Detection of Chemical Agents in Water by Membrane-Introduction Mass Spectrometry

John S. Morgan, Wayne A. Bryden, Rebecca F. Vertes, and Scott Bauer

Membrane-Introduction Mass Spectrometry (MIMS) has evolved into a powerful technique for the selective detection of volatile organic compounds in aqueous matrices. Contaminants in water samples have been analyzed at the parts-per-trillion level using hydrophobic silicone membranes. Recent advances in new membrane materials will permit the examination of polar analytes such as chemical agents. In combination with a small time-of-flight mass spectrometer, it will be possible to construct a portable detector for treaty verification, counterproliferation, and infrastructure protection. Other developments include deconvolution algorithms for complex analyte mixtures, improved understanding of analyte–water reactions, and thermal desorption of analytes from the membrane into the vacuum. (Keywords: Chemical, Mass spectrometry, Membrane, Weapons.)

INTRODUCTION

It is critically important to rapidly detect and identify chemicals during Chemical Weapons Convention (CWC) inspections. Miniaturized instrumentation with this capability can also be used to protect personnel. Small, transportable, analytical instrumentation can assist in selecting which sites are of interest for further analysis using the more definitive, but slower, analytical techniques required for establishing compliance with the CWC.

Membrane-Introduction Mass Spectrometry (MIMS) is an emerging development in chemical analysis designed for speed, selectivity, sensitivity, and real-time monitoring capabilities.[1] The technique provides an analyte separation method that can be performed in real time with minimal sample preparation.[2] With MIMS, a liquid sample containing dissolved analyte(s) is drawn past a membrane material.[3] The membrane selectively allows the diffusion of the analyte preferentially over the liquid matrix or other possible interfering compounds.[4] This selectivity enhances the sensitivity of the detection instrument because of the inherent separation of the analyte from any background. The MIMS sample introduction device is coupled to a mass spectrometer for analyte detection and determination.

Mass spectrometry is recognized as the most definitive technique for the identification and quantification of chemical compounds in the laboratory. Until recently, the size, weight, and power demands of mass

spectrometers, combined with extensive sample preparation requirements, made field measurements of trace levels of materials difficult. APL is developing a small, field-portable, time-of-flight mass spectrometer (Tiny TOF) with enhanced instrument portability, flexible design, and broad detection capabilities.[5] By integrating the simplicity and separation capability of the MIMS sample introduction technique with the portability and detection range of the Tiny TOF mass spectrometer, a powerful new technique will be available for on-site use. The technique offers reduced sample preparation requirements, excellent sensitivity, and compatibility with current gas chromatography/mass spectrometry databases needed for compound identification.

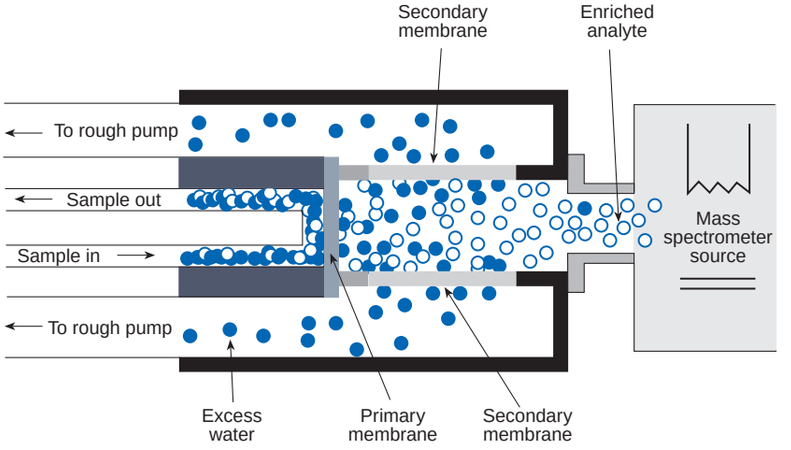

Figure 1. Direct-injection MIMS inlet with two-step analyte enrichment (closed circles = water molecules, open circles = analyte molecules). Shown are the required proximity to the mass spectrometer source, the enrichment due to the membrane's selectivity over water, and a second enrichment, sometimes used, which draws excess water from the analyte flow.

MIMS: TECHNICAL BACKGROUND

MIMS has evolved as a successful analytical technique owing to its simplicity and sensitivity. In direct-injection MIMS (Fig. 1), water samples are injected into a silicone capillary membrane located near a mass spectrometer source. An external heater elevates the temperature of the water sample, which in turn heats the membrane. Typical membrane temperatures are between 50 and 80°C. At higher temperatures, more of the sample is passed through the membrane and into the mass spectrometer source. However, more water diffuses through the membrane at high temperatures, which can increase the background pressure in the mass spectrometer and thereby deteriorate performance and sensitivity.

Analyte crosses the membrane by a three-step process called pervaporation[4] (Fig. 2), in which it

1. Adsorbs onto the surface of the membrane
2. Diffuses through the bulk of the membrane
3. Evaporates from the vacuum-side surface of the membrane into the mass spectrometer source

The most often used membrane material is silicone, which tends to exclude polar molecules because of its hydrophobic nature, i.e., polar molecules are not soluble in silicone and therefore do not readily adsorb onto the membrane surface. Also, higher molecular weight species tend to stick to the surface of the membrane and do not evaporate as readily into the vacuum. Nonpolar compounds with molecular weights under 200 amu, however, will pervaporate with high efficiency. Thus, the silicone rubber membrane provides a useful selectivity that can greatly enhance the detection of compounds that cross the membrane. For volatile organic compounds, for example, detection limits in the sub–part per billion range can be expected, as seen in

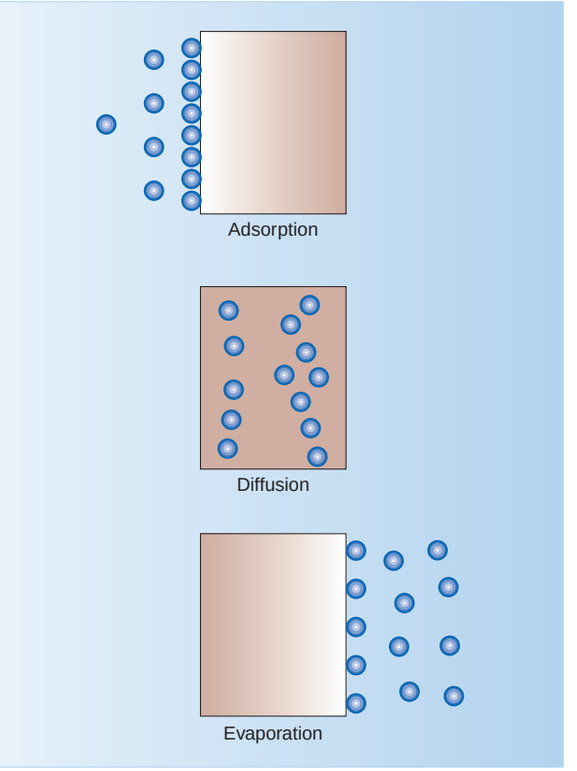

Figure 2. The pervaporation process.

Table 1. Of course, the sensitivity of the mass spectrometer also affects the detection limit. The data in Table 1 were obtained using an HP5973 quadrupole mass spectrometer. Ion trap mass spectrometers, which can collect analyte over a period of time before spectral analysis, can significantly extend the detection limit.

The mass spectrometer acquires a continuous set of spectra during a MIMS measurement interval. For example, it will scan every mass from 40 to 300 amu every few seconds. Over time, an ion current chromatogram is obtained for each mass, which can then be extracted at the end of the experiment. A typical data set is seen in Fig. 3. Since each compound has a unique mass spectrum, one can readily extract identification information from the ion chromatograms by examining the spectra integrated under each peak. Mixtures, as detailed in the following discussion, present a more difficult problem.

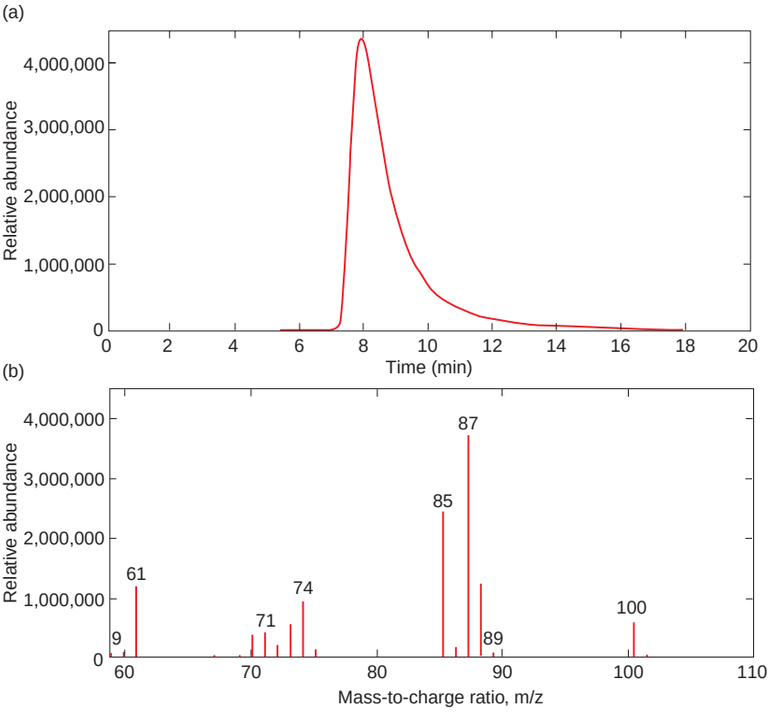

Figure 3. Typical MIMS data showing (a) the total ion chromatogram, which indicates that the analyte was passing through the membrane and into the mass spectrometer source during a 6-min interval, and (b) the mass spectrum of the analyte integrated over the interval from 7.7 to 8.5 min. The spectrum matches 2-butoxyethyl acetate, a common solvent.

CHEMICAL WEAPONS DETECTION FOR TREATY VERIFICATION

A current effort at APL and MIMS Technology, Inc., of Palm Bay, Florida, focuses on the application of MIMS for the detection of chemical weapons. Chemical weapons tend to be polar molecules with weights of 100 to 200 amu. We used simulant molecules (e.g., chemically related compounds, breakdown products, precursors of chemical agents) for testing purposes, as listed in Table 2. These analytes were chosen for their chemical similarity to common chemical warfare agents, in particular the nerve agents.

Table 1. MIMS detection limits for volatile organic compounds.

Analyte	Molecular weight	Detection limit (ppb)
Benzene	78	0.9
Diethyl ether	74	5.0
Nitrobenzene	123	1.0
o-Xylene	106	0.1
Hexachlorobutadiene	258	0.5
Chlorobenzene	112	0.1

Nerve agents, which were first developed in Germany in the 1930s and 1940s, work by attacking the human nervous system. They are all organophosphorus compounds and are closely related to insecticides, where the P(=O) is replaced by P(=S), and less reactive functional groups than fluoride or cyanide are used. These agents inhibit the ability of the enzyme cholinesterase to prevent the buildup of excess acetylcholine, which transmits nerve impulses.

The agents of German origin are identified by codes beginning with the letter "G." The three main G agents are tabun, sarin, and soman, although GF is also of note. Nerve agents of later origin include those designated "V," which tend to be more chemically stable and are roughly 10 times more toxic. The most important of these is VX. Nerve agents are further divided into volatile and persistent chemical weapon agents, depending on their tendency to evaporate. Sarin is the most volatile (17,000 mg/m^3 at 25°C) and VX the most persistent (10 mg/m^3 at 25°C) of the major nerve agents. In general, exposure to G agents is by inhalation of their volatile vapors, and exposure to V agents is

Table 2. Chemical weapon simulant compounds used in MIMS testing.

Compound	Associated chemical weapon agent(s)	Boiling point (°C)	Molecular weight (amu)
Ethyl methylphosphonate (EMPA)	G agents	109[a]	124
Pinacolyl methylphosphonate (PMPA)	G agents	96–106	180
Thiodiglycol (TDG)	VX	164–166	122
2-Chloroethylethyl sulfide (CES)	Sulfur mustard	156–157	124
Dimethyl methylphosphonate (DMMP)	G agents	181	124
Triethanolamine	Precursor, Schedule 3B (17)	190–193	149
Methylphosphonic acid (MPA)	Sarin, soman, VX	107[b]	96
Bis(2-chloroethyl)amine hydrochloride	Nitrogen mustard	212[b]	178

[a]Flash point.
[b]Melting point.

through skin contact. Thus, G agent–like chemicals are more easily detected by a MIMS-based technique, whereas V agents are less so, owing to their lower volatility.

Both MIMS Technology and APL conducted flow-injection MIMS studies using standard, 0.28-mm-thick silicone capillary membranes. At high concentrations and membrane temperatures, some of these chemical agents can be detected in aqueous solutions. For example, Fig. 4 presents a MIMS profile and mass spectrum of DMMP in a 200-ppm solution with a membrane temperature of 95°C; diagnostic ions for this compound at mass-to-charge (m/z) ratios of 79, 94, 109, and 124 are shown. These fragments correspond to the molecular ion at an m/z of 124 and successive methyl-group or formaldehyde-group losses. At lower membrane temperatures, the compound is not observed, presumably because of a low diffusion rate through the silicone membrane and the low rate of evaporation of DMMP into the vacuum system of the mass spectrometer.

Silicone membranes do not readily adsorb polar compounds such as the organophosphorus agents, so it is desirable to substitute other membrane materials for optimal performance. The silicone capillary membrane can be replaced with a flat membrane geometry, which enables the examination of a wide range of alternative materials as well as thinner silicone membranes. Johnson et al.[6] introduced liquid membrane techniques in which low vapor pressure liquids are held in place on a supporting frit by surface tension. Both alternative polymer and liquid membranes were used in this study, each having hydrophilic and hydrophobic characteristics. Among the alternatives used were

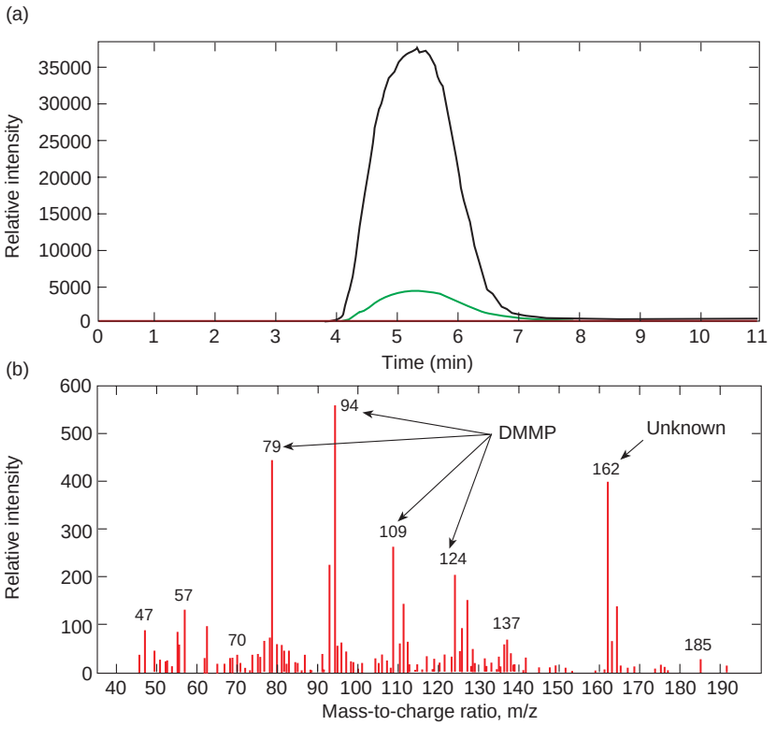

Figure 4. MIMS profile of DMMP showing (a) an ion chromatogram of the three main diagnostic ions (m/z = 94, black; m/z = 79, green; m/z = 109, red) and (b) an extracted mass spectrum that matches library data from the National Institute of Standards and Technology.

- GFT Pervap 1170: A composite membrane consisting of a silicone rubber coating on a microporous cellulose substrate
- GFT Pervap 1060: Same as 1170, except that silicone coating is half the thickness
- GFT Pervap 1000: A composite membrane consisting of a proprietary, hydrophobic coating on a microporous substrate
- Versapor 200H: A microporous membrane with hydrophobic coating
- SSP-M213: A silicone polymer treated with proprietary, hydrophilic chemicals
- SSP-M100: A proprietary, hydrophilic membrane similar to Saran wrap in appearance
- Silastic sheet (Dow Corning): A sheet version of silicone rubber tubing used in standard flow-injection MIMI instruments and serving as a benchmark

Table 3. Detection of eight chemical weapon simulants using alternative membrane materials.

Compound	Alternatives			
	GFT 1170	GFT 1060	SSP-M213	Silastic
EMPA	N	N	N	N
PMPA	Y	Y	Y	Y
TDG	N	N	N	N
CES	Y	Y	Y	Y
DMMP	Y	Y	N	N
Triethanolamine	N	N	N	N
MPA	N	N	N	N
Bis(2-chloroethyl)amine hydrochloride	Y	Y	Y	Y

In initial trials, the more hydrophilic membranes *did* allow more analyte through to the mass spectrometer source, but the higher flux of water masked the signal and eliminated any signal improvements. For example, Fig. 5 shows a typical ion current chromatogram of CES in water (20-ppm solution, 70°C membrane temperature) through a GFT Pervap 1060 membrane. Several of the compounds were detected using the Silastic membrane, GFT 1170, GFT 1060, and SSP-M100 as detailed in Table 3, although it is clear that a broader response is required. The other membrane materials showed poor response. Initial studies with liquid membranes have also been completed, but further analysis to determine the optimum membrane chemistry is needed. In these experiments, liquids such as high vacuum pump oil were supported on porous polymers, which presented a tortuous path to the analyte, thus preventing efficient transport through the membrane. Alternative supports employing small, straight pores are currently being tested.

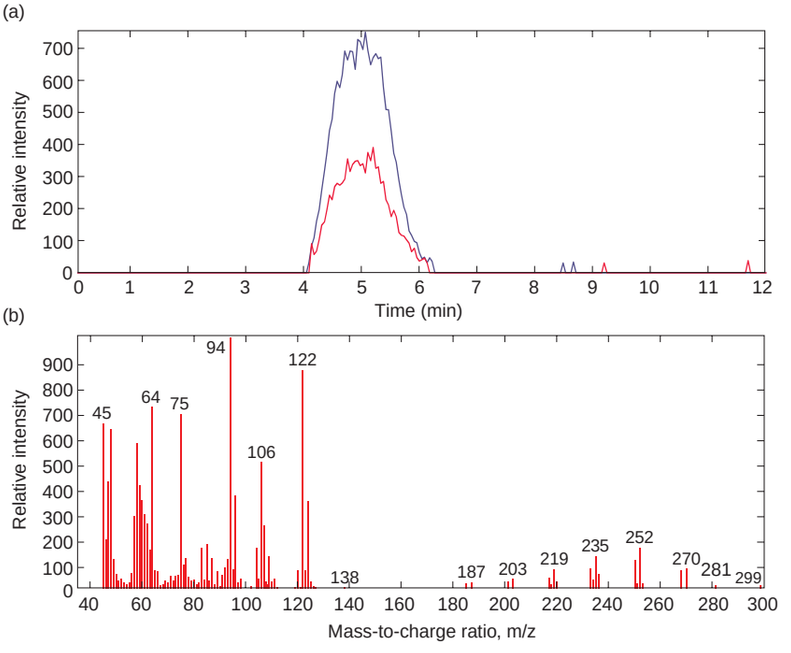

Figure 5. Ion current chromatogram of m/z = 75 (blue curve) and 124 (red curve) from CES (20 ppm) in water using a GFT Pervap 1060 membrane (a) and a MIMS mass spectrum (b).

After studies using a quadrupole mass spectrometer have determined the optimal membrane system to use for detection of chemical agents, the membrane inlet will be integrated with the APL-developed electron-impact Tiny TOF mass spectrometer. The system, as shown in Fig. 6, will be based on the Wiley-McLaren two-stage design first introduced in 1954. Here, molecules in the source are ionized by low-energy electrons (typically 70 eV).

In other Tiny TOF designs developed at APL, ionization occurs by a process known as matrix-assisted laser desorption/ionization

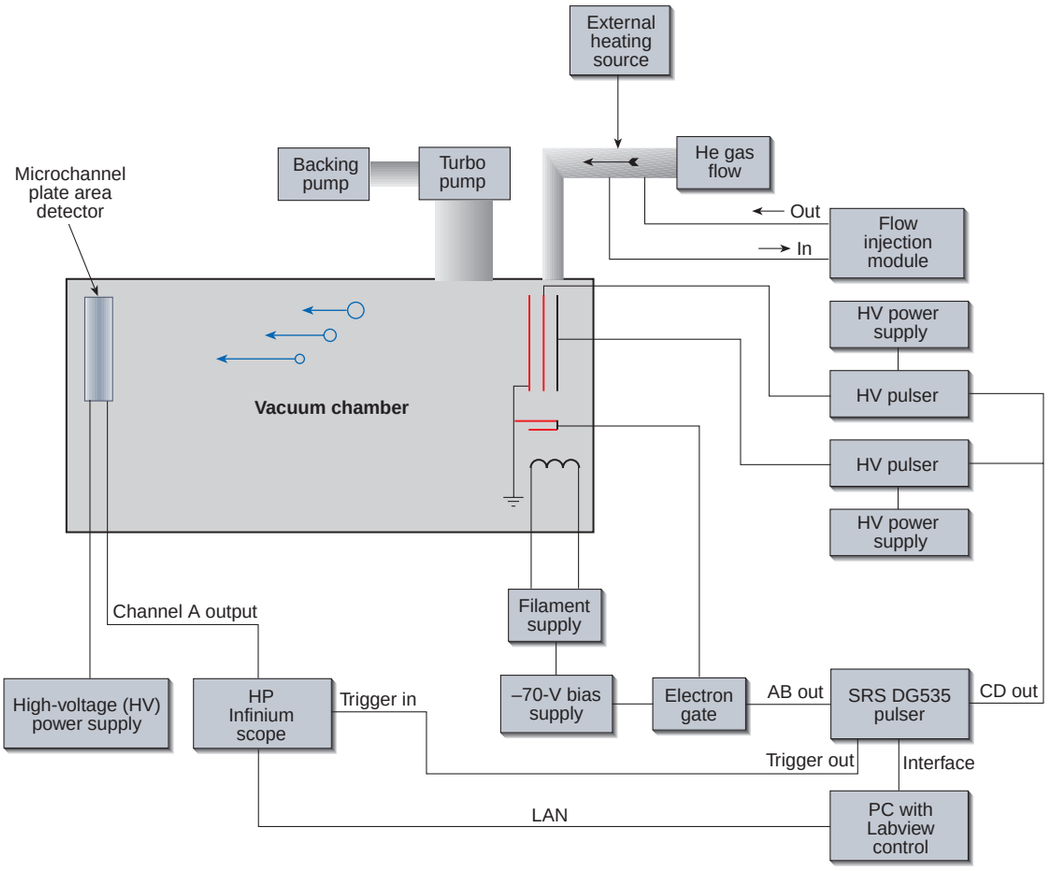

Figure 6. Block diagram of an electron-impact Tiny TOF mass spectrometer with membrane inlet sampling (LAN = local area network).

(MALDI). With this technique, a laser pulse desorbs material from a solid surface that has been co-crystallized with a matrix chemical that ionizes at the wavelength of the laser pulse. The sample is ionized by charge exchange with the matrix. Because the laser pulse occurs at a precise interval, MALDI is well suited to TOF mass spectrometry.

With an electron-impact source, the task is more difficult, since an electron pulse will extend in both space and time. Thus, molecules are ionized at different times and at different locations within the source region. This issue is addressed in two ways. First, the electron pulse is limited in space by magnetic focusing and gating in time. Thus, a small bunch of electrons will be introduced into the source in a time interval as small as 30 ns. Second, the two-stage Wiley-McLaren source corrects for spatial spreads in ions. In the first (extraction) stage, a small electric field is applied, so that ions originating in different locations in the source are not accelerated to widely different energies. In the second (acceleration) stage, a much stronger electric field accelerates the ions into the mass spectrometer flight tube. With modern electronics providing fast rise times for the voltage pulses that drive the source electric fields, the flight tube can be reduced to 13 cm, thus permitting the construction of a highly mobile, versatile MIMS system.

FUTURE OF MEMBRANE-INTRODUCTION TECHNOLOGY

The examination of alternative membrane materials potentially will allow for the detection of other compounds of interest, including those from biological specimens. Several parallel developments must be pursued to achieve the performance required to extend the capability of MIMS.

First, thermal desorption of analytes from the vacuum side of membranes should permit much greater sensitivity for detection of high molecular weight, high boiling point compounds. Many of these compounds diffuse through silicone membranes, but do not volatilize *in vacuo* owing to their low vapor pressure at typical membrane temperatures. Several methods of

thermal desorption can be applied, including the use of a continuous infrared source or laser desorption.[7]

Also, complex mixtures are difficult to completely analyze using MIMS. In gas chromatography/mass spectrometry, mixtures are separated by the gas chromatograph before introduction into the mass spectrometer. In comparison, analytes within mixtures will pervaporate through a membrane with very minimal separation in time, producing overlapping ion current peaks. To some extent, mixtures can be analyzed by comparing the mass spectra of expected components, but this does not solve the general problem. However, each analyte should diffuse through a membrane at a slightly different rate, so that the ion current chromatogram for each component in a mixture will reach a maximum at slightly different times. This does not provide the quality of separation found in gas chromatography, since the ion current profiles for different components will usually overlap significantly. Differing diffusion rates permit extraction of the components, but only by careful examination of the time at which each ion chromatogram in a data set reaches its maximum. By collecting the ion chromatograms that peak at the same time, it is possible to reconstruct the original mass spectrum of a particular chemical in a mixture. Using this and other techniques, we are developing algorithms to separate complex mixtures in MIMS data sets.

Another priority in this area is the detection of a wide range of polar chemical agents using novel membrane materials and inlet systems (e.g., trap-and-release MIMS, liquid membranes, jet separator inlets). Silicone membranes are inherently more sensitive to nonpolar analytes, which adsorb onto the surface of silicone more readily than polar chemicals. Therefore, past work in MIMS almost exclusively has involved the analysis of volatile organic compounds in various matrices, usually water. Now, semivolatile analytes, including biological compounds, can be examined with much greater sensitivity than previously possible.[8] For example, liquid membranes can be tailored to specific applications by varying the membrane chemistry. Any viscous, liquid solution can be used as a liquid membrane. Thus a solution designed to preferentially dissolve organophosphorus compounds could be used to efficiently detect the nerve agents. Since liquid membranes will allow rapid diffusion of higher molecular weight compounds, applications in biomedicine and process monitoring are also gaining interest.[9]

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