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Universal Agent Sensor for Counterproliferation Applications

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Technologies to counter the proliferation of weapons of mass destruction by rogue governments and international terrorist organizations are a top national priority. One of the top development requirements is for highly sensitive and specific detection technologies for biological warfare agents. This article describes the development of sensors for field detection of weapons of mass destruction using an advanced time-of-flight mass spectrometer system. This sensor system has the potential to provide high speed, sensitivity, and specificity across a wide range of biological agents, chemical agents, explosives, and contraband materials. In addition, the system is being engineered to be rugged, small, lightweight, and low power so that it can be deployable in the field. (Keywords: Biosensors, Counterproliferation, Mass spectrometry, Weapons of mass destruction.)

INTRODUCTION

The widespread proliferation of weapons of mass destruction along with the rise of domestic and international terrorism has led to a dramatic focusing of national attention on developing means for the rapid, mobile detection and identification of chemical, biological, and nuclear materials in the production, storage, and operational phases of deployment. Whereas detection of nuclear materials is aided by generally strong, unique, and long-range signatures derived from radioactive nuclides and their decay products, the situation is much less tractable for detection of chemical and biological materials. These substances include nerve and blister chemical agents and bacterial (including spores), viral, and toxin biological agents that have a broad range of incapacitating, and even deadly, effects. An interdepartmental team of scientists and engineers at APL has been working in a collaborative program with scientists at The Johns Hopkins University School of Medicine and the University of Maryland, Baltimore County, to develop advanced mass spectrometric sensors[1] that can rapidly detect and quantify exceedingly low levels of chemical and biological materials in the field environment.[2]

THE THREAT

Chemical and biological agents span a broad spectrum of lethality; the lethal doses of several of these materials are shown graphically in Fig. 1. Examination

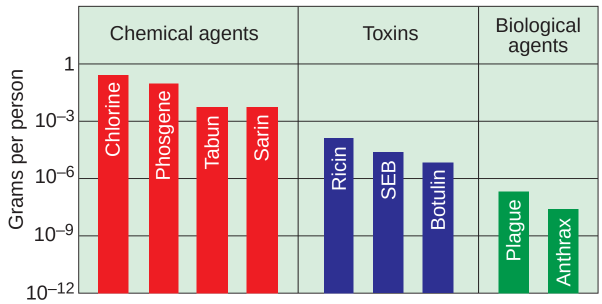

Figure 1. Graphical comparison of lethal doses of chemical agents and biologically derived toxins and infectious doses of biological agents (data from Pearson[3]). SEB = staphylococcal enterotoxin B.

of this chart shows that small doses (milligrams) of chemical agents such as the nerve gas sarin are deadly to human beings, while the biologically derived chemical toxins such as staphyloccol enterotoxin B are lethal at levels that are about 2 orders of magnitude lower. An even more dramatic threat is evident for biological agents such as anthrax, where about 8000 viable cells (nanograms of material) are an effective deadly dose for healthy human beings.

The methods of delivery of these agents include bombs, artillery shells, mortars, missiles, and even such innocuous devices as agricultural sprayers. The sprayers can dispense chemical and biological agents effectively and potentially clandestinely.[4] The effectiveness of aerial line spray techniques coupled with the extreme toxicity of the agents could potentially lead to the chilling result displayed in Fig. 2. In this figure, the lethal effects of 1000 kg of sarin (a chemical agent) and 100 kg of anthrax (a biological agent), dispensed from an aerial line sprayer, are compared. It is evident that under certain atmospheric conditions, 100 kg of anthrax has the potential to kill 1 to 3 million people over an area roughly equal to the size of Washington, D.C. The cloud released from such an attack would be completely invisible, having a density of only a few particles per liter of air. There would be no signs of this attack until the affected people started to show symptoms, about 72 h after exposure. Unfortunately, for many biological agents, if treatment is not started until after symptoms appear, the prognosis for the patient is very poor. For pulmonary anthrax, the fatality rate is about 70% for humans if treatment begins after the onset of symptoms. The sarin gas attack in the Japanese subway has also demonstrated the terrorist's potential for using low-technology delivery devices. It is believed that the terrorist who launched that attack used punctured

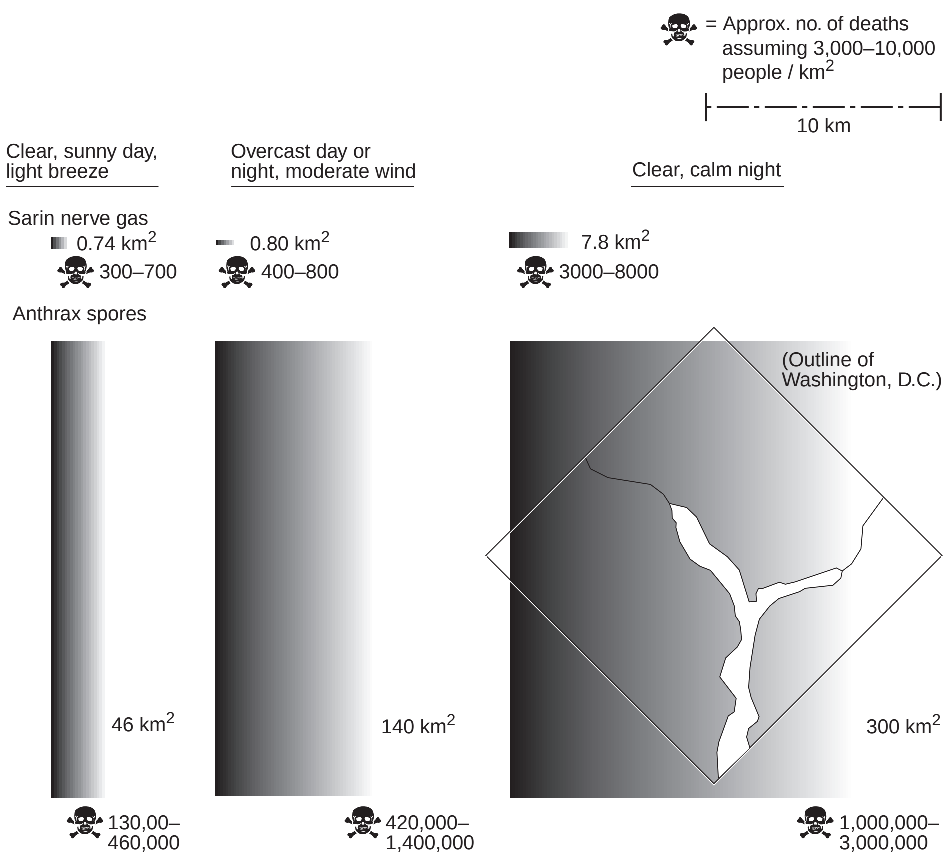

Figure 2. Comparison of lethal effects in an urban environment of a release of 1000 kg of sarin nerve gas with a release of 100 kg of anthrax spores (adapted from Ref. 4).

plastic bags as the delivery method. This attack resulted in approximately a dozen people dead and over 5000 hospitalized. It is clear, then, that there is a critical need for effective sampling methods and extremely sensitive and specific sensors for chemical and biological weapons and that detection levels be well below the lethal limit.

SENSOR SYSTEM REQUIREMENTS

Chemical and biological detection systems have widespread areas of application throughout the military and civilian communities. These applications include battlefield surveillance, passive defense for personnel, nonproliferation monitoring, treaty verification, high-value target security, intelligence collection, and counterterrorism. Each of these applications has its own specific system requirements. As an example we will focus on one of the most important national needs, protection of soldiers on the battlefield, which was brought to national attention by the events during Desert Storm. The Iraqis had carried out a systematic program to acquire and deploy weapons of mass destruction. At the time of Desert Storm, the allied arsenal had little capability for detecting biological weapons. This shortfall obviously placed personnel at risk during the war. Although the detection situation has greatly improved in years subsequent to Desert Storm, a critical need remains for a sensor that meets the following requirements:

- *High Sensitivity*. Biological and chemical weapons have extremely low thresholds for inducing fatal or incapacitating effects. It is absolutely crucial that the passive-defensive sensor be able to measure a few infective cells or deadly molecules in a huge background of benign species.
- *Speed*. The effects of chemical agents and biological toxins and the infection process for biological agents are manifested very rapidly following exposure. If troops are given sufficient warning, protective measures can be implemented that can neutralize the effects of an attack with chemical or biological agents before deadly or infectious doses are inhaled. For countermeasures to be most effective, it would be desirable to have sensor response times that are near real time.
- *Specificity*. A vast collection of chemical and biological agents exists in the world, many of which are similar to completely benign substances. In the battlefield it is necessary to unambiguously identify a specific compound or organism to avoid unnecessarily using protective postures that may compromise mission effectiveness.
- *Wide Agent Bandwidth*. Many types of sensors respond only to a specific chemical or biological agent, requiring a large array of devices to maintain readiness against the expected threat. It is highly desirable that a single sensor be developed that can simultaneously detect and identify the full set of threat compounds.
- *High Collection Efficiency*. Clouds of agent dispersed on the battlefield may be extremely diffuse when they reach the detector. A high-efficiency collection device must be effectively coupled to the sampling inlet of the sensor system.
- *Continuous Monitoring Capability*. While certain types of chemical attacks will immediately be evident, a biological attack will probably not be evident until symptoms appear. A continuous monitoring capability is essential for maintaining constant protection.
- *Remote Operation*. A remote detection capability for the sensor system is desirable in order to provide adequate response time. In fact, a high priority of the Joint Commanders-in-Chief in deterring the use of weapons of mass destruction is remote detection of biological weapons.[5] Although stand-off detection capabilities such as light detection and ranging (lidar) show promise, the current thinking of the biodetection community is that the most effective remote capability is provided by point sensors deployed on a highly mobile platform, such as an unmanned air vehicle.
- *Small, Lightweight, Low-Power System*. A necessary condition for long-term portability on a mobile platform is for the detection system to be small and lightweight and to draw small amounts of power.
- *No Fluid Consumables*. Most biosensor systems rely on biochemical reactions that are mediated by aqueous solutions. Such sensor systems require a supply of strike fluids that must be replenished periodically. This is impractical for operationally deployed sensor suites.
- *Long Shelf Life*. For ready deployment in the military setting, the sensor system must exhibit stable operation over long periods of time. Many biological sensors rely on immune reactions that use antibodies that require special handling and that, generally, do not have long shelf lives.
- *Insensitivity to Countermeasures*. Chemical and biological sensors that derive specificity from precise structural and chemical recognition probes are susceptible to agents that have been chemically or biologically reengineered to defeat the probe. Sensors that can measure all of the chemical and biological components of the agent are readily adaptable to the evolving threat and less susceptible to countermeasures.

FIELD-PORTABLE CHEMICAL AND BIOLOGICAL MASS SPECTROMETER

The mass spectrometer is the most powerful analytical tool in the laboratory for analysis of a broad spectrum of chemical and biological materials. The applicability of mass spectrometers to field detection problems has been limited given the (generally) large size, heavy weight, and prohibitive power requirements of the instrumentation. However, this situation is rapidly changing because of the need for highly capable instrumentation in several critical applications. This collaborative effort is focused on bringing small, yet powerful, time-of-flight mass spectrometer technology to bear on the problem of detecting chemical and biological agents.[1] To achieve this goal, not only must small instrumentation be developed and fielded, but validated mass spectral signatures for all of the agents of interest must be obtained. A system block diagram of required components for a chemical and biological sensor based on a mass spectrometer is shown in Fig. 3.

A mass spectrometer functions as follows: A sample derived from the environment is inserted into the vacuum space of the instrument and subjected to ionizing energy. A spectrum (intensity vs. mass-to-charge ratio) is acquired of the ions formed, and this spectrum is interpreted to identify and quantify the chemical or biological substance. The technique generally begins with samples of relatively large molecules that are intelligently cleaved into smaller fragments characteristic of the larger molecules. The spectra of these smaller fragments are then fully analyzed and refined to produce verifiable signatures of the substances of interest. Examples of categories of signature compounds for many different types of threat agents are shown in Table 1. It is evident that the mass spectrometer has the capability to be the universal agent detector for counterproliferation applications once the portability problems are solved.

The approach of our group to the problem of lack of portability has been previously described[1] and is presented in Fig. 4. The goal is to reduce the size of the mass spectrometer from the room-size equipment shown on the right of Fig. 4 to the handheld concept shown on the left of the figure while retaining the necessary analytical power to reliably measure the signature compounds in the field environment. An analysis of the systems that we are developing shows that the characteristics of the sensor match up well to the sensor requirements for several applications (Table 2).

SYSTEMS ENGINEERING CHALLENGES

It is clear from the discussion so far that mass spectrometers have the potential to be universal agent sensors for chemical and biological materials. Previous reports[1,2] have emphasized successful miniaturization of the mass spectrometer, but to fully achieve the instrument's potential, our program is actively addressing the following issues:

- Development of characteristic signatures for chemical and biological agents that are amenable to analysis

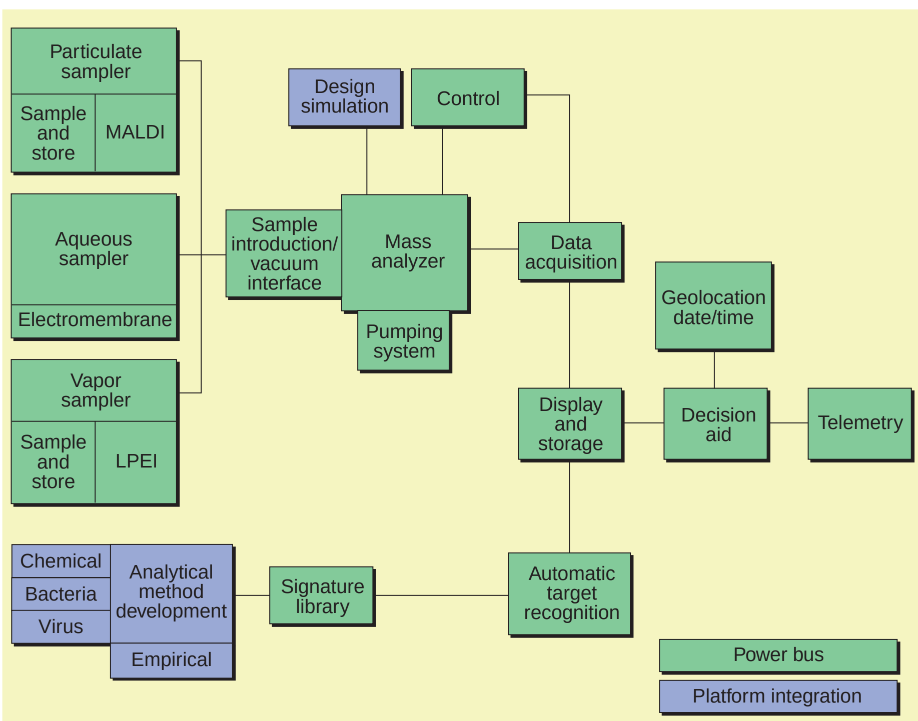

Figure 3. System block diagram indicating critical subsystem developmental items for a field-portable biosensing mass spectrometer. LPEI = low power electron impact, and MALDI = matrix-assisted laser desorption and ionization.

Table 1. Examples of mass spectral signature compounds for different types of threat agents.

Proliferant substance	Agent	Functional group	Phospholipid	Protein	Nucleic acid	Microencapsulant	Spore component	Precursor	By-product	Growth media	Breakdown product	Specific isotope
	Mass spectral signature											
Chemical	✓	✓				✓		✓	✓		✓	
Biological												
Bacteria		✓	✓	✓	✓	✓		✓	✓	✓	✓	
Spore		✓	✓	✓	✓		✓	✓	✓	✓	✓	
Virus		✓		✓	✓			✓	✓	✓	✓	
Toxin	✓	✓		✓		✓		✓	✓	✓	✓	
Nuclear												✓
Explosives	✓	✓						✓	✓		✓	

with field-portable instrumentation. The signatures for chemical agents are relatively straightforward, but for biological agents the situation is much more complicated. Current efforts are focusing on phospholipid, protein, and nucleic acid signature compounds that can be used to unambiguously identify microorganisms.

- Enhancement of signal relative to environmental background using both physical and computational techniques. The physical techniques involve implementation of tandem mass spectrometer configurations. The computational approaches are centered on advanced signal processing concepts using wavelet transforms and genetic algorithms.
- Development of novel sample collection and preparation surfaces that enhance the signal-to-environmental noise ratio. Specially tailored capture surfaces that may provide a mechanism for concentrating the specific compounds of interest are being investigated.
- Development of intelligent processing tools that will enable operators to interpret spectra to investigate the evolving threat. This effort is capturing the methodology that a mass spectroscopist uses for mass spectral interpretation into an automated computational algorithm.
- Coupling of mass spectrometer probes to efficient sample collectors. The prototypical threat cloud

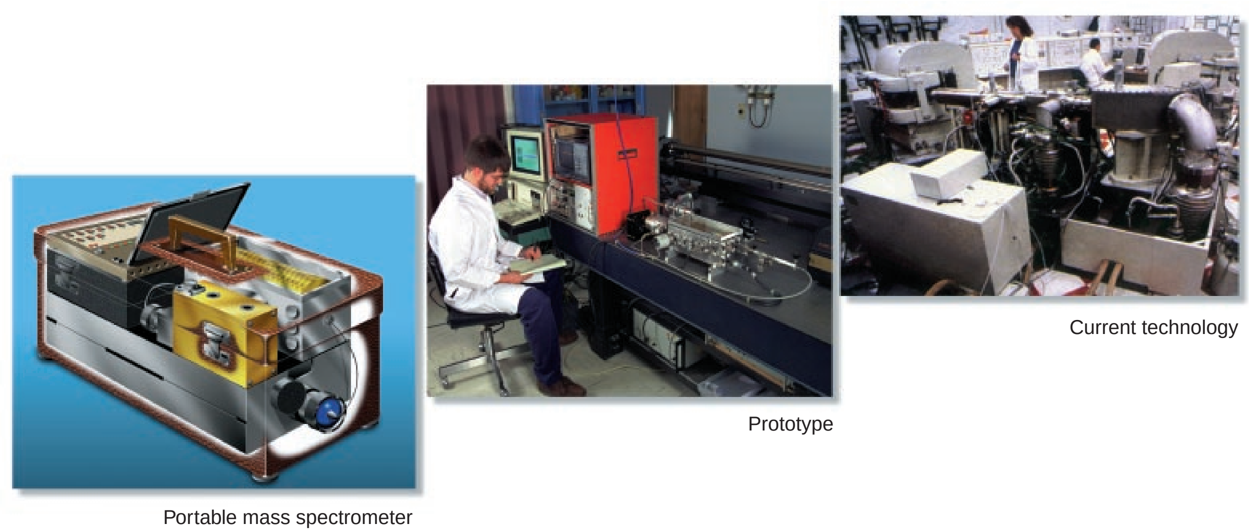

Figure 4. Conceptual diagram showing evolution of a mass spectrometer from the laboratory environment, through the current prototype stage, to the desired highly portable mass spectrometer system.

Table 2. Mass spectrometer characteristics and sensor requirements for several applications.

Characteristic	Application
High sensitivity	All
Speed	BD, TS, CT
Specificity	All
Wide agent bandwidth	All
Continuous monitoring capability	BD, TS, CT
Small, low-power operation	BD, CP, IC, CT
No consumables	BD, IC
Remote operation	BD, CP, IC, CT
Long shelf life	BD
Insensitive to countermeasures	BD, IC, TS
Low self-signature	IC

Note: BD = battlefield defense, CP = counterproliferation monitoring, IC = intelligence collection, TV = treaty verification, TS = target security, and CT = counterterrorism.

of biological agent is quite disperse. To collect sufficient sample for analysis, high-efficiency samplers must concentrate the sample onto a surface that is transferred into the mass spectrometer for analysis.

- Development of small mass spectrometer analyzers that have enhanced analytical capability. Ionization sources and time-of-flight configurations tailored for measurement of specific biomarkers in environmental samples are being developed.
- Engineering of the peripheral components of the mass spectrometer analyzer to high standards of portability. Small, low-power ionization sources, electronic components, and vacuum pumps are being developed.
- A software and display tool for the human interface that can be operated by untrained personnel. Although the mass spectrometer system is extremely powerful, it is not operationally useful until software is used to provide automatic target recognition and quantification.

CONCLUSIONS

A collaborative effort by APL, The Johns Hopkins University School of Medicine, and the University of Maryland, Baltimore County, is focused on the development of a universal agent sensor for counterproliferation applications. A small, rugged, field-portable detection system using an advanced time-of-flight mass spectrometer is being developed. This system will depend on accurate and reliable mass spectral signatures of proliferant substances for the detection methodology. A focused effort is being made to ensure that the overall system is small, low power, lightweight, and rugged and that it has an advanced user interface that enhances ease of operation.

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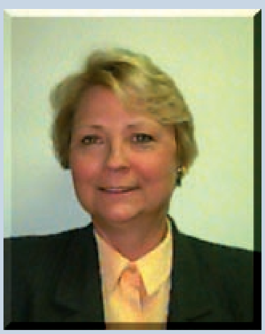

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