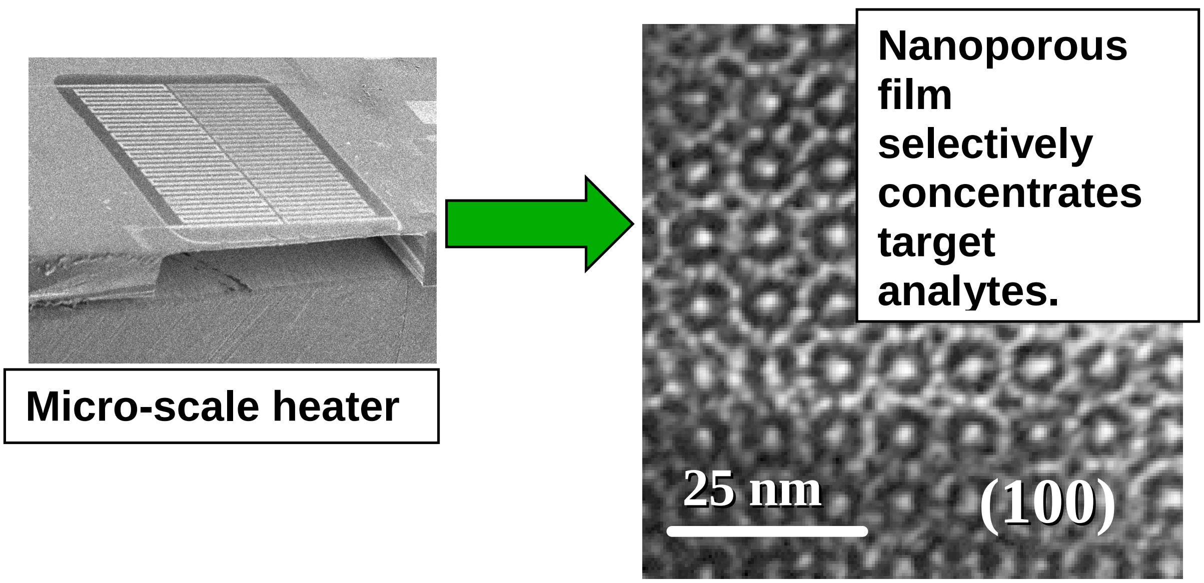
Detection and Nanoscale Properties of Materials

The future of detectors for countering chemical threats from terrorists lies in making the devices smaller and more robust. Fundamental studies in materials synthesis and processing are providing the groundwork for future developments in this area. Research into the use of templated self-assembly to create nanoporous inorganic materials may find

Nanomaterials for Integrated Chemical Analysis

Detection of low levels of chemical toxins with high reliability (low false response) is a major challenge to sensor technologies for countering terrorism. An alternative approach to improved detection sensitivity and selectivity can be realized by integrating chemical preconcentration, chemical separations, and detection into a single miniaturized total chemical analysis system. This approach relies on multiple levels of discrimination to achieve high sensitivity and low false responses.

BES-supported research has made critical contributions to the development of hand-held chemical and biological detection systems. In the example, self-assembled mesoporous sol-gel materials provide highly controlled nano-sized pores for preconcentration of chemical toxins. BES-supported research on thin film deposition processes has allowed direct integration these chemically selective films resulting in greater than one-hundred fold improvement in the miniaturized system analysis sensitivity. The improved sensitivity is critical to the overall capability for the integrated system that is now being evaluated for protection of public assets from terrorist attacks on U.S. soil.



[Sandia National Laboratories]

The micro-scale heater with its integrated nanoporous film is used in the Sandia National Laboratories developed µChemLab to provide a 100-fold boost to the performance of this hand-held total analysis system.[1]

[1] W. A. Groves, E. T. Zellers, G. C. Frye, ***Analytica Chimica Acta,*** 37 (1998), 131-143.

applications in future development of sensor platforms and separations elements. The basic principles governing self-assembly of complex hybrid interfacial and laminar species are also being addressed in parallel efforts. Novel ceramic/polymer and metal/polymer nanocomposites, prepared by employing magnetic fields, represent new classes of tailored materials with a variety of potential applications in chemical sensing. The fundamentals of thin film growth, epitaxy, and structural evolution are also being studied with a focus on elastic strain resulting from film microstructure and surface morphology. Materials containing d- and f-electrons can exhibit complex and collective states resulting from competing interactions. Research has shown that these complex states are highly susceptible to small perturbations and may form the basis for future detectors of weak magnetic fields, small temperature or volume changes, and chemical environment and incident electromagnetic radiation. The results of these studies provide important support for future development of field sensors for chemical threats.

The role of nanostructures in controlling the behavior of materials is being elucidated through fundamental research. Theoretical and experimental tools are being utilized to understand the fundamental mechanisms governing the electronic and optical properties of nanostructured materials. The basic understanding gained from these studies will lead to the discovery of new material properties and physics architectures that can be utilized for improved efficiency and sensitivity in electronic and optical detector systems. In related research, advances in our fundamental understanding of the atomic and nanostructural processes governing materials properties are being sought through the study of energetic-particle synthesis, modification, and analysis. The physics and deformations of ultrafine scale composites that exhibit extremely high specific strength levels and that can be assembled into nanostructures capable of responding to their environment are also being investigated.

The role of surfaces and interfaces in the development of new materials for detecting chemical threats is being elucidated through fundamental studies at several national laboratories and universities. The atomic-scale kinetic processes of diffusion and atom-defect interactions, as well as collective phenomena such as self-assembly, on solid surfaces are being studied. Self-assembly of metals and semiconductor materials is a promising approach to rapidly producing nanoscale sensor arrays and quantum dot networks that may be employed in future chemical threat detection devices. An atomistic understanding of the chemical and physical interactions that control solid/solid and solid/liquid interface formation is important for developing predictive models of adhesive bond strength, interfacial stability, and flow kinetics. Understanding these phenomena will assist in tailoring material surfaces for use in sensing applications. Surface phenomena in thin films are likely to be the basis of microelectromechanical sensors of the future. Studies of surface acoustic waves (Raleigh waves) in thin films can serve as the basis for future developments in this important area. Modification of Raleigh wave velocity resulting from surface modification may be used to detect airborne chemical agents.

Finally, detectors of chemical threats will continue to get smaller and less expensive through the advances in the area of microfabrication. Research has led to the development of high-throughput x-ray microtomography, capable of providing full reconstructions of micron-size parts, and high-resolution 3D imaging. Advances in lithography, electroforming, and molding (LIGA) research is providing the fundamental knowledge required to produce many of the micron-sized parts that will be required in detectors of the future.

3.2.2 Preparedness

An important aspect of countering terrorism is maintaining a state of preparedness. Remaining prepared may require that detection devices be deployed with an onboard power source. When an event occurs, devices need to operate reliably, without a power-source failure. Maximizing the power and lifetime of batteries is important to maintaining a state of preparedness. Fundamental research into the synthesis and properties of materials for thin film rechargeable lithium batteries has examined the physical vapor deposition and properties of electrochemically active thin film materials between 50 nm and 5 microns thick. The resulting batteries are very thin, less than 15 microns, and exceptionally stable, and they provide both a long cycle life and a long shelf life in the charged state. Design changes required to achieve the optimal low cost and environmentally benign rechargeable lithium batteries are being addressed. The high costs and environmental unacceptability of cobalt containing electrodes is an important issue addressed in this research. The formation and control of interfacial films that form on the electrode surfaces as a result of chemical reactions between the electrodes and electrolytes are also being addressed, along with overcharge and overdischarge problems, and mass transport at electrodes.

3.2.3 Prevention

Preventing terrorist attacks is the ultimate goal of many agencies and the focus of much fundamental and applied research. Basic research into amorphous and aperiodic materials is being conducted with the goal of understanding the effects of initial atomic arrangements on devitrification and deformation behavior. The influence of crystal chemistry on the structural stability of aperiodic systems and atomic mobility in these systems plays key roles in determining the physical properties of the materials. This research is laying the groundwork for the development of improved heat-resistant materials, longer-lived insulators, and ultra-hard materials. Such materials would potentially be harder to breach, harder to damage, and even less susceptible to fire.

3.2.4 Protection

If a terrorist event occurs, the first responders are typically local emergency personnel. Fundamental research may result in materials that better protect first responders. Investigations into the fabrication of carbon nanotube membranes may lead to new adsorbent barriers. Membranes consisting of well-defined arrays of small, aligned graphitic pores are being sought to separate energy-related molecules such as hydrogen, methane, carbon monoxide, and carbon dioxide. Extending the results from this work to the adsorption of larger molecules used as chemical threats may contribute significantly to the personal protective equipment of the future. In related research, mesoporous materials containing mesostructures characterized by a precise periodic arrangement of inorganic and organic constituents on the 1–50 nm scale can be prepared by evaporation-driven self-assembly. Scientists have shown that the pore size can be controlled in thin films prepared by the process. The synthetic method holds potential for the preparation of new materials with membrane/filtration applications.

Adsorption, absorption, filtration, and separation are processes that can potentially remove selectively targeted chemical agents from the environment. A unique high-pressure adsorption process has been discovered in fully hydrated zeolites. Superhydrated nanoporous materials can retain an excess of water after pressure release, thus permitting selective adsorption, immobilization, and storage of chemical species. At high pressures, the pores of zeolites expand because of the excess of water, allowing larger cations to enter the nanopores. After the pressure release, the pores contract and trap cations. Superhydrated zeolites and nanoporous materials can find application in waste remediation and immobilization (separation) of chemical and biological material.

Fundamental catalysis studies are examining the reactivity of Au/TiO_2 catalyst. A unique activity of this system for destruction of SO_2 has been discovered for catalysts of Au/TiO2, and related gold/oxide catalysts may find utility in the destruction of sulfur mustard chemical agents. Research has shown that chemical species adsorbed onto the surface of oxides, such as silica, alumina, and zirconia, undergo radiolytic processes more efficiently. A combination of sonication and radiolysis enhances the efficiency of remediation even more. Sensitized large-gap semiconducting nanocrystals (ZnO, porous Si) are being used to detect the presence of chemical vapors. Frontier research supported by BES in surface-supported polymerization and supported-polymer phase formation holds promise for future advances in lightweight protective clothing.

3.2.5 Response and Recovery

In open environments, even semi-volatile chemical agents and TIMs will dissipate. Nonporous surfaces are readily decontaminated with existing products. However, when semi-volatile chemicals diffuse into porous building materials, they become much more difficult to decontaminate, and they can form slowly emitting sources of low-level concentrations of agent. Research into the fundamental aspects of advanced oxidation processes may play a significant role in the development of future decontamination strategies for porous materials.

Photo- and ionizing-radiation induced effects at nonocrystalline oxide materials are being investigated. Photolytically and radiolytically formed species in heterogeneous system may degrade, neutralize, and destroy toxins, chemical agents, and TIMs. By chemical modification of the oxide surface a selective adsorption and destruction of reactants may be achieved.

3.3 Scientific Issues and Research Opportunities

The scientific issues associated with countering chemical threats of terrorism are discussed below in terms of the major emphasis areas of homeland defense. The fundamental issues and the research opportunities in the areas of detection, preparedness, prevention, protection, and response and recovery fall into the BES funding areas of materials synthesis and processing, physical and chemical properties of materials, surfaces interfaces and thin films, microfabrication, catalysis and chemical transformations, separations and analysis, and atomic and molecular spectroscopy.

3.3.1 Detection

Technology Need	Present Problem
Devices to enable chemical threat detection are required for both "detect to treat" and "detect to protect" scenarios.	Sensors and detection systems must become smaller and less expensive to be available for *all* first responders and for deployment in surveillance arrays.

Micro- and nano-fabricated devices that combine separation and detection elements into an integrated device (lab-on-a-chip) are an emerging technology that will play a significant future role in countering terrorism. There is a need for sensors that respond selectively to a given analyte, as well as those that recognize and respond to a broader set of threat chemicals and/or harsh conditions that pose a health hazard. Advances in materials chemistry, such as the development of selective coatings, are needed before molecule-specific recognition elements for sensors can be realized. High information content analytical methods, such as mass spectrometry, provide means of minimizing false positives while being sufficiently sensitive to achieve zero false negatives. Fundamental advances are required to make these methods fieldable and to expand their utility. Sample collection and transport requirements will necessarily change as detection technology morphs to meet the challenges of the future. The technological frontiers associated with each of these challenges are discussed here.

Microfluidics

Although some microfabricated lab-on-a-chip technologies have already moved from the laboratory to the market, fundamental research topics remain to be addressed. In particular, fundamental understanding of electrokinetic transport is not well developed. The structure of the electrical double layer formed at the solid/liquid interface has still not been directly probed experimentally even though its existence was articulated long ago. Nonintrusive probes must be developed with nanometer spatial resolution for such studies. Additional fluid pumping mechanisms must also be developed to allow compact low-power devices to be realized.

As the lateral dimensions of microfluidic channels shrink, the surface-to-volume ratio increases, as do the demands on our ability to pacify surfaces to preclude nonspecific adsorption of liquid-borne materials. Surface characterization tools and improved micron-scale surface modification and patterning chemistries are needed to allow viable manufacture of lab-on-a-chip devices with spatially heterogeneous surface chemistry. These chemistries will also find utility in improving microfabricated gas phase separation and analysis devices.

New quantification tools are also needed for microfluidic devices. Typical analysis volumes in lab-on-a-chip devices are in the one-nanoliter range. Femtomolar concentrations in such volumes imply low numbers of molecules in the analysis volume. Measurement tools with extreme sensitivity are needed, and ideally, they should also be miniature in size and compatible with microfabrication procedures.

Nanofluidics

The transport of fluids through nanoscopic conduits is an area of study that has received very little attention, although it is fundamental to life. The fabrication of such conduits and the active transport of fluid through them are referred to as nanofluidics. Detailed understanding of nanofluidic transport will likely lead to revolutionary technological capabilities (e.g., the ability to sequence *single* molecules of DNA at rates many orders of magnitude faster than currently possible). Understanding of molecular transport in nanoscopic domains will require probing many fundamental questions in the fields of fluid dynamics and statistical physics. Theories that need to be investigated under nanoscale confinement include one- and two-dimensional fluid theories, fundamental assumptions of fluid dynamics such as "stick" or "slip" boundary conditions, the scaling of polymer structure and dynamics with chain length, and the validity of continuum theories.

Fabrication tools must be developed to realize nanofluidic devices. Although multiple strategies for formation of nanochannels appear feasible, fundamental questions regarding intrinsic surface roughness associated with each fabrication strategy will be important. Molecular-scale channels are essentially entirely interfaced with no bulk fluid; thus, understanding and control of interfacial chemistry on the nanometer scale are paramount. Molecular dynamics simulation tools will be needed to understand transport at this scale, and an understanding of the validity of continuum theories at nanometer scale must be established. Importantly, transport through molecular-scale conduits implies that quantification tools must be effective at the single molecule limit. Optical and electrochemical techniques must be developed to interrogate single molecule transport.

Chemical Sensors

Technology Need	Present Problem
Highly selective sensors are needed to identify target chemicals in complex backgrounds.	Easy-to-use chemical sensing techniques are not capable of molecule specific recognition.

The current trend in portable chemical detection is to make sensors selective to the extent of giving analyte discrimination at the molecular level. Detection with molecular specificity is a difficult challenge, and as the number of compounds posing chemical threats continues to increase, the problem only becomes increasingly difficult. Within the context of terrorist chemical threats, it is useful to consider a second paradigm—that of detecting chemical properties or environmental conditions presenting an immediate health hazard. For example, a large number of materials will hydrolyze to produce highly acidic environments that generate a health hazard. It may not be feasible to detect all these chemicals with molecular specificity; however, it is feasible to detect acidic environments. Potential targets for generalized detection schemes include molecules that bind to iron competitively with oxygen, and molecules that mimic acetylcholine. It may be useful to think of detectors for these chemical threat groups as “effects sensors,” with the emphasis on the effect, rather than on the specific chemical. Fundamental research to overcome the challenges of developing “effects sensors” should be pursued as a worthwhile target, even though the challenge may not be as great as that of molecule-selective sensor development.

Molecule-selective chemical sensors for standalone application, as well as those embedded into integrated systems discussed above, will play a crucial role in countering threats of terrorism. At the core of a threat-specific sensor is a molecular recognition event coupled to a transducer to produce a detectable signal. Many sensors employ a thin sorbent layer of chemically selective material to collect and concentrate analyte at the interface of the coating and transducer. Detection is elicited by some change in the physiochemical properties of the interface. There are a number of transducer platforms for coupling the binding event to some observable signal. Designing the coating for specific analytes so as to maximize the collection of analyte and to minimize the collection of interferents is the most significant challenge to produce an effective chemical sensor.

Chemical sensors can employ biological entities such as antibodies, enzymes, receptors, or whole cells as recognition elements, commonly referred to as biosensors. With the advent of recombinant antibodies and phage display antibody libraries, recognition elements can now be found even for analytes for which a natural receptor does not exist. However, biological receptors have rather limited chemical and physical stability that can restrict their use under harsh conditions that include high temperatures, extremes in pH, or nonaqueous media. Biomimetic receptors are attractive alternatives for these applications, since they lend themselves to rational design and chemical synthesis. In some cases, affinities and specificities that rival natural receptors have been achieved. The most successful examples of this type have been for inorganic ions as analytes. However, with targets of increasing complexity, this strategy becomes less tenable because of the synthetic challenges associated with the receptors.

New chemically selective materials are needed that can recognize complex analytes. A further requirement is that the synthesis and processing of these materials be readily incorporated into transducer platforms for use as sensors. It would also be desirable that the processes to produce these materials be amenable to existing microfabrication technologies. Strategies such as molecular imprinting offer considerable potential for making important contributions to this area. Molecularly imprinted polymers (MIPs) are robust network materials that may be tailored for specific analytes. They offer an advantage in that they can function under harsh conditions. Not surprisingly, there has been considerable effort in recent years to employ MIPs as the recognition element of chemical sensors. Basic research is needed to expand the range of targets (ligands) for which this technique can be used. Important ligands include water soluble biologicals such as peptides and proteins. Imprinted polymers are produced by bulk polymerization and, as such, are not conveniently coupled to transducer platforms. Important developments would include new imprinting formulations and processes that are amenable to thin film formation. The ability to produce selective materials that can be produced in 2D or 3D spatially resolved domains by photolithographic processes would facilitate their incorporation into devices. There is also a lack of basic understanding of how recognition sites of MIPs are produced. An understanding of this process can lead to improvements in selectivity and in convergence towards producing more uniform "monoclonal" recognition sites.

An additional approach to producing recognition elements for chemical sensors is through organic polymer nanophases grafted-from sensor platforms by surface initiated polymerization (SIP). SIP is a new and powerful method for tethering ultrathin (10–100 nm) polymer layers onto surfaces. SIP offers potential advantages over attaching preformed polymers to the surface because, for example, it is easier to achieve high grafting densities. However, most of the efforts devoted to SIP have employed standard free radical initiators, resulting in polymers with broad molecular weight distributions and limited control over polymer architecture. Only recently have methods like living radical and living ionic polymerization been used to gain better control over the SIP process. Using these methods, diblock, triblock, and other architectures could be grown from the surface, and chain end functionalization could be achieved. Block copolymer composition can be used to control nanophase formation in tethered polymer brush systems. While experimental work in this area is in its infancy, theory and simulation predict that a rich range of patterned films could be achieved by controlling block copolymer composition, architecture, grafting density, and environment. Systematic studies to synthesize well-defined block copolymer brushes by living SIP processes and to investigate their properties are needed.

Control over the spatial extent of polymerization is a critical issue for incorporating functional polymers into micro- and nano-fabricated devices by both MIPs and SIP polymer formation. The small scales of modern MEMS devices provide an additional barrier to producing polymeric recognition elements. The chemistries discussed above must be performed on platforms and within the confines of micro- and nano-channels with dimensions less than that of a human hair. The prospect of producing chemically distinct domains within these limited real-estate devices is particularly challenging. Multiple domains within a single device are one strategy for expanding system functionality.

One of the “holy grails” of trace explosives detection is the quest for detectors so sensitive that detection of low vapor pressure explosives becomes realistic. While some volatile explosives (e.g., nitroglycerin) typically have vapor pressures in the parts per million (ppm) range or higher, explosives such as RDX and PETN have vapor pressures in the low parts per trillion (ppt) range. When these compounds are incorporated into plastic explosives such as C-4, semtex, and detasheet, the vapor pressures are reduced further by matrix effects, and of course, any packaging or concealment of the explosive will further reduce the amount of vapor available for collection and analysis. As a result, actual vapor pressures in the field may be in the parts per quadrillion range or even lower. Basic research in interface and surface science, separations and analysis, and materials synthesis and processing are needed to produce the breakthrough advances required to enhance the sensitivity of existing detectors or to develop a completely new sensor with superior sensitivity. Incremental improvement in sensitivity will lead to improved vapor detection of explosives with intermediate volatilities (e.g., TNT).

Mass Spectrometry

High information content analytical methods, such as mass spectrometry, can obviate the selectivity problems that are so troublesome for MEMS-based sensors. Mass spectrometry has inherent sensitivity but is hampered by efficiency in ionization and ion detection. Tandem mass spectrometry techniques can detect targeted compounds with high confidence, but this technique is limited to analyzing one target molecule at a time. While a computer can step through the detection of up to about 50 analytes sequentially, new techniques to permit the detection of many targets without reducing the detection duty cycle will be needed to meet the requirements of TIMs detection.

Bringing the high information content and sensitivity of mass spectrometers into a size and price range that makes them widely available to first responders and as continuous monitors of air and water sources will require overcoming some fundamental barriers. Reducing the size of mass analyzers requires studies that investigate the effects of Coulomb forces on ion manipulation and analysis. Microfabricated gas phase micro-instrumentation is a rapidly emerging area of science. The development of truly miniature mass spectrometers that can be hand held could have a huge impact on our ability to monitor the air for harmful materials. Understanding of ion chemistry and physics in confined spaces must be developed. Small lateral dimensions for gas phase devices also implies increased interaction with container walls. Small mass spectrometers may also allow operation at relatively small mean free path conditions (high pressure), and new quantification tools for ions may be needed.

There is also a need for advances in laboratory-based approaches to separations and analysis. The recent anthrax terrorist attack on the U.S. has shown how quickly our analytical laboratory capacity can become overwhelmed. New methods of applying high information content analytical methodologies will provide faster sample throughput and improve the accuracy of analysis.

Technology Need	Present Problem
Chemical signatures must be extracted from gas, liquid, and solid sources.	Develop versatile collection approaches that couple well with miniaturized sensor systems.

One of the principal basic research areas related to chemical detection is the development of adsorptive materials for the collection of chemical agents, TIMs, and explosives. A common sampling application involves adsorption of gas phase species from air, but adsorption of molecules from other media such as water is also important. Selective adsorption from air by molecular recognition processes represents a fundamental research problem with the potential for enhancing detection levels and reducing background interference.

Sample Collection and Transport

Fundamental research in polymer films and molecular recognition that will lead to advances in selective sensing elements is directly relevant to selective sampling. In addition to SIP and MIP soft materials, several other materials offer promise in this area, including sol-gels, carbon-based materials such as carbon foams or carbon-nanotubes, and composite materials. Several properties are needed for a material to be a good adsorbent for chemical agents, TIMs, or explosives. The material needs to have a high adsorption efficiency for the molecules of interest——as close to 100% as possible. For low volatility species such as some explosives, it may be relatively easy to find such a material, but the problem becomes more difficult as the volatility of the species to be trapped increases. The adsorptive material should also have a high surface area, which combined with efficient adsorption would result in a high adsorptive capacity for the analytes of interest. For reactive chemical agents and explosives, it is also necessary for the adsorptive material to release the analyte collected to a detector with minimal decomposition. One common means of releasing the analyte from the adsorbent is via surface heating, and with some current adsorbent/analyte pairs, this can lead to significant sample loss through decomposition. For use in real-world settings, the adsorbent ought to be robust, difficult to poison, and easily regenerable if degradation over time is a problem. Future research in materials synthesis and processing and separations and analysis will provide enhancements for chemical threat detection devices of the future.

Sample transport is another key issue associated with sampling of chemical agents and explosives. This is most likely to be important with low vapor pressure species, where detection in air will rely upon either very low amounts of vapor or airborne particles. Both experimental and modeling studies of particle dispersion and transport in air can be useful in addressing these issues. Such studies can, for example, help to establish how much sample is available in air under different environmental conditions, when a low vapor pressure dictates the need to detect particulate matter. Several sampling issues are more likely to arise during the detection of explosives rather than chemical agents. These issues are mainly related to the lower vapor pressures of many explosives, so they may also arise in the detection of some chemical agents with relatively low volatilities. When relying on particles to perform trace chemical detection, it will often be necessary to dislodge particles from various surfaces as a first step in sample collection. Low vapor pressure explosives are so adsorptive that they will adhere to almost any surface at room temperature.

Development of a material that shows little adsorption of these compounds at room temperature could enhance detection systems by reducing adsorptive losses on ductwork and other surfaces during transport. Dislodging material for sampling can employ either direct physical contact (swiping) or air flow methods (e.g., air jets). In either case, optimization of the sampling procedure can be critical. While this area is somewhat applied, there are fundamental aspects of particle physics, surface and interface science, and fundamental interactions that are at the heart of particle sampling under realistic conditions.

Technology Need	Present Problem
Standoff detection of chemical toxins.	Improvements in range, portability, and sensitivity are required.

In addition to the technological needs in support of new sensors discussed above, advances in stand-off detection methods for field use are necessary for countering future chemical threats. In stand-off detection, the sample is not physically transferred to the detection device, as required for the sensing and analytical methods discussed above. Instead it is interrogated from some distance based on a physical or spectral property of the material.

Atomic and Molecular Spectroscopy

Remote laser induced fluorescence (LIF) sensing has been widely used for atmospheric monitoring, especially for the detection of small molecules such as OH, NO_2, and SO_2. An interesting modification to the LIF method is to perform laser-induced photodissociation on the species of interest and then measure LIF of a sensitive fragment molecule. This photofragmentation LIF approach has been used to detect 2,4,6-trinitrotoluene (TNT) vapor in air with a limit of detection of 8 ppb.[5] Detection of fluorescence from photodissociated NO makes this method somewhat selective; however, the bulk of the equipment required and the associated laser hazards currently make this technique impractical for hand-held field use.

Laser induced breakdown spectroscopy (LIBS) is another laser-based method beginning to be used for the characterization of many solid materials, including single particles. LIBS is an atomic emission spectroscopy technique that uses a laser-induced microplasma, functioning as both the sample volume and the excitation source. The laser-induced breakdown itself can be defined as the generation of a near totally ionized gas (i.e., plasma) by the end of the initiating laser pulse. Advances in laser technology are required to bring these analytical methods out of the laboratory. Vibrational spectroscopy has found practical use as a stand-off detection method. Laser induced Raman (LIR) spectroscopy is a highly informative technique for molecule detection. Excellent selectivity has already been demonstrated for many of the substances of interest to homeland security. While it is less sensitive than LIF or LIBS, it is clearly useful as a remote probe for the detection of what are essentially pure substances. It also has the inherent advantage, shared with LIF, of having the potential to probe large areas of sample, using powerful expanded lasers and highly selective imaging detectors, although this is incompatible with easily transportable hand-held systems.

No single laser-based spectroscopic technique can be expected to detect the wide range of chemical compounds with the necessary sensitivity and selectivity. However, each method has important merits, and some combination of these methods could form the basis for a powerful and highly useful routine monitoring instrument. Fundamental issues that remain to be addressed include a lack of basic spectroscopic data (LIBS, LIF, and LRS) for some species, improvement in overall sensitivity for all methods, and sampling statistics (especially for LIBS). High-throughput applications may require new imaging detection systems with improved sensitivity.

3.3.2 Prevention

Technology Need	Present Problem
Widespread use of TIMs in industry creates targets for terrorists.	Minimize or eliminate inventories of TIMs by developing alternative chemistries and processes to reduce TIMs inventories.

Many of the opportunities for preventing future acts of terrorism with chemical threats involve limiting access to materials through institutional controls. However, opportunities exist for fundamental research to assist in countering terrorism through the development of new chemical processes that assist in reducing inventories and access to highly toxic industrial materials. Industrial processing centers that use large quantities of TIMs are significant targets of opportunity for terrorist attacks because of the potential release of these dangerous materials and their impact on the public. Significant opportunities exist to develop new chemistries that minimize or eliminate the use of TIMs and to reduce inventories of these materials. For example, since the accidental release in Bhopal, many chemical manufacturers have found ways to make pesticides either without using or without storing large amounts of methyl isocyanide. Development of alternative synthetic chemistries, new robust catalysts, and production and processing systems that minimize the use of hazardous materials significantly reduce the threat to the public from terrorist actions. An example would be the development of robust solid acid catalysts to eliminate the use of liquid HF in petroleum processing.

3.3.3 Protection, Response, and Recovery

Technology Need	Present Problem
Personal protective equipment and barrier materials require further development.	Current barrier materials are cumbersome to use.
Advances in filtration technologies are needed.	Knowledge must be developed to design better, more efficient, stable, and selective catalysts for chemical threat destruction with no toxic byproducts
Lighter weight protective clothing is required.	Fundamental research at the forefront of materials chemistry must be developed.

Personal protective equipment to guard against the effects of chemical agents and TIMs has existed for many years, yet there are many opportunities for fundamental research to provide a basis for improved systems. Technological barriers impede the development of catalytic materials that operate under ambient conditions to decompose chemical agents and TIMs. Catalysis research sponsored by BES can address these issues. Materials synthesis and processing advances hold promise for developing lightweight barrier materials for comfortable protective clothing. The porous nature of common building materials coupled with uncertainties about the lifetime of chemical agents in environmental settings presents technological challenges to decontamination in a post-event recovery after a chemical attack. These issues, along with the need for stronger barrier materials, present a set of technological challenges for future protection, response, and recovery aspects of homeland defense.

Current filtration technologies remove nerve agents by adsorption, whereas more volatile reagents (e.g., blood, choke, and blister agents) are removed through a combined process of catalytic decomposition and adsorption. Advances in filtration technology will leverage a significant BES investment in catalysis and chemical transformations. Adsorption of reactive chemical agents and TIMs onto different substrates is insufficiently understood. Data for adsorption on metal oxides, surfaces of plastics, fibers, and lipid bilayers (e.g., cellular membranes) are needed. Fundamental studies will allow a systematic mapping of adsorption properties of chemical threat agents and their analogues. Little is known about surface chemistry of G-agents, and even less is known about the complex reactivity of VX,[6] and their analogues or simulants. Current detoxification, decontamination, neutralization, and destruction schemes do not involve catalysis, and fundamental investigations of homogeneous and heterogeneous catalysis are warranted. Surface science studies of model compounds related to chemical threat agents would lead to an improved understanding of the fundamental principles of bond activation on surfaces of oxide, metals, and supported metal catalysts. Fundamental studies are required to develop model catalytic systems that operate at ambient temperatures and are resistant to poisoning. The ultimate product from these studies would be the knowledge required to design better, more efficient, stable, and selective catalysts for chemical threat destruction with no toxic byproducts.

Solvated electron technology (SET) is one of several alternatives tested for chemical threat agent destruction. Little is known about details of this reaction on molecular scale. The reactivity of solvated electrons and reactions of materials called electrides with chemical threat agents or suitable analogues is an area that needs further investigation.[7] In addition, sodium vapor reduction of CFC may have potential for chemical threat agent destruction.

Protective clothing to guard against the effects of chemical agents will be made of lighter weight materials than current protective suits. Permeability of materials to chemical threats is directly related to the underlying chemical structure of the material. Fundamental research at the forefront of materials chemistry will lead the way to lighter weight materials. Both military and civilian personnel need clothing that is lightweight, inexpensive, and comfortable to wear, while providing protection against chemical agents. Block copolymers are one obvious candidate for such applications because of their low cost and ease of processing.

In preliminary experiments, it has been demonstrated that linear triblock copolymers based on a continuous phase of butyl rubber with dispersed nanodomains of partially sulfonated polystyrene fulfill many of these characteristics. They allow water vapor to transport through the material while preventing the passage of common toxic chemical agents. However, both the mechanical properties and permselectivity of these materials require further improvement. Simultaneously, work has been conducted that demonstrates the strong impact of changing polymer architecture (linear diblock triblock versus branched graft copolymer architectures) on permeability characteristics and mechanical properties. Introduction of controlled branching into block copolymers is thus a tool that can be used to enhance both mechanical properties and permselectivity. Both these areas are only beginning to be explored systematically, and much fundamental research needs to be conducted in these areas. Small angle neutron scattering (SANS) and neutron reflectivity are powerful tools for studying the structures of such materials. DOE facilities for neutron studies of soft materials will be highly utilized in these studies.

Technology Need	Present Problem
Volatile and semi-volatile chemical agents in a confined area will adhere to surfaces and diffuse into pores and open spaces.	Fundamental studies are needed to further determine the lifetime of chemical agents and TIMs in porous building materials, soils, and natural environments.
Self-cleaning and self-decontaminating titanium dioxide surfaces technology may not be adequate for the rigors of counter-terrorism response and recovery applications.	Fundamental research is required to increase the photoefficiency of TiO_2-containing barriers and improve their function.

Volatile and semi-volatile chemical agents will dissipate in an open environment, but in a confined area, they will adhere to surfaces and diffuse into pores and open spaces. Decontaminating exterior surfaces can be achieved in a number of ways; however, the pores may be inaccessible, and the remaining material can slowly diffuse from the pores providing long-term, low-level human exposure. Fundamental studies are needed to further determine the lifetime of chemical agents and TIMs in porous building materials, soils, and natural environments. Vapor phase decontaminants are limited in number and scope, and additional approaches to this problem are required. One approach is to apply an overlayer of titanium dioxide (TiO_2) material to catalytically decompose the chemical agent or TIMs as they diffuse out of the contaminated media. Photocatalytic materials can bring about the oxidation of a wide range of organic and some inorganic substances. Photocatalytic particles, coatings, and thin films have been demonstrated to oxidize (or reduce) a very wide range of organic and inorganic compounds at ambient temperatures, pressures, and humidities.

Self-cleaning and self-decontaminating titanium dioxide surfaces are well demonstrated. The current technology, however, may not be adequate for the rigors of counter-terrorism response and recovery applications. Fundamental research is required to increase the photoefficiency of TiO_2-containing barriers and improve their function. The nature of active sites involved in chemical processes at the air/solid interface is not understood, and the mechanism of photocatalytic oxidation is worthy of further study. The role of noble metals deposited on TiO_2 for specific reactions is not understood, and catalyst deactivation by inorganic reaction residues remains a problem. In addition to these fundamental technological barriers, durable catalyst coatings for high-wear situations and new methods to incorporate photocatalysts into textiles and filter media are engineering challenges to be overcome in order to apply photocatalyst to problems of response and recovery from chemical acts of terrorism. Other technical challenges include the development of new, light transmission materials to distribute light to catalyst sites for uniform illumination, polymers or functional structure coatings for photocatalytic surfaces to increase reactivity, and formation of nano-textured surface structures to effect catalytic activity, selective adsorption, or light adsorption.

Technology Need	Present Problem
Materials are needed that can contain or protect against the effects of an explosives detonation.	Current materials can't combine low weight, impact resistance, and low cost.

In the area of explosives protection/mitigation, there is a need for the development of materials that can be used to contain or protect against the effects of an explosives detonation. Applications of such a material might include containers for luggage/cargo being transported in airplanes or other vehicles, barriers within high-security buildings, barriers to protect VIPs at high profile events, and stronger building materials. The desired properties of such a material would include high blast resistance, low frangibility (i.e., if the material is breached by a blast, it should not shatter into many airborne pieces, but should allow pressure to escape through cracks or holes), light weight, and low-to-moderate cost. The Federal Aviation Administration has funded some work in this area, but fundamental materials synthesis and processing research is needed with a focus on engineering the desired properties into the materials.

Technology Need	Present Problem
Presymptomatic diagnosis of exposure to chemical threat agents at sub-lethal levels is needed.	Medical diagnostic tools to detect early signs of exposure to a chemical threat agent require development.

An additional important aspect of response and recovery is the presymptomatic diagnosis of exposure to chemical threat agents at sub-lethal levels. This is particularly important in addressing social issues associated with a terrorist chemical attack by providing a means of gauging exposure and preventing public hysteria. Medical diagnostic tools capable of detecting early signs of exposure to a chemical threat agent would also reduce stress levels in the medical community under pressure to manage a crisis situation. Biological markers of exposure to a chemical agent will be formed, as the result of cellular processes, long before the clinical presentation of symptoms of exposure. Identifying the biological markers of exposure will allow early screening and detection of exposure to facilitate treatment of only those individuals exposed to a chemical agent. Once these marker compounds are identified, new analytical techniques for the rapid and confident detection of these compounds in physiological media (blood, saliva, sputum, etc.) will be required. As in the case of detection of chemical agents themselves, research in separations and analysis, and materials chemistry could provide detection systems that could be used by medical personnel to assess public exposure to chemical threats.

3.3.4 Preparedness

Technology Need	Present Problem
Needs include the development materials and deposition processes to fabricate bipolar thin-film battery stacks and development of alternative battery chemistries for low-voltage batteries	Fundamental research is needed to identify mechanisms, flaws, or film properties that limit the fabrication yield for thin-film batteries.
Fieldable detection and mitigation devices are needed.	Fuel cell research is required.

Basic research needs for improved batteries and miniaturized fuel cells will contribute to future developments in the homeland defense area of preparedness. Fundamental research is needed to identify mechanisms, flaws, or film properties that limit the fabrication yield for thin-film batteries. Mechanisms leading to degraded performance after storage or use of batteries at elevated temperatures (60–100 °C) need to be identified. In addition, synthetic methods need to be adapted to allow fabrication at low temperatures, very thin, and inexpensive substrates (e.g., plastics) and to facilitate direct integration of the battery with integrated circuits. Development of improved packaging for the thin-film batteries is also needed. Long-term research needs include the development materials and deposition processes to fabricate bipolar thin-film battery stacks and development of alternative battery chemistries for low-voltage batteries.

Miniaturized fuel cells offer alternatives to batteries for powering more demanding fieldable detection and mitigation devices. Fundamental research is needed in the area of membrane technology for ion and small molecule transport and separation. Chemical reactions and stability at electrode-electrolyte interfaces is a topic for future research from both experimental and computational approaches. Mechanisms of corrosion also remain a topic of importance for the future of fuel-cell research.

3.4 Research Needs

To seize the research opportunities discussed above and address the scientific issues associated with countering chemical terrorism, several research needs must be met.

3.4.1 Scientific Issues

Miniaturized Integrated Systems

Miniaturization and integration research themes underlie future ability to develop inexpensive and reliable devices for first responders. Critical research issues include microfluid and nanofluid transport, surface treatment and functionalization, combination of top-down and bottom-up fabrication techniques, and coupling of nanoscale and continuum models for mass transport.

Chemical Recognition

Research is required to enable highly selective sensors capable of identifying target chemicals in complex backgrounds. Critical research topics include the use of biological or biomimetic receptor elements, imprinted polymers, nanophase grafted polymers, and miniaturized mass spectroscopy.

Interfacial Chemistry

Fundamental theoretical and experimental tools and models to probe molecular interactions with solid and liquid surfaces will be critical to development of new, selective chemical sensors, transport and fate models for toxic chemicals that are released into a wide range of environmental conditions, development of improved separations chemistry, and the development of new protective barrier and catalytic materials for protective clothing and toxin neutralization.

Novel Materials

A wide range of novel and nanophase materials will be critical for the development of new catalysts to break down chemical toxins, strong and lightweight materials to contain explosive blasts, as well as nanoporous and membrane materials for advanced battery and fuel cell miniaturized power supplies.

Computing, Modeling, and Theory

It will be critical to fully understand and predict the equilibrium and kinetic chemical interactions in flow fields and at solid interfaces. Models will be important for predicting the fate of chemical toxins in a wide range of environmental conditions and for predicting the performance characteristics of sensors and chemical preconcentration and sampling approaches. Modeling will also contribute to a broad range materials development and optimization tasks associated with detection, protection, and response to chemical threats.

Nanoscale Science

Many critical scientific issues and challenges associated with chemical threats are rooted at the nanoscale behavior of materials and interfaces. New tools for fabricating nanoscale structures, probing structure and chemistry at the nanoscale, and modeling properties and behavior will be needed. The Nanoscale Science Research Centers currently being developed by BES can play a critical role in providing the tools and research environment needed to address these critical problems.

3.4.2 Research Environment and Infrastructure

Existing BES scientific user facilities at DOE laboratories and universities, coupled with those currently under construction, such as the Nanoscale Science Research Centers, will provide many important capabilities needed to address critical scientific issues associated with chemical-based threats of terrorism. However, it is important to recognize that because no single institution possesses all the required assets, it is vitally important that future research programs be multi-institutional to ensure that all research needs are met. It will be essential to initiate collaborative projects that promote the formation of cross-disciplinary and cross-institutional teams to address these complex and critical challenges. For example, although surrogate chemical threats may work fine for much of the fundamental research discussed above, at some point it becomes important to test fundamental principles using real chemical threats. The necessary facilities for handling these materials safely, especially chemical warfare agents, are not and should not be available at all DOE sites and universities. Many tools for characterization and analysis of both hard and soft materials will be available in the nanoscience research centers being developed at several sites throughout the DOE laboratory system and at other existing and developing BES resources.

The Office of Basic Energy Sciences possesses many unique resources, in the form of scientific user facilities that can contribute to developing the fundamental knowledge base required to counter future acts of terrorism involving chemical threats. The four BES synchrotron radiation light sources provide access to radiation ranging from x-rays through the infrared region for spectroscopic and structural studies. Four high-flux neutron sources will provide the neutron scattering and materials irradiation resources to meet the fundamental research needs. Four BES electron beam and micro-characterization centers are among the world's best high-resolution electron-optical microcharacterization and analytical facilities. These facilities will be crucial for characterizing fundamental advances in materials research. BES-funded specialized single-purpose centers including the Materials Preparation Center at Ames, the Surface Modification and Characterization Research Center at Oak Ridge, the James R. Macdonald Laboratory at Kansas State University, and the Pulse Radiolysis Facility at Notre Dame provide additional resources.

3.4.3 Relationships with Other Programs

3.4.4 Dual-Use Opportunities

The very fundamental nature of the advances required for countering future chemical threats by terrorist organizations opens the door to many dual-use opportunities. The more applied programs within DOE that look to BES for fundamental scientific advances will directly benefit from basic research applied to counter terrorism. For example, miniaturization and integration of separations and analyses systems will find use in field analysis for environmental monitoring in support of remediation efforts. Small, inexpensive sensors with high chemical selectivity will play a significant role in environmental monitoring. Selective sensors deployed in a monitoring network can potentially save millions of dollars each year in manual sample collection and fixed laboratory analysis costs. New fundamental knowledge in the areas of materials and interfacial chemistry will provide breakthrough advances in many areas, including increased energy efficiency in lighter weight vehicles and stronger composites for industrial applications. The knowledge base for improved adsorption and catalytic decomposition of chemical agents and TIMs will certainly lead to better catalytic materials and processes for environmental restoration and environmental protection through reduced emissions. Advances in nanotechnology are going to influence developments in virtually every area of science and technology, making the dual-use opportunities endless.

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4 Biological Threats

4.1 Terrorism Threats and Technology Needs

The challenges we face from biological threat agents are increasing. While microbes continue to evolve and biotechnology becomes more powerful, the inherent hazards to humans, plants, and animals from infectious microorganisms are greatly increased by their intentional use by terrorists. The recent mailing of anthrax-laced letters to our political leaders and members of the press demonstrated how simply a pathogen can be used to kill, instill fear, and radically disrupt normal societal activities. The need for faster and better capabilities for warning, response, and cleanup was painfully evident as we responded to this one case of a small-scale deployment of a noncontagious, naturally occurring pathogen. The specter of terrorist use of other biological agents that could result in far greater loss of life has risen in our consciousness—agents that might be contagious or perhaps engineered for increased virulence and resistance to our medical treatments such as antibiotics and vaccines. In this context, we must recognize that as microbes evolve and compete for survival, we also face naturally emerging threats that we must be able to quickly identify and distinguish from a suspected terrorist act.

While today's focus on bioterrorism is being driven primarily by concerns about attacks on humans, attacks on livestock and/or crops can be just as devastating. The recent outbreak of foot and mouth disease in Great Britain demonstrates the devastating impact microbes can have on livestock, and the consequent impact on food supply and economies. We know, for example from the work of the United Nations inspectors in Iraq, that rogue nation's have actively explored both animal and plant pathogens as weapons. This report was written with strong reference to attacks directly on humans, however, the science and technology base needed to protect crops and livestock is highly related.

The biological threat is real, and we must tap into new science and technologies in order to reduce that threat. Advances in material and chemical sciences not traditionally applied to biothreat reduction technology requirements hold great promise for rapid improvements in the U.S. counter-bioterrorism posture. Fundamental advances are needed to fill gaps in our needs and to develop the next-generation technologies for

- Detection and identification
- Medical diagnostics

- Protection
- Decontamination and remediation

The Department of Energy (DOE) materials and chemical sciences research and development (R&D) programs in Basic Energy Science (BES) are poised to make significant contributions to reducing the biothreat through scientific advances that have great potential for transition to other developmental efforts that focus on shorter term deployment of technology to address the biological threat, including the DOE National Nuclear Security Administration (NNSA) Chemical and Biological National Security Program (CBNP). A multidisciplinary approach that leverages advances in the chemical and physical sciences holds great potential for decreasing our vulnerabilities. The advances envisioned in this report would provide quantum leaps in technology that will alter existing approaches to prevention, response, and mitigation of the biological threat. In addition, the technology will enjoy wide application in resolving related public health challenges from infectious diseases.

The Department of Defense has addressed the biological threat in the context of the battlefield. However, biothreat reduction in the context of the civilian population is very different. For example, the average civilian is not trained or equipped for response, the public health system is not supported with the kind of central command and control systems associated with the military, different requirements exist on sensitivity and different levels of tolerance for false positives and false negatives, and there is a need for dealing with a broader set of potential agents. Also, much higher sensitivity is required for Counter Terrorism (CT) detection, raising substantial technology challenges and the need to assess background interferences that will be much more significant for low-level detection/monitoring issues.

Scientific research and technology development to reduce the threat from bioterrorism must be conducted in an environment that has strong multidisciplinary capabilities, that includes biology along with materials and chemical sciences, that has the infrastructure to support large teams and projects, and that has the ability to separate and compartmentalize work that must be classified or protected while still being able to attract the best scientists and technologists.

The technological challenges that need to be addressed are significant and diverse. Some examples that will be specifically addressed in this report are the following:

Environmental backgrounds. In general, backgrounds are complex with an imponderable diversity of biology. They are not well characterized, are highly variable (in time and space), and can contain measurable levels of the "smoking gun" chemicals from normal industrial activities. False positive and false negative detections of biological agents will be extremely unpredictable without a more thorough understanding of the chemical and biological environments being sampled.

Transport and transformation in the environment. Understanding the fate of signature species in the environment is required to minimize large uncertainties. Few studies have examined the natural distribution and survival capabilities of pathogens like *Bacillus anthracis* in even the most common environments.

Sample collection. Means for collection, concentration, and separation of low-level agents in highly variable, complex environments are required for reliable detection of many agents. The development of materials and systems that achieve this task with high efficiency is a significant challenge.

Development and characterization of new materials. New materials for many applications are needed (e.g., remediation and decontamination materials that can be rapidly deployed to mitigate initial impacts and that are environmentally friendly, coatings and materials to protect against hazardous substances, and materials for new sensors and diagnostics).

Coupling sensitivity, selectivity, and reliability. Many systems with the required sensitivities are prone to false alarms.

Developing durable and reliable unattended systems. To achieve broad area surveillance, some detection systems may need to be left in place with little oversight for years of time and need to be stable, subject to reliability checks, etc.

Speed. High-speed, secure, reliable information flow can be critical to screening of high volumes of materials (e.g., travel bags, shipping containers) or providing adequate time for a response (e.g., shutting down an air handling system or taking some neutralizing counter-measure).

Complexity. The ability of biological agents to mutate or to be manipulated and the inherent diversity of the biosphere are challenges in this regard. Also, large volumes of complex data need to be processed and analyzed rapidly in order to make sound decisions (e.g., through artificial intelligence).

Development of new trigger systems. Rapid response to bioterrorist threats has been hampered by the focus on initial detection that relies upon highly specific and expensive detection systems. Techniques that detect simple environmental changes that are easily measured (e.g., rapid increases in total bacteria numbers or highly conserved biosignatures unrelated to any other changes in the environment) could provide much better and cheaper initial warning systems for first responders.

4.2 BES Research Accomplishments and Implications

DOE's Basic Energy Sciences program has supported research and development in many areas that are critical to advancing our capabilities for addressing the emerging biological threat, including the threat posed by potential terrorism. These areas include basic research and technology development relating to molecular recognition, integrated molecular systems, interfacial science, novel materials development, nanoscience and technology, spectroscopy, computing, modeling and simulation, and integrated devices, as well as advanced instrumentation and the development of large-scale facilities for materials and molecular characterization. A few examples are given here of BES research accomplishments that highlight fundamental advances in these areas.

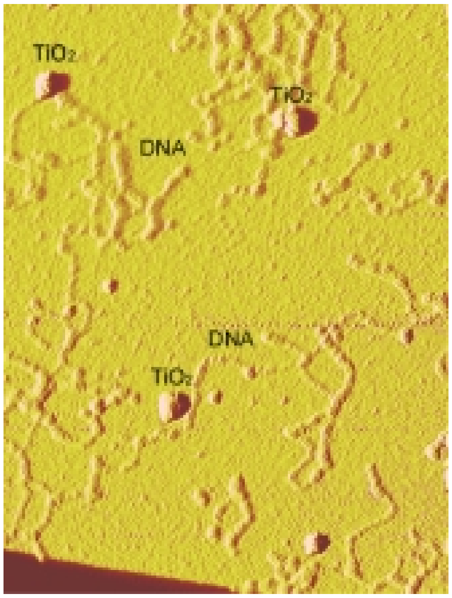
4.2.1 Nanophase Materials

BES is one of the larger sponsors of research that addresses fundamental issues controlling the synthesis, characterization, and properties of nanophase materials. Materials that are structured on the same scale as the molecular machinery of life offer extraordinary approaches to address complex biological problems. Current research is being pursued in areas including the development of new semiconductors for spectroscopic analysis of bio-agents, membranes and nanoporous materials for detection and protective applications, and nanocrystals that can be used to provide new approaches for molecular recognition for detection, medical diagnostics, and response and recovery.

Nanoparticles for Novel DNA and Protein Sensing Technology

BES-sponsored research has led to the development of new methods for chemically coupling biomolecules to metal oxide nanoparticles, opening up opportunities for development of new families of electronic sensors of DNA hybridization (bio-chips), protein binding, and in situ DNA imaging. Single-strand DNA-linked nanoparticles retain the ability to hybridize to complementary DNA and to carry out sequence-specific, light-triggered DNA recognition. Light-generated silver deposition on metal oxide nanoparticles is observed only when attached DNA sequences are in a double helix form. This allows the electronic sensing of the DNA double helix, as well as the development of new electrochemical probes for DNA-binding. This system also extends to detection of DNA binding polymers because of a change in redox properties of DNA after binding to proteins as well as detection of protein-protein interactions.

[Argonne National Laboratory]

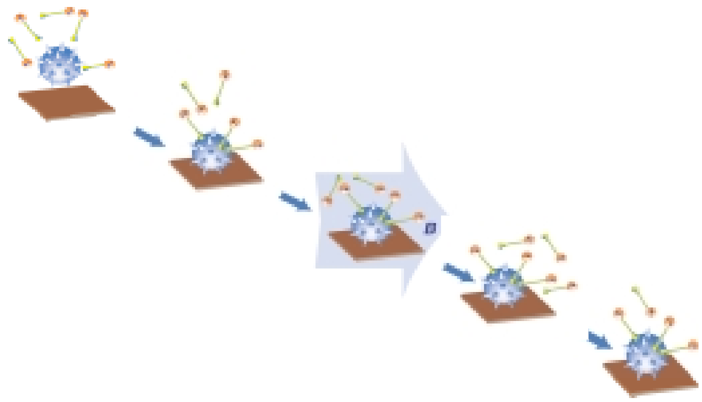


Electron micrograph of titanium oxide nanoparticles with attached DNA

SQUID-Based Pathogen Detection

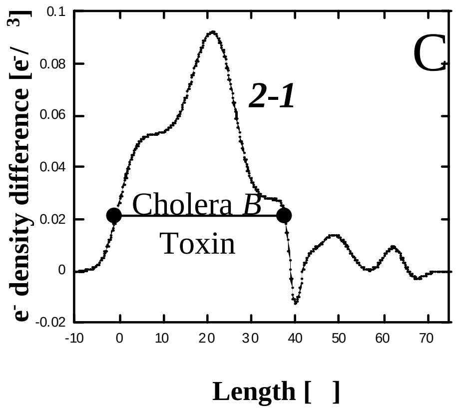
BES sponsored researchers are developing a sensitive, fast, and versatile new technique for detecting pathogenic organisms or molecules using a "microscope" based on a Superconducting Quantum Interference Device (SQUID).

[*Lawrence Berkeley National Laboratory]*



Magnetic particles labeled with molecular recognition elements bind target if present. After 1-second pulse of magnetic field, only bound particles send relaxation signal for detection in the next second. No more than 2000 magnetic particles are required, which, for detection of bacteria or viruses, could translate into fewer than 10 targets.

Host-Pathogen Interactions Probed Using Neutron and X-Ray Scattering

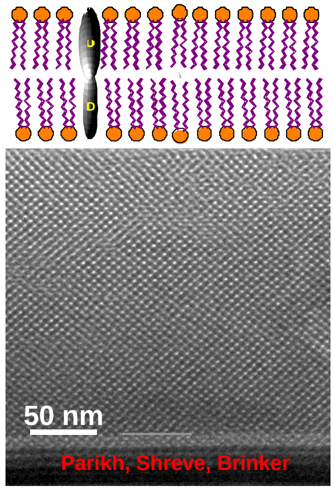


Electron density of cholera B5 binding to GM1 in a phospholipid monolayer.

Neutron and x-ray diffraction and reflectometry experiments being performed at the BES-supported Los Alamos Neutron Science Center have been used to probe the molecular recognition interaction of cholera toxin with its natural receptor, GM1, on a cell membrane surface. Binding of the cholera B5 subunit to a phospholipid monolayer containing GM1 in a Langmuir Blodgett trough results in an ordered array of cholera with electron density distribution shown in the Figure. Binding of the full cholera protein, AB5, results in disruption of the order in the aliphatic portion of the phospholipid monolayer, possibly indicating incorporation of the A subunit into the membrane. Improved models for toxin molecular recognition can contribute to the development of new biomimetic sensor technology as well as the development of improved human vaccines.

[Los Alamos National Laboratory]

Nanostructured, Interfacial Materials for Biosensors



Nanostructure supported ion channel system.

BES-supported research is exploring the use of templated self-assembly approaches to create nanoporous inorganic materials and hybrid organic/inorganic materials that could serve as novel platforms for bio- or chem-sensors and as separation elements in purification and filtration devices. While molecular self-assembly is routinely used to precisely control nano-scale porous materials, new research focuses on the co-assembly of soft organic structures within more robust inorganic scaffolds. Specific examples include the co-assembly of lipid bilayers within sol-gel silica meso-porous materials. Results show that the co-assembled lipid membranes retain their biomimetic sensing capabilities while the hybrid composite material provides greater stability and ease of processing. The emphasis of this research is on the development of material preparation strategies, on characterization of the resulting materials, and on understanding the interaction of these materials with other nanostructured components such as biological membranes or electronically active macromolecular systems.

[Los Alamos and Sandia National Laboratories]

4.2.2 Interfaces

The structure and properties of interfaces between living systems and man-made materials play an extremely important role in technologies related to the detection, medical diagnostics, protection, and response to biological threats. BES research has led to the development and application of experimental and theoretical tools that are providing new insights into the structure and dynamics of these interfaces. Developments include local and scanning probe techniques for measuring structure and molecular interactions, time resolved spectroscopic tools to examine interfacial energy transfer, X-ray and neutron tools to determine detailed molecular structure, and a wide range of computational tools.

4.2.3 Integrated Systems

Integrated systems for chip-based detection and diagnostics are already being developed to counter biological terrorism threats. BES research has played a pioneering role in the development of these technologies by providing underpinning science addressing microfabrication, integration of new materials and synthesis approaches, fluid and energy transport at small dimensions, and the control of interfacial properties and interactions.

4.2.4 Atomic and Molecular Spectroscopy

Advanced spectroscopic tools being developed in BES research programs have significant impact on technologies for detection and source attribution of biological agents. Developments included high-resolution mass spectroscopy for identifying bacteria or other biological agents, laser-based spectroscopy for both microanalysis and stand-off detection and identification of bioagents, and nuclear isotope detection that can help in identifying the source of specific bioagents.

In addition to the individual research projects highlighted above, BES is developing a major new initiative to establish a number of Nanoscale Science Research Centers: Molecular Foundry (LBNL), Center for Nanoscale Materials Sciences Science (ORNL), and Center for Integrated Nanotechnology (Sandia/LANL). The research centers will provide facilities and support collaborative research that will bring together the best researchers in the national laboratories, academia, and industry with the latest technologies to carry out breakthrough research and development in nanoscience and technology. These intellectual and resource centers will be major assets in advancing the research and development needed for biothreat reduction applications described in this report.

Finally, BES is steward of a number of the nation's major facilities for materials and molecular characterization; specifically synchrotron (Advanced Photon Source, National Synchrotron Light Source, Stanford Synchrotron Radiation Laboratory, Advanced Light Source) and neutron scattering (Spallation Neutron Source, High Flux Reactor [HIFR], Intense Pulsed Neutron Source, and Los Alamos Neutron Science Center) facilities that each year serve hundreds of users. These facilities will play a key role in advancing the materials and chemical sciences underpinning advances in biothreat technologies.

Biocavity Laser for Real-Time Detection of Pathogens

BES-funded research on nanostructured compound semiconductor light emitters has supported the development of a highly sensitive micro laser device, the Biocavity Laser. Consisting of a microfluid channel introduced into the optical cavity of a quantum-well semiconductor laser, the Biocavity Laser has been successfully demonstrated for rapidly screening human cells for abnormalities (e.g., brain tumors and sickle cell anemia). The power of this approach relies on the intimate coupling of solid-state nanostructured materials with living biological systems. Operationally, the bio agent, suspended in a fluid, enters the optical cavity of the laser via the microfluid channel and becomes a part of the cavity, impressing bio agent information on the spectral output of the laser. Spectral analysis using a laptop computer leads to the identification of the agent. While this work has focused on human disease detection, it is directly applicable to the rapid identification of potential biowarfare agents in the form of tiny pathogens like bacteria, spores, or viral particles.

[Sandia National Laboratories]

[1] P. L. Gourley and D. Y. Sasaki, "Biocavity lasers," *American Scientist*, v. 89(#2) pp. 152-159 Mar-Apr 2001.

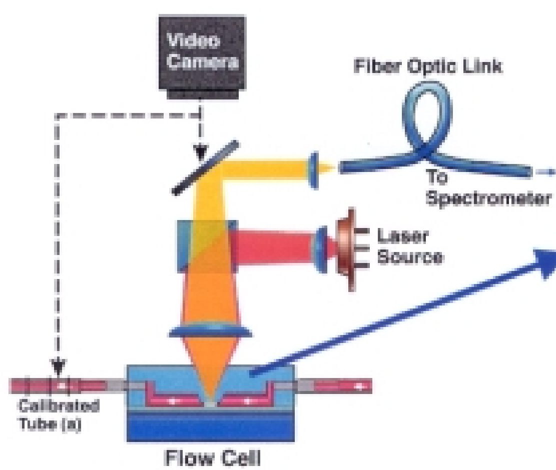
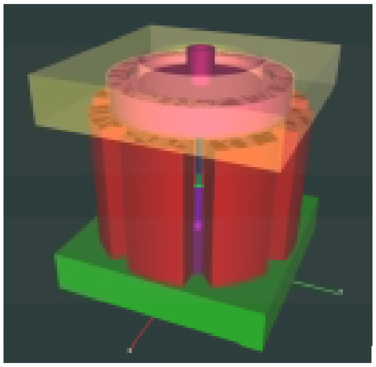


Fig. 2. Compact microfluidic system for reading nanolaser chip output spectra and images for high throughput analysis of endospores.

Fig. 1. Electron micrograph of biocavity laser and a bacillus endospore approximately 1 micron in diameter.

Mass Spectrometry Based Bio-Agent Detection



PNNL's advanced ion trap is used to perform full 3-D modeling and simulation calculations

Fourier Transform Ion Trap (FTICR) mass spectrometry has already demonstrated. Preliminary work has already demonstrated the usefulness of this approach, providing advanced designs that have many of the features needed for reliable field instrumentation with the required performance. It has the required mass range, sensitivity and resolution. However, significant advances are needed to turn this instrument into a sufficiently small, rugged, reliable, and easily used instrument for routine work outside a research laboratory. To this end, numerous issues associated with the fundamental physics of these instruments are being investigated in BES research projects. Perhaps the most important problems are those associated with electric and magnetic field quality.

[Pacific Northwest National Laboratory]

4.3 Scientific Issues and Opportunities

To keep the focus clearly on the goals of biothreat reduction, this part of the report is organized around the four critical application areas broadly recognized as key to our ultimate defense against biological threats: (1) Detection and Identification, (2) Medical Diagnostics, (3) Protection, and (4) Decontamination and Remediation. Each of these areas will be discussed in terms of the specific scientific issues and opportunities. The common themes emerging from these discussions are summarized at the end under Research Needs, which will also consider infrastructure, research environment, and relationship to other programs.

4.3.1 Detection and Identification

Technology Need	Present Problem
Identify biohazards in wide variety of ambient settings.	Need improved techniques to rapidly and selectively sample biohazards from complex biomaterial backgrounds.

Here we consider detection and identification technologies needed across the full spectrum of intervention scenarios: indications and warning, environmental surveillance, diagnostics, residual hazard surveys, and attribution and forensics. The key attributes required for effective detection and identification technologies across this entire spectrum include high sensitivity, specificity, speed, no false positives or false negatives, reliable discernment of targets against complex backgrounds, simple operation, inexpensive to deploy for broad coverage devices, systems integration, and size (potential for miniaturization, microfluidics, portability). We will consider these attributes as we address the issues and needs for different phases of detection: sampling and collection, triggers, early warning and point sensors, and characterization and forensics.

Sampling and Collection

Biohazards will be presented in the context of an already complex environment that is rich with materials that both dilute and interfere with the intended detection signal. Sampling technologies are required to improve the sensitivity and specificity of detection and analysis methods for assessment of contamination of the environment as well as the related personnel and surfaces. Of particular importance is the characterization of aerosol hazards using systems that can be automated and allow operational simplicity. System attributes should include means for selective concentration of the species of concern to avoid complications from the widely varying and complex background.

Extraction, Purification, and Concentrating Technologies. There is a clear need for novel technologies for the extraction, purification, and concentration of bio-agents. Key to this technology will be molecules that exhibit very high affinity and specificity for the agent of interest. These molecules may be synthetic, such as abiotic receptors, polymers imprinted to achieve high specificity, or biological molecules selected from large, diverse libraries for their high affinity and specificity to the agent of interest, such as single-chain antibody variable domains. Methods to engineer high stability into these specific ligands represent an important challenge for this problem, as well as the development of detectors and point sensors discussed below.

Affinity purification will require molecules designed for specific recognition and binding followed by reversible release of the targets so that they can be recovered. Scaling down to the use of microfluidic devices, including flow cytometry to select specifically labeled cells or size selected cells and the ability to lyse cells for further analysis, are all capabilities that need to be developed significantly to make possible extraction of agents from small, dirty samples in the field. New materials for separations, such as novel polymer resins for column chromatography will need to be developed that are robust, reusable, and inert to environmental contaminants.

Sampling and Collection Materials. Selective adsorbents for pathogens that are compatible with biomaterials are needed to collect environmental samples from both the aqueous and gas phase. These materials must be designed both to specifically entrap the pathogens, via molecular or shape recognition, and to maintain the biomaterial's structure and function. Molecular or shape recognition can be pursued using biologically or synthetically derived receptors that can be engineered onto various surfaces/materials. The supporting surface or material must not only support functionalization for specific binding of the biomaterial, but must also be engineered to resist nonspecific adhesion of the biomaterial. Besides the main issue of nonselective capture of the biomaterials from the environment, nonspecific adsorption of biomaterials can lead to numerous additional problems. For proteins, nonspecific adsorption often will lead to denaturation, thereby changing the function of the protein as well as its affinity characteristics to sensor systems downstream. Denaturation also can mean tenacious binding of the protein to the surface and thus ineffective desorption of the protein for subsequent identification. Cellular adhesion to surfaces can also run into similar problems and even lead to cell lysis, again rendering downstream detection schemes useless. Surfaces coated with polymers (e.g., surface grafted polymers, block copolymers, or dendrimers) or self-assembled materials (e.g., SAMs, lipid bilayers, or liquid crystals) with unique functionality (e.g., PEG, PNIPAM, or polysaccharides) have proven effective as biomaterial-passive coatings, but further advances in the materials with regard to molecular-level structure, nano- and micro-scale patterning, functional group orientation and placement, and post-functionalization capability would greatly improve upon existing systems.

The sampling and collection materials must not only possess the ability to capture the bioagent but must also reversibly desorb the captured agent. In that sense, the receptor sites, and the material, must have either reasonably low on/off rates, such that relatively small changes in temperature can effect biomaterial desorption, or the ability to reversibly alter its structure to reduce ligand affinity on command. Reversible structure schemes could be triggered by temperature, light, or chemical treatment. For any scheme to succeed, the material must be robust to the physical or chemically changes used to impose desorption.

Triggers

Technology Need	Present Problem
Simple, inexpensive triggers that alert the need for detailed biohazard analysis.	Current biomolecular analysis approaches not suited to widespread and continuous applications.
Stand-off detection of biohazards.	Laser-based techniques must become more portable with greater range and sensitivity.

It can be very expensive and challenging to deploy sensing systems that detect biological agents with reliability adequate for taking actions that may have major economic impact or cause significant societal disruption. An alternative is to deploy less definitive and less expensive devices for providing information that would “trigger” further analysis and sample collection for definitive decision making. Trigger sensors fall into two general types, point sensors and stand-off sensors. Point sensors are described in their own section as they can play roles as either trigger of definitive sensors depending on their characteristics. We consider here the needs for development of improved stand-off sensors.

Laser-Based Remote Detection Methods. Laser based detection systems are inherently capable of remote real-time characterization. Their value as triggers for biothreat agents will be determined only by research leading to the development of advanced tools to enable exhaustive characterization of ambient microflora versus biothreat clouds, demonstration of detection above background, and identification of organisms in different states. Next generation instruments will be more portable, more sensitive, lower in cost, and more reliable. X-ray fluorescence and synchrotron FTIR may prove to be valuable tools for obtaining materials properties leading to remote trigger detection methods. Creation of mathematical tools (e.g., artificial intelligence) for the extraction of reliable information from large volumes of complex data will be a valuable adjunct to any trigger system.

Fundamental issues that must be addressed include a lack of basic spectroscopic data for bio-particles such as bacteria, improvement in overall sensitivity for all of these methods, sampling statistics, and the ever-present issue of eye safety that must be adequately addressed if such instruments are ever to find widespread use in commercial and industrial environments. High-throughput applications may require new imaging detection systems with improved sensitivity. Examples of three applications of lasers to remote sensing are given below.

Laser Induced Breakdown Spectroscopy (LIBS). Characterization of many solid materials, including single particles, can be accomplished using LIBS, an atomic emission spectroscopy technique that uses a laser-induced microplasma for the highly efficient dissociation of the components of fine particulates (~10 microns diameter) producing light emission characteristic of the atomic constituents. Detection of the emission can be used for chemical analysis at a distance of up to 24 m and for about 75% of the known elements. Research is needed to evaluate and extend the sensitivity (current detection limits are of the order of tens of ppm for most elements) and selectivity of this technique for characterization of aerosol dispersed biological agents, as well as chemical agents and explosives.

Laser Induced Fluorescence (LIF). For substances that luminesce, which include most bioaerosols and many organic aerosols, LIF is a sensitive remote characterization method.[1,2] Detection of small molecules can be highly sensitive with limits of detection in the tens of parts per trillion levels.[3,4] The simple presence of particle luminescence can be used to distinguish between biological and nonbiological particles, and the spectra of individual particles can often be used for more detailed identification. Successful applications have included detecting allergens and spores. However, spectral similarities have made it difficult to identify specific bacteria. Research is needed to better understand the photophysical processes leading to fluorescence from dispersed biological agents to extend the diagnostic potential of LIF for stand-off detection in complex atmospheric environments. A modification to the LIF method as applied to volatile explosives at the ppb levels is to perform laser-induced photodissociation on the species of interest and then measure LIF of a fluorescent fragment molecule.

Laser Raman Spectroscopy (LRS). An inherently remote method, LRS can provide functional group specific spectral information over a distance of tens of meters. Recent advances in laser Raman spectroscopy are from the development of spectroscopic systems using UV excitation for resonance enhancement, near-IR excitation for freedom from fluorescence background, sensitive array detectors, and Fourier transform techniques. Research is needed to continue the recent advances in spectral selectivity (i.e., using acousto-optic tunable filters) and sensitive optical detection schemes. Raman characterization of individual particles currently requires that the particle under study be held stationary using relatively simple electromagnetic or electrostatic particle traps in order to have sufficient time to acquire adequate signal-to-noise ratios. Spectra of particles of less than 1 μm diameter have been obtained in this manner. While these techniques have so far only been used in the laboratory, they could be promising approaches for field detection of a wide variety of toxic particles in air. Researchers have found that bacteria can be readily distinguished by their Raman spectra, as can explosives. Raman spectroscopy is the least sensitive of the laser techniques but can be the most specific.

Early Warning and Point Sensors

Technology Need	Present Problem
Point sensors for early warning detection.	Present sensors cannot combine rapid, sensitive and specific detection.
Real-time continuous biohazard monitoring.	Sensors will have to become more robust, reliable and able to operate at low power in air.

Advanced point sensors for environmental detection of biological pathogens are critical for early warning and for assessing possible contamination. Sensor systems capable of rapid, sensitive, and specific detection of biothreat agents are needed to deal with not only the terrorist threat, but also naturally emerging biological threats. Environmental point sensors could be used by first responders (firemen, police, hazmat personnel, etc.) as portal monitors or in sensor networks. The sensors must be simple, robust, reliable, compact, and, in many instances, battery operated. They must also be able to differentiate between pathogens in the context of the inherently complex environment. These attributes are difficult to achieve for environmental sensing. Moreover, there is a pressing need for real-time and continuous monitoring, and for the sensor system to operate directly in air with no prior aerosol collection. What is addressed here is the basic science that underpins the development of advanced sensor systems and entirely new detection methods.

Molecular Recognition. Molecular recognition (the process by which two molecules come together, recognize one another, and initiate the process by which they finally bind in a specific, high-affinity interaction) is one of the most important processes in any technology to detect biological (or chemical) agents. However, the chemistry and physics of the recognition process, which involves initially weak interactions, are poorly understood. Questions that arise when considering molecular recognition in the biological arena are: How does the binding site of proteins convert from a typically disordered state to one that achieves strong ligand recognition? How does a disordered loop of peptide on the surface of a protein recognize a small molecule? How can the interaction of the small molecule lead to the formation of a stable, protein–small-molecule complex? How is the specificity and affinity of the interaction coded into the structure of the binding partners prior to their interaction? We need to find answers to these fundamental questions to make progress in engineering host-guest complexes that will be important for design of sensors, whether they use biological or inorganic molecules as components.

Engineering of Robust Ligands. There is a huge need for highly specific ligands that are robust for use in field detectors, as well as in collection devices. One option for these ligands is to use polymers treated by molecular imprinting to provide specificity. Another approach is to utilize carbohydrates and small peptides (7–20 mers) that are inherently stable.[5] Both of these approaches satisfy the need for stability but suffer from low affinities and relatively poor specificity owing to cross reactivity to multiple biomolecules. A third method is the engineering of proteins or DNA/RNA aptamers obtained from large, diverse molecular libraries.[6,7] For instance, antibodies have many properties that are highly favorable for use in sensors (or collectors), but often lack the stability required for use in the field or for long-term storage. Structure-based engineering of antibody domains can be used to create hyper-stable, single-chain variable domains. Alternative approaches involve the use of other scaffolds that have greater intrinsic stability.

Structural Biology of Surface Epitopes and Macromolecular Complexes. Protein-based detection of bioagents will depend on interaction of a detector molecule(s) (such as a single-chain antibody variable domain) and a surface epitope of the agent. Characterization of the surface epitopes can be carried out either through the crystallographic analysis of structural proteins that make up the surface of the agent,[8] or through epitope analysis using libraries of antibodies displayed on the surface of phage particles. Screening of antibody libraries will lead to the identification of those with affinity for surface epitopes of the agent. The epitope can then be identified by screening peptide sequences, which may or may not be derived from the gene of interest, displayed on the surface of phage particles. Characterization of the specificity of the antibody will provide the identification of the epitope. Identification of these epitopes is a significant step towards an understanding of the parameters needed for vaccine design, design of drugs targeting the adhesion molecules of the agents, or the design of drugs involved in agent neutralization.

Signaling and Amplification. Cell signaling in nature is an exquisitely sensitive molecular cascade that converts a highly specific molecular recognition event to a macroscopic change. Nature does this by directly coupling a molecular recognition event to a signal, often a structural change that is then amplified through the enzymatic production of secondary messenger molecules that open, for example, ion channels.

There is continued need to develop new molecular transduction approaches that mimic cell signaling in increasingly innovative ways.

Examples of recent advances in signal transduction and amplification include the coupling of novel electronic and photonic materials to recognition. Conducting polymers have been used to provide amplification through the fluorescence quenching of the entire polymer by a single molecule.[9] Similar approaches have been taken with carbon nanotubes and related "molecular" wires to provide exquisitely sensitive response to a molecular-level event. Molecular recognition has also been used to open and close ion channels to provide signal amplification that mimics nature.[10]

In addition to new transduction approaches that build on novel new materials, entirely new approaches are needed to provide the level of specificity and sensitivity inherent in high-affinity recognition ligands yet with lower affinity permitting continuous monitoring. Current approaches based on immuno-assays are, in effect, irreversible. Mammalian olfaction is an example of how nature utilizes low affinity but highly specific recognition to achieve rapid reversibility of an event and avoid saturation. The development of new sensing approaches that build on biomimicry and biomimetic materials could well provide the underlying scientific foundation for near real-time continuous monitors for environmental sensing of threat agents.

Interfacial Phenomena. Sensors that are based on mimicking biological recognition and response must be able to interface the biomimetic system with a sensor platform that can interpret the signals. Biochemically based identification devices correspondingly require quantification tools that approach single molecule sensitivities. Moreover, technologies that have features with small (< 10 µm) length scales necessarily have high surface-to-volume ratios increasing the importance of understanding interfacial chemistry. Understanding how ultrasensitive spectroscopy and interfacial phenomena interrelate is fundamental to developing more sophisticated, robust sensors. Spectroscopic probes can be applied to condensed-phase systems and have applications in both biological and materials sciences.[11,12] These ultrasensitive laser-based probes have been used to interrogate physical and chemical interactions in micro- and nano-domains and at interfaces. These probes can now be used to study systems where biological or biomimetic molecules interact with hard and soft materials.

Dry Sensors. Environmental sensing of biological markers generally requires an aerosol collection followed by sample injection. It would be highly desirable to develop sensors that could directly respond to biological markers dissolved in aerosols without first concentrating the aerosol. Such "dry" sensors may need a permeable barrier material that separates the air to be monitored from the active element of the sensor system. Mesoporous materials (sol-gel, hydrogel, aerogel, block-copolymers, etc.) with controlled pore size and character (hydrophilicity and functionality) could be used to separate the air to be sampled from the active sensor elements. Ideally, these would be hybrid materials where proteins or genes could be, for example, electrophoretically (or physically) driven across the membrane barrier into the active sensor region. Other transduction approaches that use biomimetic materials that incorporate recognition and reporter molecules in a stable fluid media (e.g., membrane mimetic architectures) also have promise as dry sensors.

Single Particle Methods. Instrumentation is becoming available for the rapid, real-time analysis of individual aerosol particles. Such instrumentation can be highly diagnostic, as it does not average information about a specific agent with that from background constituents—finding the needles in the haystack by rapidly looking at a large number of individual "straws." Many field-portable instruments have been developed that follow an initial sorting of the aerosols by their aerodynamic size with a volatilization, fragmentation, and ionization step (sometimes through the use of lasers) and mass spectral characterization of the ionic fragments.[13,14] Instruments using ion traps for mass analysis are especially powerful because of their MS/MS capability, permitting the generation of sequence tags for protein identification, for example.[15,16,17,18] Research into laser material interactions is needed to improve the quantitative aspects of such instruments, with particular attention to characterization of biological agents and explosive materials. Aerodynamic sorting can also be followed by deposition of the aerosols on a substrate for later laboratory analyses. Recent advances allow elemental analyses on tens of thousands of individual particles (as small as 0.1 μm) to be performed via automated electron induced x-ray emission detection. Advances in high-resolution mass spectrometry indicate the potential for direct biological species identification through detection of highly specific signature molecules, following laser ablation of molecules from the surface of an individual spore, for example. These recent examples show that there is much to be gained in the speed and certainty of detection of biological agents through additional research into methods of single particle analysis.

Miniaturization. Among the technologies needed for addressing the identification of biological threat agents will be microfabricated devices. Different aspects of R&D needed to achieve miniaturization will be described here.

Microfluidics. Microfluidics enables samples and reagents to be easily manipulated, analyzed, and detected "on-chip." This suggests the eventual ability to perform virtually any type of "wet-chemical" bench procedure on a microfabricated device.[19,20,21] This moving of the chemical or biological laboratory to a microchip includes the advantages of reducing reagent volumes, automating material manipulation without human intervention, reducing capital costs, parallel processing, faster analysis, and remote operation away from large laboratories. The volume of fluids manipulated or dispensed in the microfluidic structures depends on the channel dimensions but is typically on the order of picoliters to nanoliters. By implementing multiple processes in a single device (serial integration), these small fluid quantities can be manipulated from process to process efficiently and automatically under computer control. An operator would only have to load the sample to be analyzed. This serial integration of multiple analysis steps can be combined with parallel processing by replicating microfabricated structures on the same device.

Although significant progress has been made, microfluidic devices need to reach the next level of sophistication to contribute significantly to deterring terrorism. Fundamental research issues include materials development, novel fabrication techniques, fluid transport phenomena, and system integration. Developments with microfabricated fluidic devices would need to parallel advances in biochemical assays for future integration.

Nanofluidics. Understanding the chemistry and physics of molecular transport through fabricated channels with molecular-scale lateral dimension is fundamental to developing the next generation of biological sensors. Although such transport is fundamental to life, there is little molecular scale understanding of the requirements for such processes. Studying such phenomena using well-characterized nanometer scale channels fabricated in substrates such as silicon, quartz, or other materials is one approach.[22,23] Fundamental transport issues for fluids and solutes need to be studied within these nanoscale conduits.[24,25] These studies should include chemistry and physics issues related to hard materials (the materials that form the fluid enclosures), soft materials (fluids, molecular coatings, and biological molecules), and the interface between the two types of materials. Fundamental questions that need to be addressed include phase transitions and scaling of polymer transport through nanoconduits, the validity of continuum fluid mechanics at the nanoscale, and fundamental limits of forming nanoscale conduits.

Miniature Gas Phase Analysis; Mass Spectrometry. The inherent selectivity and speed of mass spectrometry has the potential to provide significant capability for rapid identification of biological agents. The idea of advanced, selective miniature mass spectrometer-based sensor systems is intriguing.[26,27] Experimental and computational approaches to study the fundamental chemical and physical processes that permit the reduction of size, cost, and analysis speed for mass spectrometer systems would be needed. Evidence suggests that the fundamental processes underpinning laboratory scale mass spectrometry will not scale with size when moving from the centimeter to the micrometer domain (and beyond). Thus, transitioning mass spectrometry from laboratory to small-scale (hand-held) sensor devices will require the study and understanding of fundamental phenomena in the new size regime both to determine the limits of scale as well as to identify and exploit new opportunities. These phenomena include ion transport, ion energetics, and gas phase ion and ion-ion chemistry at micrometer dimensions.[28,29]

Characterization, Attribution, and Forensics

Technology Need	Present Problem
Rapidly characterize and attribute the origin of biohazard material.	New methods must provide rapid species analysis and stain specific detection.

For bioagent characterizations, a variety of technologies ranging from compact fieldable sensors to elegant laboratory-based bioanalytical methods are needed. The discussion above for sample collection and environmental point sensors applies equally to forensics and attribution. Forensics and attribution can also be achieved by isotopic and elemental analysis of nonbiological constituents of a sample, as well as by DNA analyses for the species and strain identification. Analysis of DNA variations using Amplified Fragment Length Polymorphism (AFLP), Multiple Locus Variable number tandem repeat Analysis (MLVA), and single nucleotide polymorphism (SNPs) have proven invaluable in characterizing agents. These DNA-based techniques will remain important, but we also need novel methods that will provide for faster analysis for species and, if possible, strain-specific detection and characterization. In this section, we will concentrate on technologies needed for attribution and forensics applications of isotopic analysis and high-throughput bioassays.

Isotopic Signatures for Attribution. Sensitive techniques for stable isotope separation provide a means of determining the origin of biological agents in forensic reconstructions. A specific example of this kind of application is the potential use of Sr and Pb isotopic compositions in tracing the source of the anthrax causing B. anthracis recently sent through the mail system, either through the composition of the spores themselves or of their carrier medium. In the natural environment, different sources of Sr and Pb can have different isotopic compositions because of decay of ^{87}Rb to ^{87}Sr, ^{235}U, ^{238}U, and ^{232}Th to isotopes of Pb, coupled with variable time integrated Rb/Sr, U/Pb, and Th/Pb ratios in different natural materials. This variation, related to underlying regional geology, imparts to different fresh-water sources contrasting Sr and Pb isotopic composition that can be used to constrain geographically the source of fresh water. For example, water from the Connecticut River has a distinct range in Sr and Pb isotopic composition from water from the Sacramento River (in contrast, while the Pb isotopic composition of seawater is variable, the world's oceans are essentially homogeneous in Sr isotopic composition). Likewise, the trace amounts of Sr and Pb in chemical reagents are likely to have distinct isotopic compositions. When Bacillus anthracis sporulates, it incorporates small amounts of Sr and Pb, faithfully recording the Sr and Pb isotopic composition of the growth medium. This provides then an isotopic fingerprint of the source of the spores. This can be used to not only compare different aliquots of the spores, but could also potentially provide clues to the geographic origin of spore production or to sources of utilized reagents.

High-Throughput Assays for Agent Characterization. There are many instances (e.g., distinguishing a pathogenic agent from a vaccine strain) where it is critical to be able to rapidly characterize biothreat agents in the field.

Gene Probe and Protein Chip-Based Assays. Immunological (protein based) and DNA or RNA (gene based) detection currently provides sufficient accuracy for identification and characterization. Microarrays provide an efficient way of performing large numbers of nucleic acid hybridizations or protein-protein interactions simultaneously, but there are challenges concerning costs and quality control. They rely at the moment on the arraying of nucleic acids or proteins on glass slides or membranes. Protein arrays still rely on sandwich assay formats that require both capture and reporter antibodies. For this reason, protein arrays suffer from problems of relatively low affinities (the weaker of the antigen's affinities to the capture or reporter antibodies) and higher levels of cross reactivity relative to gene arrays.[30] New reagent-free assay formats that build in higher binding affinities, and simple chemistries to pattern recognition ligands onto chips are needed. In addition, advances in reactive chemistries to improve binding of these ligands to the array matrix, as well as the development of modified or synthetic ligands to improve the stability of ligands (to permit reuse of arrays, for example) would make these techniques more robust. In addition, construction of hybrid organic sol-gel materials or modified semiconductor materials (e.g., Nanogen's chip technology) may provide rapid, more reproducible fabrication methods. There are also issues concerning cost and quality control to be addressed before this technology can be broadly applied to the biothreat problem.

Next-generation microarray technology likely will involve the elimination of confocal optical techniques for readout and will, rather, integrate the molecular interactions with signal transduction at the silicon surface, or in thin film composites. Current directions in BES Nanoscience and Technology are already producing prototype devices demonstrating what might be possible.

Single Molecule DNA Sequencing. The possibility of sequencing single molecules of DNA at kilohertz rates using nanotechnologies would be essential for real-time, high-sensitivity identification of pathogens or real-time DNA fingerprinting of individuals at portals. One approach to the sequencing of single polynucleotide molecules is to use conductance probes within a molecular-scale aperture. There have recently been intriguing suggestions about how one might rapidly determine the sequence of a single DNA molecule contained in a buffer solution by transporting it through a voltage-biased nanoscale aperture while monitoring the ionic current through that aperture.[31,32]

Fundamental research issues are to develop fabrication strategies for forming nanometer-scale structures, understand limits to dimensional stability and surface roughness, evaluate transport for solvated ions and polyelectrolytes in confined fluids, investigate polymer dynamics in confined spaces, and interface nanostructured material to the "real-world." These investigations should be pursued both experimentally and theoretically.

4.4 Medical Diagnostics

Technology Need	Present Problem
Rapid diagnosis of infection or detection of human exposure.	Clinical diagnosis is too slow for effective early treatment approaches.
Diagnostic tools for use in point-of-care facilities.	Instruments need to become simpler, less expensive, and able to operate after prolonged storage times.

In the event of a bioterrorist attack, it will be essential to have technologies that can be used to rapidly detect infection from, or exposure to, biothreat agents within potentially large human populations. Early diagnosis of infection or detection of exposure can make all the difference in successfully treating victims and in minimizing the impact to the local medical community. For example, if intoxication by botulinum neurotoxin (BoNT) can be detected prior to clinical diagnosis, this disease can be effectively treated with therapeutic antibodies; if not, the only recourse is respiratory aid for 6–8 weeks in an intensive care unit.[33] Even a limited terrorist attack with BoNT could paralyze the medical community. Medical diagnosis will, most likely, take place in a doctor's office or point-of-care facility. Given the expected low incidence of events, diagnostic instrumentation or sensors will be used sparingly, if at all, to address biothreat attacks. Accordingly, it is critical that they have dual use capabilities and be used regularly to address common infectious disease, or they are likely to be ineffective in the event of a real biothreat attack.[34] Other attributes, such as cost, speed, and simplicity of use are also important. The most important contributions of BES are likely to come from the preparation and characterization of novel materials for new diagnostic or therapeutic devices, from the development of new tools for diagnosis and the development and application of new materials and tools to study host-pathogen interactions at a fundamental level.

Bio-Compatible Materials for Therapeutic and Diagnostic Applications

New bio-compatible materials are need for a variety of biomedical applications encompassing diagnosis and treatment. These include optoelectronic materials that have ideal light-emitting characteristics for probing biological systems. The ability to implant macro- and nano-structured materials for detecting disease, monitoring exposure, and therapy after exposure is also an area to explore.

New Materials for Diagnostic Devices

This area of research seeks to apply materials (self-assembled, semiconductor, glass, and polymer) science and technology toward early detection of infection by biomedical analysis of blood, body fluids, and tissues in real time at a point-of-care setting. Such detection includes measuring the response of the human immune system to invading viral and bacterial pathogens as well as detecting markers of the pathogens themselves. Important candidate technologies include novel microfabricated and nanofabricated structures and devices that are integrated with cells, microorganisms, or biomolecules for analysis, separation, or processing. They exploit the interplay of the microfabricated structure/device materials and architectures with the biosystem by interrogating the biophysical or biochemical properties of bioparticles. Such materials may be used for in vitro detection, in noninvasive monitoring as in ex vivo detectors and dermal contact sensors, or in vivo for detection, imaging, and therapy.[35]

Microfabricated and nanofabricated materials for optical-electrical-mechanical systems enable characterization techniques that offer higher speed, sensitivity, and efficiency over conventional methods. Such structures or devices could include microfabricated flow structures; micro-cytometers for cell analysis, identification, and sorting; DNA, RNA, and protein sequencing; insulin or glucose detectors; antibody and virus detectors.[36]

This area will need modeling and simulation to better understand and predict the material or biosystem interactions at micro- or nano-meter scales. Examples include the studies of the surface modification of semiconductors and biocompatible materials (semiconductors, glasses, and polymers) integrated at the wafer level (lab on a chip), optical microcavities or porous fabricated materials containing biological fluids under analysis or modification by enhanced physical or chemical effects, and micromanipulation of molecules/cells/particulates by microfabricated devices. Also included are nanostructured surfaces that exploit enhanced surface effects to study, modify, or manipulate cells, molecules, or particulates; surface-enhanced phenomena arising from direct contact of biosystems with materials; biomimetic materials such as membrane mimetic architectures; and hybrid organic-inorganic materials.

It is evident that the research opportunities include a broad range of materials science such as self-assembled and hybrid materials, semiconductors (silicon, III-Vs, and other compounds) insulators (glasses, dielectrics, fibers), and organics (polymers). The essential focus is on understanding and making very small structures and devices from these materials and applying them to the flow, capture, detection, or processing of biological species. Novel theories of substrate-organism interactions, experimental techniques, fundamental materials science, and materials processing are all included.

Spectromicroscopic Imaging at Molecular and Cellular Levels

Imaging technologies have experienced great advances in recent years, and their use in biology has been increasingly exploited for both research and medical diagnostics. The traditional imaging techniques such as MRI and CT, for example, can generate highly detailed spatial images, but the observed contrast does not directly contain useful biochemical information. If one could obtain a *biomolecular image* of tissues or cells, it would be possible to discern the structurally specific chemical basis of dynamic biological processes or take advantage of the combination of shape and unique chemical composition of individual cells to obtain fingerprint signatures, including diseased cells and pathogenic bacteria, without the addition of dyes or labels. Vibrational imaging technologies that correlate molecular spectral (intensity as a function of energy) data with spatial variables can provide such a molecular map. The primary challenges to the development of this approach include needed improvements in the sensitive detection of vibrational images and development of image understanding tools to extract relevant information. These problems may be addressed using infrared and coherent anti-stokes Raman (CARS) methods as outlined below.[37]

FTIR Detection of Pathogens in Cells

Fourier transform infrared (FTIR) spectromicroscopy is a technology that may be enabling for new detection techniques for pathogens in infected cells, as well as in the environment.[38] FTIR has the advantage of a wide spectrum, very bright beam that can interrogate surfaces with living intact cells. It has been recently demonstrated that high-brightness synchrotron radiation-FTIR (SR-FTIR) spectromicroscopy with a spatial resolution of less than 10 um has the ability to detect many biochemical changes, such as different phases of the cell cycle and exposure to very dilute chemical agents (e.g., 10^{-11} M of dioxin).[39] It also allows one to use the beam to study localized cellular processes. This research also indicates that synchrotron infrared photons do not induce detectable intracellular chemistry changes or physiological effects (long term or short term) on cells that are exposed to the synchrotron infrared beam. The reflected spectra can show unique responses in particular wavelengths that indicate compounds or suites of compounds that are unique to that organism or indicate metabolic/biochemical changes that have occurred in a host cell in response to infection or toxicity. FTIR spectromicroscopy is sensitive enough to detect reproducibly distinct (spectral) changes in a single hydrated and living fibroblast (lung) cell as the cell undergoes different stages of its cell cycle. Thus, sputum samples from exposed individuals could be examined to determine if they have been infected, prior to showing any symptoms. In addition, the spectra from environmental samples have been used to identify bacteria on environmental surfaces and demonstrate their juxtaposition to substrates. Once the spectra that are critical have been identified, then a small tuned laser system that might even be handheld would enable rapid field detection both by first responders and clinicians.

IR Focal Plane Arrays for Hyperspectral Imaging

SR-FTIR shows great promise as a research tool to further unravel what can be learned about disease using spectromicoscopy techniques. It is not, however, practical to rely on limited high-brightness sources for rapid diagnosis that will be needed in the event of a terrorist attack. For this reason, it is important to continue to develop more flexible approaches based on advanced detector systems and more conventional sources that could be deployed in a doctor's office. The recent deployment of multichannel 2-D focal plane array (FPA) detectors including InSb, HgCdTe (MCT), and quantum-well infrared photoconductors (QWIP) on the infrared microscope has facilitated the application of hyperspectral imaging to vibrational microspectroscopy. These array-based technologies are being actively developed, with sensitivity and spatial resolution issues still to be fully characterized and optimized.

Coherent Anti-Stokes Raman Scattering (CARS)

Recently, nonlinear multiphoton techniques have been applied to fluorescence imaging. In these experiments, femtosecond pulses of near-infrared light are tightly focused on the sample. Two-photon absorption will occur only from within the focal volume where the light intensity is high; hence, fluorescence originates only from the focal volume. Similarly, nonlinear optical techniques for vibrational spectroscopy have many benefits for chemical imaging. CARS is a nonlinear Raman technique that produces coherent emission of Raman radiation.[37] The primary value of CARS includes its superior resolution capability (sub-diffraction) and, as a stimulated process, its high signal levels. Even more important is the fact that it does not require dye-labeling as do may fluorescent probe methods. Molecule specific imaging is possible in unmodified cells or tissues, greatly simplifying sample preparation and other issues related to medical applications of laser based imaging methods.

Image Understanding

While vibrational spectroscopy can provide chemical information for all species present, the sheer volume of information generated can make data analysis problematic. As each chemical species gives rise to many vibrational modes, the measured spectrum will be comprised of contributions from all of these. A similar problem has already been successfully addressed using an alternate technique based on "evolutionary algorithms." The macroscopic applications of astronomy and satellite-based surveillance systems have made use of hyperspectral imaging, and the data analysis routines used in these disciplines have attained fairly high levels of sophistication. Two approaches, both separately and in combination, will improve the utility of vibrational images: (1) genetic learning algorithms that use a library of signatures and user-selected screening algorithms to categorize individual and combined elements within an image and (2) the application of a multiscale, multiresolution algorithms to both compress and optimally select the discriminating characteristics of vibrational images.

The realistic potential for correlating molecular images of cells to disease states offers enormous technical benefits, which would accrue from better understanding the relevant biochemical foundations of cellular responses. In both the biological and the materials science arenas, the instrumentation and analysis techniques proposed here will yield information with an unprecedented level of spatial and chemical detail, and ultimately allow the examination of how heterogeneous molecular-level structure influences and controls macroscopic function.

New Materials and Tools to Study Host Pathogen Interactions

An understanding of how pathogens invade the host can help guide the development of both diagnostic and therapeutic tools. One example is the mechanisms of cellular invasion of viruses and bacterial protein toxins. In both cases, the cellular invasion mechanism always involves pathogen recognition of multiple receptors on the surface of targeted cells. A clear understanding of the ligand-receptor interactions can be used to design man-made receptors that bind the active receptor site of the pathogen more tightly than the natural receptors. These man-made receptors can then be used for inhibition to block the pathogen's invasion of cells or as recognition molecules for sensitive detection of the pathogen. Structural biology (neutron and x-ray diffraction as well as electron microscopy) can be used to clarify the receptor binding sites to guide the synthesis of man-made receptors with high binding affinities.[40]

The mechanisms of translocation of a bacterial toxin or viral particle (or its genetic information and core proteins) across the cell membrane is understood for only a limited number of pathogens. Often, the pathogen-receptor complex further aggregates on the surface of the cell membrane, resulting in structural changes that open a channel for translocation of, for example, the enzymatic subunit of a protein toxin. Understanding the detailed invasion mechanism could provide the insight to develop entirely new ways to detect and treat. In this case, new membrane mimetic architectures and research tools that can be used to directly study the invasion mechanisms would help to develop that understanding. For example, the use of neutron or x-ray reflectometry and low angle diffraction to study protein toxins interacting with natural receptors at the surface of a fluid phospholipid bilayers could help in developing a more detailed understanding of host-pathogen interactions.[41] There are a number if other imaging (e.g., scanning probe microscopy[42] and various electron microscopies) and spectroscopic techniques (above) that could also shed light on host-pathogen interactions. Single molecule spectroscopic and imaging methods have recently been developed that allow real-time imaging of the entire process of viral attack, invasion, and control, providing valuable kinetic data as a complement to these structural studies of the mechanism.

Synthesis and Study of Molecular Prophylactics and Therapeutics

Materials with molecular recognition moieties that are attached to carrier vehicles could provide excellent drug delivery systems for pathogens either in vivo as a therapeutic or in solution as a decontaminant.[43] These same materials could also be used to detect and image disease by incorporating imaging molecules or materials (e.g., radionuclides and magnetic or fluorescent molecules). Functionalized polymers and self-assembled structures (e.g., liposomes, liposome-coated particles, micelles, dendrimers, and cage structures) have the properties to physically and/or chemically carry therapeutic agents to the pathogen. Cell or tissue-targeting molecules attached to these or other materials could offer the targeting as well as release mechanism for drug delivery. It has recently been possible to select peptides and single chain antibodies that both target specific cell/tissue types and also effect the translocation of phage particles across the cell membrane. These molecules are obtained using phage display methods where the selection pressure requires both recognition and endocytosis and are remarkable in their specificity in targeting specific cell or tissue types and in being able to distinguish between healthy and sick cells. Schemes to link these cell/tissue targeting molecules with the drug delivery particles must also be further developed. Moreover, these hybrid materials that couple cell/tissue targeting molecules with drug-, gene-, or imaging-containing particles must be made to be stealthy in the vascular system. In the future, it may also be possible to design and fabricate nano-structured hybrid materials where highly specific recognition events between the cell/tissue targeting molecules and the targeted cells/tissues triggers the generation of a measurable signal or the activation and release of therapeutic agents.

Synthetic agents that can neutralize the pathogen by mimicking the target receptor or docking area at the cell surface could significantly reduce the risk of infection. To address this area, an in-depth understanding of the modus operandi of the pathogen must be addressed. Structural analyses of biotoxins, viral particles, and organisms on lipid membranes should be probed at the nanoscale and in real time. Techniques of relevant use include scanning probes, neutron and light scattering, and modeling simulations. By thoroughly characterizing the path of pathogen attack, weaknesses in its cell invasive mechanism will become clear. Through this effort, small molecule reagents could be developed to attack the pathogen during its cellular invasion, as well as decoys prepared with cell surface mimics.

4.4.1 Protection

Technology Need	Present Problem
Protect people, animals, crops and living spaces..	Current approaches not able to meet practical needs of large populations and indoor spaces.

Devices and systems are required to protect at-risk people, animals, crops, and material from the adverse impacts associated with biological threat agents. The need to protect-to-warn to facilitate protection of people is discussed in previous sections. The risk of infectious disease also extends to animals (e.g., impact on security dogs employed to protect facilities) and materials (e.g., microorganisms released into fuel storage systems can cause significant adverse impacts).

Functional devices are available to remove biological threat agents from air and water, and the agents can be killed in foods. However, the current protective equipment suffers from significant practical limitations, in particular for protection of large populations and indoor spaces. Limitations are associated with excessive unit costs (e.g., high efficiency particulate filters), operational costs (e.g., fitting and certification of respirators), and impairment of function (e.g., respiratory burden of negative pressure protective masks). Aspects of the critical infrastructure are at risk from microorganisms that can degrade or interfere with industrial and other large-scale processes (e.g., fuel storage).

Research has been conducted to incrementally improve protective equipment along traditional lines of inquiry. However, advances in BES areas of research suggest great advances in protective equipment can be realized as described below.

Individual Protection

There is a clear need for advanced materials from which to construct next-generation personnel protection equipment (PPE). For example, considerable waste could be eliminated by designing HEPA filter canisters that contain a color indicator to indicate when the filter has reached a conservative limit of capacity upon exposure to biological (and chemical) agents. Such an indicator could also provide the user with an additional degree of confidence that the filter was performing its function. The indicator would preferably be a colorimetric scheme (e.g., blue to red) that allows a distinct and rapid assessment of the material's state. The color-change mechanism should be linked to a specific chemical recognition scheme that is activated at a threshold value. More than one color-changing material specific to different agents could be incorporated into the filters to provide additional information to the user about the environment he was exposed to.

New materials for protective outer garments are especially needed. Even the more durable military garments must be discarded after exposure to agents, as there is no means of assessing the remaining protective capacity of the suits (short of sensory detection of the suit no longer functioning!). SBCCOM is already investigating membrane technologies for the next-generation JSLIST suit, and DOE's materials research programs could accelerate this development through the development of specialized polymers, as well as coating fabrics or other textiles with reactive surfaces of either chemical or enzymatic nature that could detoxify CB agents on contact (e.g., Tiller et al. at MIT recently reported that certain polymers, such as HexylPVP, can kill 95% of bacteria on contact). Materials that can enzymatically cleave amide bonds could neutralize the majority of biotoxins by degrading them to small inactive pieces. Studies of the surface structure of whole organisms or viral particles, on the other hand, could provide insights into means of inactivating pathogens using unique chemistries or materials to inactivate them via cross linking or synthetic enzymatic processes that change the organism/particle coat characteristics.

Collective Protection

The terrorist dispersal of *B. anthracis* spores through the U.S. mail system, contaminating USPS facilities, the Hart Senate Office Building, and other buildings through which the mail passed and was opened, revealed a new mode for deployment of biological agents. HVAC systems as currently designed also make it difficult to prevent re-aerosolization of settled agent, and hinder decontamination efforts. Immediate measures have been taken to decontaminate mail, and mail handlers have been advised to scrutinize mail for indications that might suggest suspicious contents. These measures are clearly reactionary, and active measures to detect and prevent the spread of biological contamination are necessary. Such protective measures would also be applicable to transportable shelters and mobile platforms.

Respiratory protection, as described above, is largely accomplished through the use of HEPA filtration given current technology. In the case of buildings, new approaches to air filtration, from the design of more effective air handling and prefilters, to advanced materials to increase the duty cycle and durability of the filter matrix are necessary. Selective filtration materials may be desirable to control influent air, along with recirculation within a building or work area. Such materials could also find use in the physical handling of mail and packages to provide worker protection. The use of novel reactive or absorptive materials that would inactivate any biological agent on contact would represent a quantum leap over current technology. These materials would also have the collateral benefit of providing solutions to so-called “sick building syndrome,” which is caused by a variety of fungi, especially *Stachybotris spp*. This problem is so endemic and difficult to combat in the U.S. that many homeowners’ insurance policies specifically exclude coverage for this problem. This also represents a significant component of the problem in the workplace.

4.4.2 Decontamination and Remediation

Technology Need	Present Problem
Biological decontamination of people, surfaces, and buildings.	Need to develop decontamination approaches that are effective, efficient, environmentally benign, and not harmful to humans or materials.

In the event of a release of biothreat agents, decontamination of people, surfaces, and spaces will be required to facilitate crisis response and consequence management. Decontamination will limit spread of the biohazard and facilitate prompt medical treatment to save lives. Following resolution of the incident, remediation of residual hazards will be required to return property, equipment, and personal belongings, at an acceptable level of risk, to owners.

Operational requirements for decontamination and remediation are associated with identification and quantification of hazard levels, and removal and/or killing of microorganisms. Biological threat agents (e.g., spores and some viruses) can be extremely stable in the environment, and contamination may be widespread and of low concentration. In addition, microorganisms may be stabilized against environmental stresses to enhance their effectiveness. Development of reactive chemicals and materials that kill microorganisms and have acceptable levels of environmental, health, and material risk has not been achieved.

Spaces to be decontaminated/sterilized range from large outdoor and indoor areas to complicated building ventilation systems. Materials requiring treatment range from construction materials to high-value art work (e.g., Senate Hart Building). Contaminated and infected people pose additional challenges. Current decontamination and sterilization agents and application equipment do not provide effective, efficient, and environmentally benign decontamination and remediation capabilities to address biothreats.

Fundamental scientific issues must be pursued to develop required capabilities described above. Research needs reside within many of the focus areas of the BES program. Of principal interest are scientific advances that will allow large-scale inexpensive production of effective materials that are highly specific in their destruction of microorganisms. Potential methods for the decontamination of sensitive equipment and valuable art include supercritical CO_2, environmentally friendly solvent wash systems, thermal approaches, and plasma approaches. For ductwork and other “hard to reach” places, methods to vaporize or encapsulate existing or newly developed noncorrosive chemistries or the development or identification of noncorrosive gases is needed. These chemistries may be agent-specific, since the primary use would be for facility restoration. Methods could be developed for deactivation and destruction of agents rapidly by solid matrices for remediation of bulk agents. This could include methods such as reactive nanoparticles, reactive microparticles, adsorption, and highly reactive surface chemistries.

Encapsulating Materials

Many objects that may be contaminated like desktops, chairs, large machines (e.g., letter sorters, etc.), and fixed equipment are too large to be quickly and efficiently decontaminated. In addition, many biocides may also be toxic or have damaging effects on objects being treated (e.g., oxidation, depolymerization, etc.). Thus, a simple inert material that can quickly and fully encapsulate an object to contain a diverse array of biological threats is highly desirable. The problem with many current materials like polyurethane foam is that they are too porous to be effective in containing spores. The ideal encapsulating material would be inert, transparent, thin, resilient to normal handling, applied as an aerosol, and easily applied by a first responder. Plastics and polymers research will find application in this area.

Irradiation

Microwave irradiation would become a viable technique for destroying *Bacillus anthracis* or other bacterial spores if the spores were found to have absorption lines in the few GHz region. Such specific absorption lines would then couple power into the spore, in analogy with the 2.45 GHz line of water exploited in microwave cooking. Research is required to determine if bacterial spores do have such absorption bands. If this were the case, then radio frequency (RF) power sources with relatively low powers of about 10 kW could potentially provide an effective method for selectively destroying bacterial spores.

In the case of a federal need for sterilization of a significant mail stream using electron irradiation, BES research expertise in the design of specialized linear accelerators could be brought to bear on this problem. There are a number of approaches, requiring R&D, that could provide sources superior to those presently available including, for example, (1) an integrated sheet-beam-klystron and linac that would provide a very compact device using sheet electron beam technology to spread the energy dissipation over larger areas than a conventional round beam, thus allowing higher average powers to be reached before destruction of the irradiated mail and (2) magnetron driven systems that would result in low-cost, very robust linear accelerators suitable for widespread deployment.

Nanoparticle Fluorescence

High affinity ligands, with an attached reporter, in a nano-material structure may be used for identification of surface contamination to guide decontamination treatment. Success of this effort will require directed synthesis of highly specific binding agents, which are attached to nano-structures. The process must be amenable to large-quantity, low-cost manufacturing.

Laser-Induced Fluorescence from Semiconductor Nanoparticles

This area of research encompasses surface functionalized semiconductor quantum dot particles equipped with specified bulk optical properties for interacting with external electromagnetic fields generated by lasers. The surfaces are functionalized for selective binding to cell membranes or pathogens.[44] One use of these luminescent semiconductor nanoparticles is to label cell membranes, organelles, or cytoplasmic molecules for the purpose of imaging the cell structure. They have advantages over conventional fluorescent molecular probes, including ease of synthesis, broadband absorption, narrowband emission, and wavelength selection by quantum size effects.[45,46] An array of such nanoparticles tailored to emit at selected discrete wavelengths can be used to identify pathogens, for example, in microfluidic systems in real time in a field setting for evaluating residual agent levels and hence risk.

Reactive Chemistry

Develop noncorrosive, materials compatible, nontoxic, and environmentally friendly oxidative or enzymatic chemical and biological decontaminants (both aqueous and nonaqueous) to replace current toxic and corrosive formulations for use in first response and facility restoration. These formulations should be capable of neutralizing CBW agents at material-friendly pH of 7.5–9.5 by either oxidation or displacement reactions yielding acceptable reaction products. The decontaminants should be effective against standard CBW agents, TICs, and TIMs, and other biological pathogens. Formulations should be inexpensive and easily deployable in the field.

Agent Targeted Remediation

Advances in ligand design and synthesis, when combined with reactive chemistries and novel materials hold the potential for development of decontamination systems that are selectively targeted at biological threat agents and that can self-activate upon recognition of the target substrate. Development of this capability would require interdisciplinary basic research and cross-functional coordination between researchers engaged in ligand and decontaminant development. Bacterial chemotaxis is an example of a simple chemoreceptor system that directly activates a response. A molecular system that contains a specific receptor that then activates the release of a biocide is an exciting possibility and within the realm of the Nanoscience and Nanotechnology programs.

4.5 Research Needs

A number of themes that emerged from the discussion of scientific issues and opportunities build on the areas of strength in the BES research program.

4.5.1 Scientific Issues

Molecular Recognition

Molecular recognition is an underlying research theme for almost every aspect of biothreat reduction discussed. There are research needs for ligand design in terms of specificity, desired affinities and kinetics of binding, robustness, and manufacturability. Biological and abiotic ligands are relevant. The structural biology of receptors and complexes with receptors will be important in detection and in therapies designed to block infection by mimicking key receptors required for pathogen invasion and proliferation.

Integrated Molecular Systems

Sensing biological agents and medical diagnostics depend upon being able to integrate recognition with signaling and amplification. Technologies for detecting small toxins such as aflatoxin and small peptides are needed.

Interfacial Science

Like molecular recognition, interfacial science is an underlying theme of every aspect of biothreat reduction. Nano-bio interfaces, transport at interfaces, functional interfaces through the attachment of recognition molecules, stability of layered materials (phase control, adhesion), and transport and fate of pathogens in the environment all depend on understanding and advances in interfacial science.

Novel Materials

New materials with novel properties are needed for detection, diagnostics, protection, decontamination, and remediation. Nano-bio materials, hybrid materials and systems, self-organized materials, patterned surfaces, reactive materials, molecular electronics will all be important.

Nanoscience and Technology

Detection, diagnostic, decontamination, and remediation technologies that build upon the principles of molecular recognition, signaling, and amplification require tools for studying nanostructures and nanostructured materials,

Spectroscopy

Spectroscopic tools will be needed as sensitive, specific probes of molecular and nano-scale structures, for probing interfacial phenomena, as stand-off detection systems, for sensing, for single particle analysis, etc.

Computing, Modeling, and Simulation

Molecular dynamics simulations will be important for understanding recognition, collective phenomena, materials properties, and interfacial interactions. High-speed data analysis is important for analyzing array data, data from distributed sensors or trigger systems. Intelligent control systems to coordinate multiple components of integrated sensor systems or networks of sensors will be important to efficient operation of complex systems triggered by sentinel detectors, and to interpretation of responses from multiple sensors.

Advanced Instrumentation

New advanced instrumentation is needed for materials and interfacial characterizations, high-resolution bio-imaging, mass spectrometry (precision, portable, high-mass analysis), and stand-off detection using laser systems, spectroscopy, or hyperspectral imaging.

Integrated Devices

Integrated devices require research and development in microfluidics and nanofluidics, optoelectronics, microelectronics, MEMS, and a wide range of functional materials. Achieving these integration goals will require new experimental tools and modeling approaches that are able to address materials interfaces, energy and information transfer, device manufacturing, and materials assembly.

4.5.2 Research Environment and Infrastructure Requirements

Addressing the R&D needs of such a complex problem as biothreat reduction requires an unusual hybrid environment that includes elements from both academic, industry, and defense-related research environments. For example, the best scientists and technologists must be attracted; there must be mechanisms to support large, cross-disciplinary teams from across the community; and major facilities for molecular and materials characterization are needed in a research environment that is juxtaposed with secure environments. Specific to countering the biological terrorist threat is the need for a biology expertise that can interact with physical and chemical sciences as well as engineering and computational science.

Special Facilities and Large-Scale User Facilities

Synchrotron and neutron scattering facilities will be needed for materials characterization and structural biology. State-of-the-art macromolecular crystallography that can be carried out possibly in a secure location or with Biosafety Level 3 (BSL-3) capabilities might be an asset to consider at one of the synchrotron facilities. A “biosurety” program and specialized facilities for handling pathogens, such as Biological Safety level-2 and -3 laboratories are critical. All of these elements are contained within the DOE complex of national laboratories. Mechanisms should be put in place to make the appropriate facilities available these teams of research scientists and engineers.

Nanoscale Science Research Centers

Facilities for nanoscience and technology, including fabrication, will be key for many aspects of biothreat reduction. The Nanoscale Science Research Centers will also be centers of excellence for interfacial science, synthesis of nanomaterials, self-assembly, novel materials, biomimetics, and more.

4.5.3 Relationships with Other Programs

The DOE Basic Energy Science program is partnered with other major programs that bring critical expertise to the problem of reducing the threat from bioterrorism. For example, there are programs in Environmental Management (EM), Super Computing (ASCR), and Biological and Environmental Research (BER). In particular, a partnership with the BER and its genomic science capabilities will be a critical. Through the Joint Genome Institute, the department has highly competitive genomic sequencing capabilities in terms of both cost and throughput. These sequencing capabilities can provide a wealth of information on human, plant, and animal pathogens and the host systems they attack. The BER/ASCR initiative, Genomes to Life, explicitly targets genome scale analyses that will yield systems-level information on the composition and function of the biochemical components, networks, and pathways that carry out the fundamental processes governing life. The initiative will also develop the computational tools and infrastructure for integrating and understanding the vast amount of data that will be generated and then used to gain predictive understanding of the fundamental processes in biology. This initiative promises to be a rich source of information on protein complexes, regulatory networks, and microbial communities that will significantly enhance the potential for success in the material and chemical science programs within BES efforts that will focus on specific bio-molecular assemblies and interfacial systems for biothreat reduction technologies. The BER program in climate modeling and atmospherics is also an important potential partner in the race to develop the best defense technologies against biothreats.

The NNSA, within DOE, can be a powerful ally with BES in the fight against bio-terrorism. The mission of the NNSA's Chemical and Biological National Security Program (CBNP) is to develop, demonstrate, and deliver technologies and systems that will help the nation prepare for, recognize, and respond to chemical or biological attacks on the civilian population. The focus of this program is on developing new technologies that can be deployed on a 3–5 year time scale. In addition, the NNSA's nonproliferation mission has been expanded explicitly to include chemical and biological weapons of mass destruction. The longer term R&D focus of BES, and BER, will be important fuel for CBNP's future generations of technology development.

It will be key for DOE to develop strategic alliances with other offices or agencies with expertise and research and development capabilities for different aspects of anti-bioterrorism. Perhaps most importantly among these will be the Health and Human Services' National Institutes of Health (NIH) and Centers for Disease Control and Prevention (CDC), the Department of Defense, and the Department of Agriculture. Some interactions have already formed and only need to be strengthened and solidified. It will also be key to interface with the ultimate users of the technologies being developed in order to understand the operational needs, such as first responders, public health, Department of Transportation, Immigration and Naturalization, military, and law enforcement.

4.5.4 Dual-Use Opportunities

The detection, identification, medical diagnostics, and clean up capabilities needed to protect our citizens against the bio-terrorist threat will also serve to strengthen our public health infrastructure in general and provide increased protection against naturally emerging infectious diseases. Also, the application of these technologies to agricultural threats will aid in protecting our food supplies and ensure its safety.

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5 Workshop Conclusions and Recommendations

The goal of this workshop was to identify the critical scientific issues and opportunities where basic research supported by the Department of Energy (DOE) Office of Basic Energy Sciences can have an impact on our nation's ability to counter terrorism. The two days of workshop presentations and discussions clearly showed how many of the research directions currently supported by BES are either currently having an impact or may potentially have a direct impact on important technology needs for countering terrorism. In addition, the facilities and scientific capabilities that BES supports at the DOE national laboratories and universities were identified as having extremely high value to our nation's war on terrorism. It was concluded that the DOE national laboratories and the BES special and user facilities can be expected to play a continued and increasing role in our nation's efforts to counter terrorism.

In this final section of the report, we turned to the advice provided by our plenary speakers to develop a set of recommendations that will help BES and other basic research organizations further increase the impact of its research capabilities on problems associated with countering terrorism.

- Invest Strategically – Here, we focus on ***Cross-Cutting Research*** that has the potential to have an impact on a broad set of technology needs, thereby providing the greatest return on the research investment.

- Build Team Efforts – We addressed team efforts in two contexts: (1) ***Research Environments and Infrastructures*** that encourage and enable cross-disciplinary science and technology teams to explore and integrate new scientific discoveries and (2) Exploring ***Relationships with Other Programs*** that will build connections between scientific advances and those groups responsible for technology development and implementation.

- Consider Dual Use – We have identified areas of research that present significant ***Dual-Use Opportunities*** for application to countering terrorism and other complementary technology needs.

5.1 Cross-Cutting Research

Sections 2–4 of this report provide detailed descriptions of critical scientific issues and their relevance to technology needs associated with Radiological and Nuclear, Chemical, and Biological threats. From these underlying scientific issues, a number of cross-cutting research themes emerged.

Recommendation: *We recommend continued or increased funding for the following research directions since they underpin many technologies that have high probability to impact our nation's ability to counter terrorism.*

***Novel Materials* –** A wide range of new and nanophase materials will be needed as catalysts, sensors, semiconductor detectors and solid-state lasers, membranes, lightweight structures, and molecular electronic and optical materials. Capabilities are needed in synthesis and characterization of self- and directed assembly, nano-bio hybrids, complex functional materials, and patterned and templated surfaces. Characterization will require a suite of tools ranging from large user-based x-ray and neutron scattering facilities to novel local probes. The materials development will require an underpinning in predictive modeling and theory.

***Interfacial Chemistry* –** Fundamental theoretical and experimental tools and models to probe molecular interactions with solid/vapor and solid/liquid interfaces will be critical to development of new selective sensors, transport and fate models, development of improved separations chemistry, and development of new protective barrier and catalytic materials for protective clothing and toxin neutralization. Research challenges include development of accurate thermodynamic and kinetic models for interfacial behavior and ultra-fast local probes to study interfacial molecular interactions.

***Chemical and Molecular Recognition* –** Molecule/ion selective receptors could have an impact on a wide range of detection, protection, and response technology needs. Progress will require the development and application of new theoretical and experimental tools as well as new combinations of tools and expertise spanning physics, chemistry, and biology. It will be important to develop integrated receptors that provide pathways for transducing recognition events to surrounding structures and devices.

***Laser and Mass Spectroscopy* –** Laser spectroscopy is expected to play a key role in stand-off detection and integrated systems. Research needs include new, compact, solid-state laser sources, semiconductor/biological interfaces, luminescent nanoparticles, and improved data analysis and data mining algorithms. Mass spectroscopy offers the ultimate in specific recognition, but investment is needed to develop more compact and portable approaches.

***Nanoscale Science*–** Many critical scientific issues and challenges associated with each threat area are rooted at the nanoscale behavior of materials and interfaces. New tools for fabricating nanoscale structures, probing structure and properties at the nanoscale, modeling properties and behavior, and integrating across multiple-length scales will be needed. The Nanoscale Science Research Centers being developed by BES can play a critical role in providing the tools and research environment needed to address these critical problems.

***Miniaturized Integrated Systems* –** Miniaturization and integration research themes underlie future ability to develop inexpensive and reliable devices for first responders. Critical research issues include microfluid and nanofluid transport, surface treatment and functionalization, combination of top-down and bottom-up fabrication techniques, and coupling of nanoscale and continuum models for mass and energy transport.

***Computing, Modeling, and Theory* –** Reliable predictive models will be required for all research directions identified in this report. The capabilities must span from large-scale continuum models for fate and transport to quantum chemical models that can predict molecular recognition events. The challenge is to not to just span these multiple length scales, but to provide continuity between the multiple techniques needed to cover these multiple length and time domains.

5.2 Research Environments and Infrastructures

The presentations and discussions at this meeting have made it abundantly clear that progress toward countering terrorism will require the formation of science and technology teams that combine multiple scientific disciplines and span from basic research to systems engineering and manufacturing. Given this need for broad research and technology teams, it is important to explore new opportunities to improve the coupling between academic, national laboratory, and industrial research and development communities. The workshop participants agreed that the DOE national laboratories, in general, and the highly collaborative research facilities such as the Combustion Research Facility, the Environmental Molecular Sciences Laboratory, or the newly initiated Nanoscale Science Research Centers, in particular, could provide a fertile environment for nucleating these new research teams and associated collaborative science and technology projects.

Recommendation: *We recommend the development of new collaborative programs that can help to stimulate the formation of, and provide needed resources for, cross-disciplinary and multi-institutional collaborations focused on critical needs for countering terrorism.*

The workshop discussions also pointed out the importance of DOE specialized and user facilities. Existing BES scientific user facilities at DOE laboratories and universities, coupled with those currently under development, such as the Nanoscale Science Research Centers, will provide many important capabilities needed to address critical scientific issues associated with threats of terrorism. However, we recognize that no single institution possesses all the required assets to address these complex problems. It will be important that research and technology teams are able to take full advantage of the spectrum of capabilities available at the DOE national laboratories and university-based programs.

Recommendation: *We recommend continued investment in DOE specialized and user facilities and explore new mechanisms that enable research teams to "mix and match" capabilities needed for larger collaborative projects.*

The topic of radiological and nuclear threats presents a unique situation in which the Office of Science has the stewardship role for fundamental research in these areas. Resources allocated to these areas have, in general, been decreasing over the last three decades, resulting in a net loss of personnel and aging infrastructure, including a lack of modern equipment. These problems are not only acute at the national laboratories, but are also reflected at universities where faculty positions and studies in radiochemistry and nuclear chemistry have been rapidly declining.

Recommendation: *We recommend exploring approaches to stabilize or increase the basic research funding in radiation effects and nuclear and radiological materials programs particularly as they apply to terrorist threat reduction and defense programs.*

5.3 Relationships with Other Programs

The task of countering terrorism provides challenges that are extremely complex and broad. Advice from our plenary speakers and the results of our own technical and scientific discussions served to reinforce the point that no one organization or federal agency will be able to provide all of the tools and capabilities that are needed to meet this challenge. This report cites examples that show how pooling the strengths of various organizations within the DOE itself could provide greater opportunity to address the complex problems associated with countering terrorism. In addition, it will be important for DOE to develop strategic alliances with other federal agencies whose missions and capabilities strongly complement those of the DOE.

The examples cited in this report range from agreements that would provide the research community with appropriate access to specialized facilities for handling chemical and biological toxins to alliances that would facilitate the communication of new scientific developments and accelerate their application to important counter terrorism applications.

Recommendation: *We recommend evaluation of complementary relationships with other organizations and agencies and, where appropriate, work to develop agreements that facilitate the formation of multi-organizational teams and the sharing of capabilities that will improve our nation's ability to counter the threat of terrorism.*

5.4 Dual-Use Opportunities

Many examples cited in this report show how critical science and technology challenges associated with countering terrorism could also impact important needs in energy, national defense, environment, and human health care. However, the key requirements for the success of any of these dual-use opportunities are as follows: (1) a clear understanding of the technology needs and (2) an effective pathway to move from laboratory / bench-top demonstrations and prototypes to low-cost, manufacturable technologies that can be widely implemented. In fact, the key requirements serve to further reinforce the value of strong technical teams and complementary relationships with other organizations, especially including industry. The simple fact is that no new scientific discovery or technological solution will benefit our nation's counter-terrorism effort or any other important national need if we are unable to translate that new science into useful and cost-effective technology.

Appendix I - CT Roster

BES Lead

Walter Stevens, SC-14

Workshop Chair

Terry Michalske, SNL

Biological Threat Group

Chair: Jill Trewhella (LANL)
Lee Makowski (ANL)
Basil Swanson (LANL)
Steve Colson (PNNL)
Terry Hazen (LBNL)
Frank Roberto (INEEL)
David Franz (Southern Res. Inst.)
Gary Resnick (LANL)
Stephen Jacobson (ORNL)
Jay Valdez (Army SBCCOM)
Paul Gourley (SNL)
Maher Tadros (SNL)

Chemical Threat Group

Chair: Michael Sigman (ORNL)
Michael Sailor (UC San Diego)
Mike Ramsey (ORNL)
Ben Smith (U. Florida)
Ken Shea (UC Irvine)
Jan Hrbek (BNL)
Phil Rodacy (SNL)
David Tevault (Army SBCCOM)

Radiological/Nuclear Threat Group

Chair: Norman Edelstein (LBNL)
James Beitz (ANL)
Carol Burns (LANL)
Greg Choppin (FSU)
Sue Clark (WSU)
Mark Deitz (ANL)
Robin Rogers (U. Alabama)
Sam Traina (OSU)

Thirteen National Laboratories Represented and 8 Non-BES Organizations

Additional Laboratory Participants

David Baldwin, AMES
Marion Thurnauer, ANL
Greg Hall, BNL
Leonard Newman, BNL
David Miller, INEEL
Harriet Kung, LANL
Don Parkin, LANL
David Shuh, LBNL
Henry Shaw, LLNL
Lou Terminello, LLNL
Dan Meisel, Notre Dame Rad Lab
Dan Blake, NREL
Michelle Buchanan, ORNL
James Roberto, ORNL
Steve Colson, PNNL
Robert Carling, SNL-CA
George Samara, SNL-NM
Darryl Sasaki, SNL-NM
Piero Pianetta, SSRL

Non-BES Attendees

Brendlyn Faison, BER
David Thomassen, BER
Teresa Fryberger, BER
Gerald Kiernan, NNSA
Mike Kreisler, NNSA
Larry Morgan, NNSA
Janice Hicks, NSF
Joe Dehmer, NSF
Larry Kerr, OSTP
Ben Smith, U. of FL
Jimmy Mays, U. of TN
Sue Clark, Wash. State. U.