A Time-of-Flight Mini-Mass Spectrometer: Aerosol Collection, Capture, and Load-Lock System

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Time-of-flight (TOF) mass spectrometry has many applications for the precise analysis and identification of biological and chemical agents. The large size and weight of conventional mass spectrometers limit their portability, delaying sample processing. Miniaturization of TOF detectors should significantly reduce the delay between sample collection and final identification by making available self-contained portable devices. APL has designed and begun integration of a miniaturized TOF spectrometer for completing rapid *in situ* measurements. This article describes the major components of the system, including an automatic aerosol collector, a sample processor, and a mass spectrometer vacuum chamber load lock. A sample collection tape ties the components together by capturing samples from the collector, transporting the samples through a chemical processing stage, and introducing the samples into the mass spectrometer detector. The tape replaces collection filters, processing slides, and insertion probes normally used to introduce samples into a spectrometer vacuum chamber. (Keywords: Aerosol collector, Mass spectrometer, Particle separator, Vacuum load lock.)

INTRODUCTION

The objective of the Time-of-Flight Mini-Mass Spectrometer System (TOF-MMS) Project is to develop a mass spectrometer–based analysis system for the rapid, unambiguous, *in situ* identification of a wide range of microbial organisms and toxic substances. The precise identification and quantification of microbial organisms has particular application for infectious agents. The major subsystems of the TOF-MMS are the sample collection stage, a compact TOF spectrometer, and a data collection/analysis computer (Fig. 1). The sample collection stage comprises an air pump and particle collector, capture tape and transport device, and components to prepare the collected samples for TOF analysis.

This design has the unique characteristics of combining sample collection, preparation, measurement, and analysis in one automated system. The conventional approach separates these functions, requiring an operator to manually perform each processing step. It may help to explain the mechanics of the typical

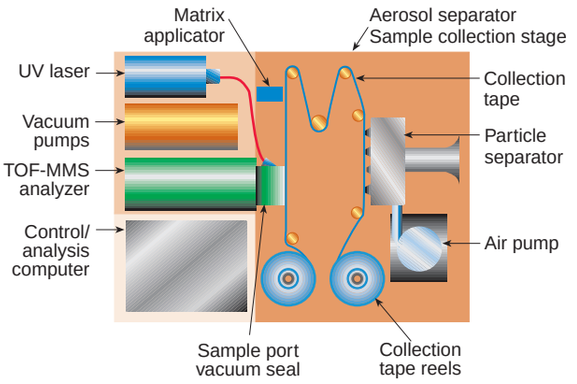

Figure 1. Time-of-Flight Mass Spectrometer collection and analysis system.

laboratory TOF measurement process so the reader may better grasp the constraints and the design of this aerosol collection system. Background information on the mechanics of operating a mass spectrometer and a brief description of traditional aerosol collection systems are included in the next section for readers unfamiliar with these processes.

BACKGROUND

Traditional TOF Mass Spectrometer Processing

The TOF-MMS uses a coaxial TOF mass spectrometer analyzer[1] and a chemical matrix-assisted laser desorption/ionization (MALDI)[2] treatment technique. In typical laboratory applications, one initiates the identification process by capturing aerosols onto a medium such as filter paper using a collector that functions like a common vacuum cleaner. The particles collected are washed, separated, and mixed with a chemical used in the desorption matrix, and a pipette is used to place a small drop of the sample on the tip of a test probe. When the solution dries, the technician slides the probe through a series of seals and a valve mechanism into an ionization/desorption cell of the mass spectrometer's vacuum chamber. A pulsed laser beam then irradiates the sample, which induces ionization and desorption of the molecules.

Before ionization, a voltage potential is formed between a backing plate on the probe tip and a fine screen, called an extraction grid, separated from the tip by a few millimeters. The voltage potential accelerates the desorbed molecules through the grid toward a detector. Low-mass molecules will have greater acceleration than high-mass molecules.[3] Measurement of the TOF of the ionized molecules correlates with the molecular mass of the sample constituents. Repeated laser pulses on a single sample spot will create an ensemble of strong, weak, and noisy mass spectra. Analysis of the ensemble mass spectra provides a classification of the aerosol constituents. Further signal processing techniques produce enhanced identification through noise cancellation and pattern matching.

The number of laser pulses required to produce the ensemble spectra depends on the concentration of agent-containing particles (ACPs) in the sample area, the sample area irradiated by the laser, laser fluence (energy/unit area),[4] the matrix effectiveness, etc. These factors have important implications in the design of an automated aerosol collector and mass spectrometer instrument.

Aerosol Collection Techniques

Airborne particulates come in many shapes and masses, and the temporal and spatial size distributions of most aerosols found in the atmosphere are influenced by natural and man-made activities. The EPA has initiated regulatory actions for particulate matter bracketing a 2.5-mm diameter ($PM_{2.5}$) since these particles can easily enter the lungs and serve as an indicator of potential adverse health effects.[5] Identifying the constituents in atmospheric particulate, i.e., aerosols, requires tools for collection and methods to define aerosol properties to design those tools. For this purpose, the field of aerosol science uses many of the dimensional and nondimensional constants in fluid dynamics, beginning with a basic definition of a particle's equivalent diameter to describe particle size. Factors that define an equivalent diameter may account for particle shape, mass density, median mass density, etc. The most common definition of equivalent diameter is the aerodynamic diameter of a given particle, i.e., the diameter of a spherical particle of unit-density (e.g., 1 g/cm^3) that settles in still air at the same velocity. Any interpretation of aerosol data requires a clear definition of the particular equivalent diameter used; for example, the subscript for $PM_{2.5}$ refers to aerodynamic diameter.

Aerosols vary in size from thousandths to hundreds of micrometers. Those of particular concern to health include viral and bacterial agents that agglomerate into particles that easily enter and lodge in the respiratory system. For the TOF-MMS application, microbial agents of interest tend to agglomerate as aerosols with an aerodynamic diameter of 0.5 to 10 μm and are of interest in average concentrations of approximately 15 ACPs per liter of air.[6] Typically, aerosols over 10 to 20 μm fall out of the air rapidly and do not carry far from their origin, whereas the particles of interest will stay airborne for long periods. Natural background in the 2.5-μm range typically consists of low molecular weight molecules,[5] making it easier for a TOF mass spectrometer to differentiate from the high molecular weight microbial agents of the same aerosol size range.

Common techniques used for aerosol collection involve the use of filtration,[7] settling, and particle inertia. Filters have such wide use that we will dispense with a detailed description of their design. Suffice it to say that as the air flows through a porous medium the particulate impacts the filter material and sticks. Probably the least sophisticated collection technique simply uses gravitational forces to gradually settle aerosol particles onto a collection surface, analogous to dust collecting on a dining room table. Filtering and settling techniques collect particulate in relatively low-density concentrations for a given time and capture area, and gather particles of nearly all sizes. Analysis of the particles requires additional steps to wash, size-segregate, and concentrate the particulate from the collection surfaces. The increased time and effort interfere with rapid classification and identification.

One can better separate and collect aerosols in a highly concentrated form by using controlled inertial methods, which operate by moving the particle-containing airflow through curved pathways. Particles with low enough mass tend to follow the air streamlines, regardless of the curvature, while larger mass particles tend to cross streamlines having small radii of curvature to streamlines of greater curvature. Adjusting the flow velocity and path geometry determines which particles will follow the streamlines and which will cross them. The reader may notice this effect while driving an automobile.[8] You may see that most airborne material directly in your path—whether snow, rain, or insects—tends to hit the windshield. If you look closely (preferably not as the driver), you should see that many small objects flow over and around the windshield. By changing vehicle speed, you have some control over the size of particle that hits the windshield.

Although the inertial separation technique provides a means to collect particles of specific sizes, it has stochastic properties that require statistical characterization. A typical particle separator will divide the airflow into two paths, each containing large and small particles characterized by an equivalent diameter cut-point. The cut-point defines the size at which 50% of the particles above and below that size follow each path. Some separator designs will produce sharp divisions between the particles that follow each of the paths. Aerosol collectors with high collection efficiency will then capture nearly all the particles in one or both of the paths.

Inertial devices come in a variety of geometries, flow rates, and cut-points. Maddox[9] reported on an apparatus he designed to reduce the time from collection to examination. It used convection air currents and particle inertia to concentrate and capture aerosols onto small areas that could easily be viewed under a microscope. Inertial collectors today have characteristics similar to the design by Maddox, such as a simple low-volume fixed body impactor.[8] This impactor consists of a fixed plate positioned in a forced airflow, which captures particles too large to flow around the plate.

Cyclone separators probably best exemplify high-volume inertial separators used in industry. Air flowing through the cyclone tubes forms a vortex in the tube that induces high centrifugal forces on the particles. The rotational forces segregate the larger particles to the outside of the tube. Variations in the tube diameter, length, taper angle, and flow velocity determine particle separation size. One may then capture particles with a cyclone by letting the particles slide down the tube walls into a filter bag or by washing the walls with a liquid and capturing the concentrate in a basin. Home and industrial dust collectors[10] often use cyclones to remove sawdust and other particulates from the air.

One of the most common separation techniques for scientific study is the conventional impactor,[11] which works by directing the particle-containing air through a nozzle onto a collection plate (Fig. 2a). Adjusting the nozzle, plate geometry, and flow parameters of the impactor determines the cut-point for the size that hits the plate and gets captured. A variation of the conventional impactor is the virtual impactor (Fig. 2b),[8] which operates by directing the airstream from the nozzle to an opening with a restricted flow. Larger particles enter the opening, which forms a virtual surface, and become entrained in a minor flow of reduced velocity, while smaller particles follow the major flow. The virtual impactor has the benefit of concentrating particle quantity from low density in the high-volume flow to high density in the low-volume flow. The minor flow may capture 80 or 90% of the particles above the cut-point and have a volume flow rate around one-tenth the total flow.

Conventional and virtual impactors use a variety of nozzle shapes and arrangements. The most common ones consist of round nozzles arranged in large two-dimensional arrays that easily allow concentrations from virtual impactors into cylindrical plenums. The minor flow then goes through conventional impactors onto filter paper. An alternative design uses a long slit,[12] which simplifies fabrication and reduces the space requirements for a given airflow. Individual nozzle and plate separation geometries have dimensions in the 1-mm range and may run velocities well over 100 m/s.

The properties of the capture plate material affect particle adhesion to the capture surfaces. The base material may be glass, metal, plastic, or paper. To create a sticky surface, the material can be coated with glycerin, oils, greases, or adhesives. Alternatively, the surface may be wetted, or fluid traps containing pure water or other low-viscosity fluid may be used. Fluid trap designs allow recycling of the fluid to produce high sample concentrations, although they have constraints on their orientation and require dedicated fluid reservoirs, pumps, filters, etc.

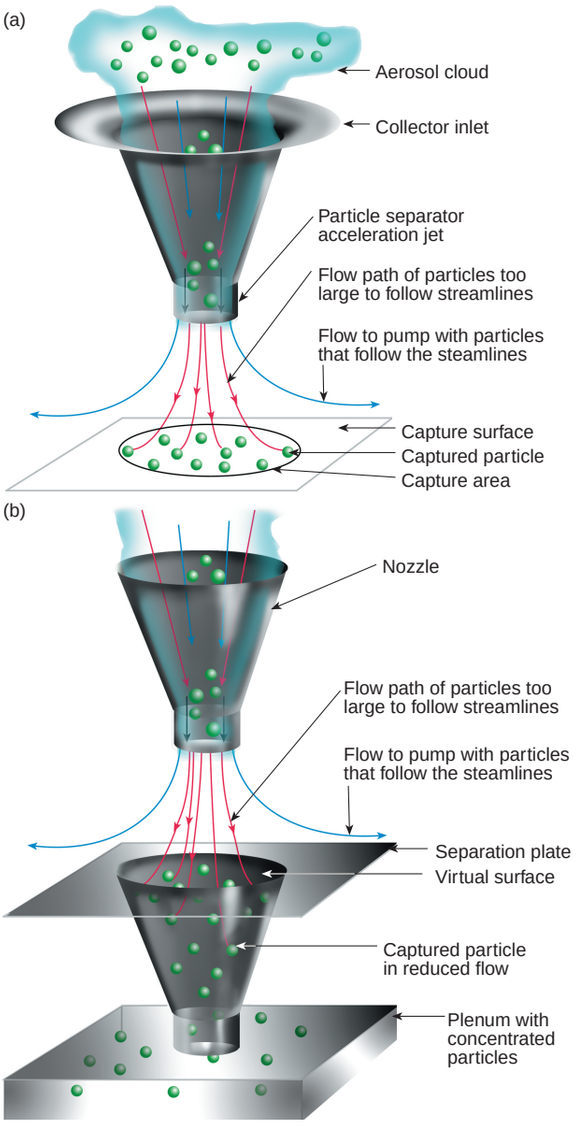

Figure 2. Impactors: (a) conventional, and (b) virtual.

Configurations using a series of cyclones (e.g., In-Tox Cascade Cyclone[13]) or impactors and virtual impactors (e.g., Grasby-Andersen Marple Cascade Impactor[14]) can route the particles in the major and minor airflow through a cascade of separators.[15] Each stage resolves the aerosol into fine divisions, selectively separating particles into bins of 1- or 2-μm widths.

TOF-MMS AEROSOL COLLECTION DESIGN APPROACH

In general, the objective of the aerosol sampling system for the TOF-MMS is to create a design that accomplishes the following activities:

- Collect, concentrate, and separate aerosols from breathable ambient air at concentrations of 15 ACPs per liter of air and of 0.5- to 10.0-μm aerodynamic diameter
- Capture infectious and toxic agents on a substrate in small spots that allow maximum coverage by an irradiating laser beam no larger than 1.0 mm in diameter
- Prepare the sample for the MALDI process by adding a matrix
- Introduce prepared samples directly into the TOF-MMS
- Archive samples for postanalysis confirmation by storing processed samples and saving an unprocessed sample from each collection period

Since these activities must be performed using a portable instrument, the process should also

- Minimize the time needed for collection and agent identification, not to exceed 5 min
- Automatically perform all functions with no operator interaction
- Have portability and reliability to survive transportation on a range of vehicles, to allow handling by two persons, and to operate from a portable power source

The design of a typical aerosol collection system primarily depends on the total airflow and the aerosol particle collection and rejection cut-point. Several factors in this spectrometry process impose additional constraints on an automated aerosol collection design, the most obvious being the requirement to automate the mechanics of the actions performed by a laboratory technician during sample preparation. In a manual process, this complicated operation involves sample collection and preparation, placement of the sample on the probe tip, and insertion of the probe into the vacuum chamber. An automated system should perform these functions with mechanical components having minimal complexity (e.g., eliminate the need to place a sample on a probe that must slide into the chamber through seals and a valve). More subtle constraints on this system derive from the chemical matrix effectiveness and the interaction between the laser beam and the sample within the ionization/desorption cell, since only sample material irradiated by the laser beam will ionize and desorb to produce a mass spectrum.

Ideally, the aerosol collection system will separate ACPs from the air and capture them on a spot that can be covered completely by the irradiating laser beam (Fig. 3). For a given fluence, the signal can significantly be improved by maximizing the irradiated area.[16] In conventional aerosol collection, the size of the captured sample spot rarely matters since the agents are removed from the collection medium for further processing and analysis. In this application, the practical

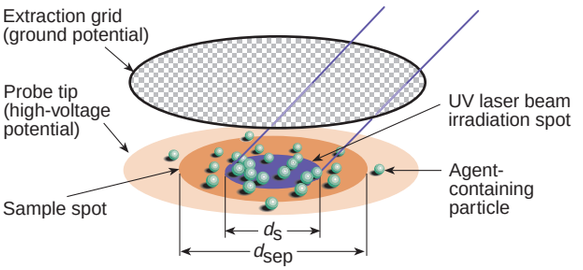

Figure 3. Ionization/desorption cell geometry (d_s = diameter of laser beam field of view, d_{sep} = diameter of particle separator capture area).

beam diameter has a maximum limit of 1 mm, based on the physical constraints of the laser optics, ionization/desorption cell geometry, vacuum sealing techniques, etc. Suitable UV lasers produce a 120- to 300-μJ/pulse,[17] which will exceed minimal fluence[4,18] of 1 to 5 mJ/cm^2 and can exceed fluence of 20 to 40 mJ/cm^2 similar to that used in commercial MALDI spectrometers (private communication, A. Bowdler, Kratos Analytical Ltd., Manchester, England, 1998). Imposing this 1-mm-diameter limit on the sample capture spot drives the collector impactor design.

Fortunately, MALDI-TOF mass spectrometry has a significant advantage: Damage that reduces the survivability of captured microbial material does not necessarily impair—and may even enhance—the mass spectrometer measurements. This contrasts with analysis methods that depend on agent viability for colony formation in a growth medium. Unfortunately, the MALDI process has evolved over the years from many empirical tests.[16] One cannot use calculation to determine either the number of ACPs required for identification or the number of laser pulses needed to create an adequate ensemble data set. Under extremely low background noise conditions the MALDI-TOF-MMS can resolve the molecular mass spectrum at agent quantities of femtomoles (10^{-15}).[19] Under field conditions, however, contamination from many sources may obscure the signal with background noise.

An increase in the number of ACPs available for ionization within the laser beam area will improve the strength of the ACP signal by accentuating it over the noise. Fragments of the ACPs created by mechanical stresses during the separation and collection process as well as the capture of these fragments can contribute to an improved signal-to-noise ratio. This allows for a wider range of sample collection methods, regardless of whether the methods impose high stresses on the aerosol.

Bryden et al.[1] proposed a concept for an automated TOF-MMS that combines sample preparation, introduction into the mass spectrometer, detection, analysis, and archiving into a single unit (Fig. 4). The setup includes a reel-to-reel tape collection medium to

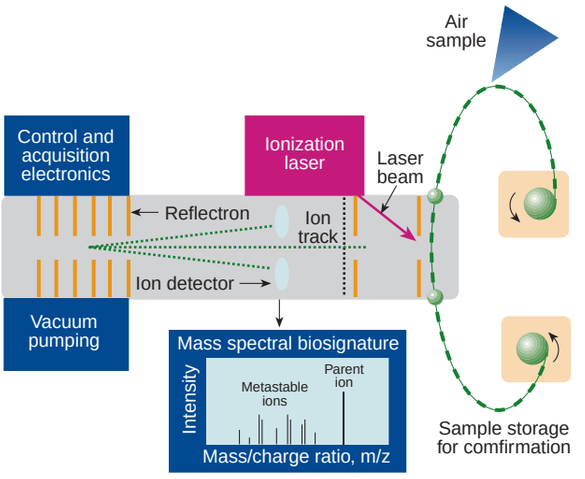

Figure 4. TOF-MMS concept.

capture and store the samples, a microchemical dispenser to prepare the samples, and a vacuum load lock to introduce the samples into the vacuum chamber. Others have developed systems for highly specific toxic gas detection using similar concepts that include continuous tape drives[20,21]; however, these systems do not have the sophistication for use with a broad-spectrum TOF mass spectrometer.

A continuous collection tape has many desirable attributes when coupled to a sample collection stage made of a bank of virtual impactor particle concentrators and a series of conventional impactor separator nozzles. One can vary the amount of sample collected by adjusting the collection time and periodically advancing the tape. Multiple impactor nozzles can easily be arranged linearly along a length of tape to simultaneously capture samples. This allows adaptive processing of the spectra while sequentially adjusting the MALDI parameters for each simultaneously collected sample. In addition to serving as a sample collection medium, the tape may include a magnetic surface for electronic data recording. This creates a compact package for collection and storage of the sample as well as data results, including collection location, time stamps, and analysis results. The design also provides all the material needed for postcollection testing and verification.

Continuous tape solves another problem: the introduction of the sample into the vacuum chamber of the mass spectrometer. We considered several methods to accomplish this, including a technique to remove portions of a sample from the tape via a punch or typewriter-key transfer. The preferred method would allow direct measurement of the sample without removal from the tape while also eliminating the need to insert a probe into the chamber. We accomplished this by replacing the probe with the tape and by using the

tape as a temporary boundary to form a vacuum chamber seal.

The approach taken in this design considered the overall objectives, and from that developed a combined aerosol separator and collector, tape drive mechanism, and vacuum chamber load lock, which follows the original concept while satisfying the specific design requirements for the automated system.

TOF-MMS AEROSOL COLLECTOR DESIGN

Aerosol Collector Description

The particle separator chosen for use with the TOF-MMS derives from high-volume impactors developed by Sioutas.[12] The impactor has a proven design based on established principles of operation. Air drawn in through a plenum (Fig. 5a) flows through 6 to 10 nozzles. Each nozzle handles 3 L/min, with a pressure drop of 5.0 kPa. Particles accelerate in the nozzles through a 0.85-mm-diameter acceleration jet to about 90 m/s and deposit by impaction on a section of tape located approximately 1 mm away.

The selection of this design resulted from an extensive review of commercial and special aerosol collection devices. The size, power, and capture medium constraints of most commercially available sampling systems do not conform well to the design of a portable spectrometer system.[22–24] The work by Sioutas on aerosol particle separation matched closely the basic format of the proposed TOF-MMS concept. Sioutas developed separators that had linear arrangements of conventional and virtual impactors. Adapting his geometry for design and fabrication at APL proved straightforward. Tests of the resulting particle separator (Fig. 6) demonstrate that it meets the criteria of a 0.5-mm cut-point, collection efficiencies in the range of 80% for 2.5- to 5-mm particles, and typical collection spot sizes in the desired range of 1 mm in diameter. The design also allows for relatively easy replacement of the nozzle plates to clean or to exchange for alternate geometries. However, variations in the mechanical properties of biological agents appear to affect the collection efficiency and the shape of the capture area for this collector. These agents seem to have a wide range of shapes, moisture content, and hardness. Particles with similar physical size and density may have characteristics analogous to those of hardballs and snowballs. Some particles may migrate from the capture spot as a result of impact with other particles[25]; some may bounce when they hit the capture surface, resulting in a loss of particles. These factors

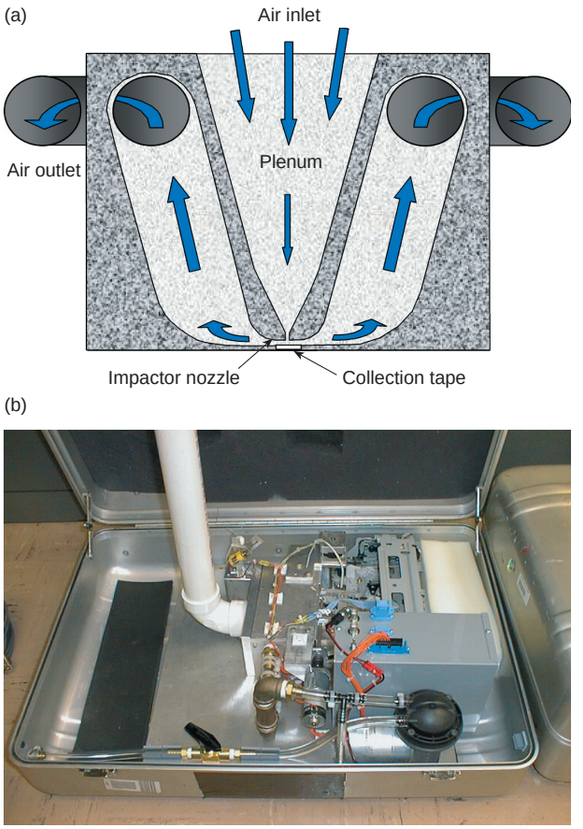

Figure 5. Aerosol impactor collector. (a) Movement of air flow. (b) The portable unit is linked by an RS-422 to a remote notebook computer that provides monitoring and high-level commands.

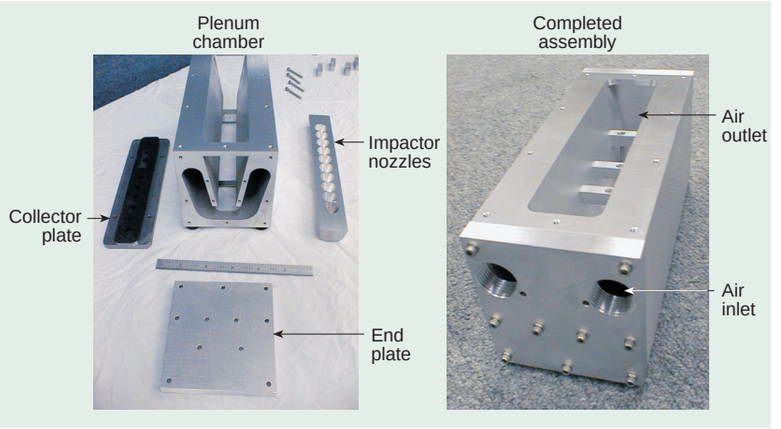

Figure 6. Multiple nozzle aerosol collector.

result in capture spots having the desired 1-mm diameter and spots that spread out to a greater diameter, beyond the reach of the laser beam (Fig. 7).

Initial laboratory tests indicated that a highly efficient aerosol capture device with the proper matrix requires an airflow rate of 30 L/m, which the Sioutas impactor design easily meets. Subsequent tests with a greater variety of agents indicate that the total flow may need to exceed 300 L/m. We accomplish this by adding to the inlet of the Sioutas collector a bank of upstream virtual impactors having a 10:1 concentration.

The higher flow rates and associated pressure drops of the virtual impactor have raised an issue of air pump efficiency. Many common air pumps, such as vacuum cleaner blowers, have efficiencies of less than 30%. In most aerosol collection systems these blowers will suffice because they connect to the public power grid. This becomes problematic in a portable unit that will ultimately operate on batteries. Commercial pumps that operate at much higher efficiencies have unacceptable pressure-drop to flow-rate relationships. We can compensate for these losses by replacing the commercial air pumps with custom turbine blade pumps having efficiencies above 50%; by improving the collector nozzle geometry; and through improvements in the MALDI process. Additionally, new collector technologies have started to emerge that take advantage of fluidics, improved manufacturing processes, and mesomachining. These proprietary designs indicate the potential for an order of magnitude reduction in power for equivalent collection capability.

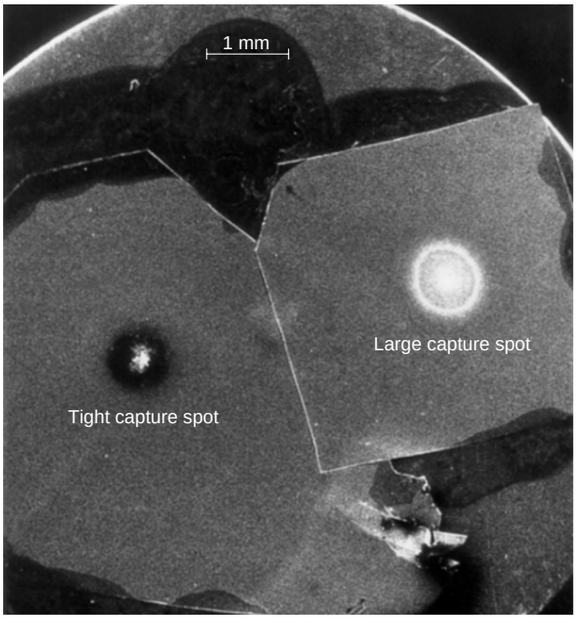

Figure 7. Aerosol capture spots (11× magnification).

Tape Aerosol Capture and Transport Mechanism

The original concept of using a flexible tape material to capture the sample and form a carrier for preparation, analysis, and storage works well for a portable mass spectrometer. This design uses a standard videotape cassette for this purpose. During collection activities a mechanism (similar in function to that used in video recorders) extracts the tape from a cartridge to form a loop between the cartridge feed and take-up reel. As the mechanism forms the loop, guide rollers align the tape with the particle separator nozzles, the microchemical matrix processor, and the spectrometer vacuum chamber inlet port.

We tested the first prototype portable aerosol collection system (Fig. 5b) at the Dugway Proving Grounds, Utah, in 1997. It uses a commercial VCR and VCR tape as the sample handling system. The system forms a prototype platform to test alternative sample collection and preparation processes. Experiments using standard VCR tape as a collection surface indicate that the material is rugged and inexpensive, and does not interfere with the ionization spectra when employed as a collection substrate. The use of VCR tape as the baseline collection and transport system also allows flexibility in future sample preparation and collection methods. Although satisfactory results were initially obtained from a standard VCR tape, investigations into collection surfaces continue in order to optimize the mechanical and chemical aspects of the capture and preparation steps. These investigations look at variations in collection surface materials, surface finishes, and different surface preparations for the MALDI matrix.

Although the prototype collection system uses a standard VCR chassis as the mechanical handling system, many problems arose when attempting to incorporate the commercial video-player tape handling system into the final design. The primary problem is that tape drive manufacturers typically update models every year. By the time a design has completed testing and enters a series of field evaluations, the availability of replacement parts disappears. Commercial VCR player components, such as motors or gears, are not very rugged or easily maintained for this application, and the VCR player mechanisms have overly complex and intricate gearing relative to that required by the MMS.

The latest mechanical design (Fig. 8) has been greatly simplified from commercially available VCR systems and also ruggedized to provide reliable tape handling in a fieldable system. The tape handling system continues to use a standard VHS tape cassette, but a manual drop-in locking interface plate replaces the standard motorized VCR player's in-and-download mechanism. Once loaded, a single lead-screw motor-drive draws out a loop of tape and aligns it with the impactors of the aerosol collector and the sample port of the mass analyzer.

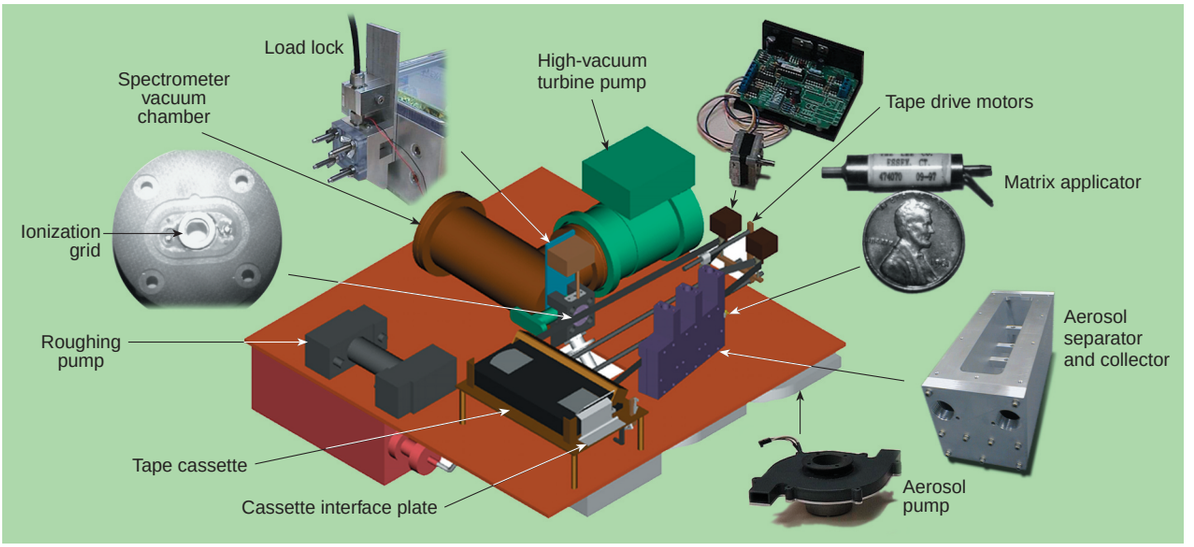

Figure 8. TOF-MMS assembly.

Simple adjustments in limit switch locations control the tape loop length. These adjustments enable installation of variously sized sample preparation, aerosol collection, and mass analyzer components.

At full extension, the lead screw places the tape in contact with two independently controlled motor pinions. A motor on the aerosol collection side advances a section of tape aligned with the aerosol collector nozzles while the mass spectrometer motor steps each collected spot past the sample preparation applicator and over the mass spectrometer ionization port. As the sample passes toward the mass analyzer port, a MEMS (microelectromechanical system) derived dispenser applies a small amount of solvent. The solvent forms a matrix with the collected sample to prepare it for the MALDI process. A spring-loaded tape-tensioner between the two motors forms a service loop of tape that allows independent movement of sections of tape driven by each motor. This arrangement allows for simultaneous collection, sample preparation, and analysis of aerosol samples.

A stepper motor controller card that plugs into a standard ISA (Instrument Society of America) slot of a computer operates the tape movement and several other actuators. The card provides 28 standard TTL (transistor–transistor logic) level digital output signals. The TTL signals couple to relays that switch both high- and low-power devices. For example, attached to the aerosol collector and the vacuum interface for the mass analyzer chamber are platens used to seal the tape to the opening. The platens operate with motors receiving digital control signals. Other output signals control the sample preparation system, laser attenuator, vacuum valve actuators, the aerosol collection pump, and the take-up reel motors. The stepper motor controller card also provides inputs for system status indicators. The card is configured for 28 digital inputs that provide end-of-travel limit switches, platen position indicators, or valve status indicators. All control-level signals are sent to the stepper motor controller card, where they are then evaluated by the system control software.

The current design is controlled using visual C++ software as the primary interface. System-level user interfaces provide flexibility in system operation for testing and debugging the entire system. By interfacing directly with the components of the system, instead of relaying information via an intermediate software environment as several commercial acquisition and control programs do, we eliminate potential timing interference. During development, the complete working system, without all the hardware connected, can be tested by simulating any of the missing components. Two system control windows are under development to provide a skilled user with multiple options for controlling the sample collection or sample acquisition systems. As certain operating parameters are fixed, they will be removed from user control. Eventually, the entire system will be operable by an unskilled user or by an automated control system. Ideally, the software may be directly loaded into an embedded microcontroller, thereby reducing the size and power of the control system.

Aerosol Collector—Mass Spectrometer Interface

Of all the major system functions, the introduction of the sample into the mass spectrometer vacuum chamber created major difficulties in transforming the proposed concept into a working system. Devices used

for vacuum chamber sample introduction are called load locks. An extensive search of commercial load locks found very complicated devices, none of which adapted to our need for rapid and repeated batch processing of small samples. The first step in solving this problem involved moving the ionization/desorption cell outside the vacuum chamber proper, between the sample tape and the vacuum isolation valve (Fig. 9a). The ionization cell normally resides within the walls of the vacuum chamber and is reachable only by a long probe. By moving it outside the chamber we eliminated the need for a long probe. This external design maintains the separation of 1 to 2 mm between the sample surface on the tape and extraction grid, leaving room for an isolation valve between the ionization grid and the inside of the chamber.

The sample collection tape now must act in place of the probe to form the vacuum seal. To do so, the tape must consist of nonporous material that holds a vacuum seal at or below micro-Torr pressure levels. One candidate material is polyester film like the kind used for magnetic recording tape. A series of vacuum tests using a helium leak detector demonstrated that a wide variety of polyester, polyamide, polytetrafluoroethylene, and other tape materials would hold an adequate vacuum. Practical limits on vacuum seal design, material availability, and cost suggested the use of 0.5-in. tape rolled in standard VHS recording cassettes.

Operation of the external ionization valve follows a few straightforward steps. Before opening the high-vacuum isolation valve, the platen compresses the tape against an O-ring surrounding a port to the ionization cell (Fig. 9b). This forms a vacuum seal. A second port attached to the ionization cavity connects to a vacuum roughing pump for removal of trapped air in the cavity. It takes approximately 10 s to rough the cavity. After removal of the air, the roughing pump valve closes and the isolation valve opens. This creates a direct straight-line path from the sample surface to the spectrometer detectors. It then takes another 20 s to pump the cavity to a micro-Torr pressure. Once at vacuum, a 4500-V potential is applied between an electrode on the contact surface inside the sealing ring of the platen and the extraction grid. A laser then ionizes the sample by firing a beam through an optically clear vacuum window to a 1-mm spot focused on the tape surface. The vacuum isolation valve closes upon completion of the spectrometer measurement, the rough port valve opens, and the platen releases, allowing the tape to advance for the next measurement. Tests thus far have demonstrated the capability to handle extraction voltages exceeding 6000 V.

A pressure differential between the two sides of the sample tape may cause deformation. To solve this problem, the platen design contains a port opening on the backside of the tape. The port connects to a compensating vacuum formed by the main vacuum chamber roughing pump. This compensating vacuum significantly reduces the differential pressure forces, thereby preventing unacceptable tape deflection.

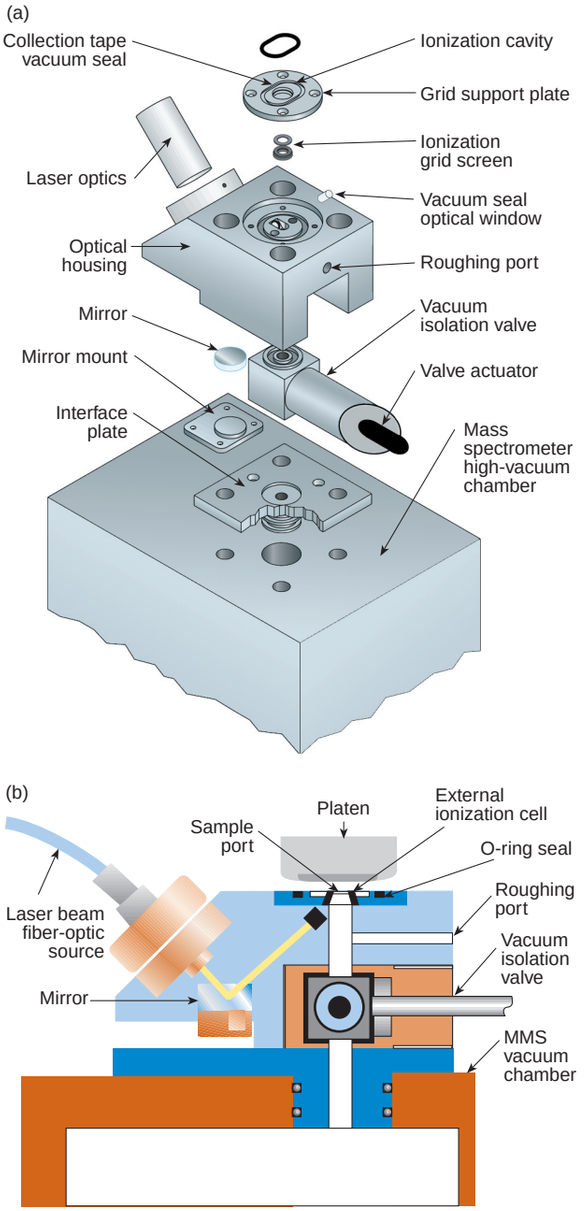

Figure 9. External ionization grid assembly (a) and port (b).

The external extraction grid design shows the most promise for rapid sample injection, given the trade-offs of sample contamination, effectiveness in vacuum sealing, and complexity. Of the designs considered, it has the least cross-contamination potential during real-time sampling. Admittedly, the sample surface immediately

around the extraction opening does contact all samples, which may cause cross-contamination around the sealing area. However, the key sample site at the point of laser beam impact remains uncontaminated. This technique can also allow for some degree of postprocessing of the sample tape since each sample remains on the tape.

SUMMARY

APL has under development an automatic aerosol collection and MALDI-TOF-MMS. Based on an idea suggested by Bryden et al.,[1] the TOF-MMS combines in one unit the sample collection, preparation, introduction into the mass spectrometer, analysis, and sample archiving. This concept consists of a reel-to-reel tape collection medium used to capture and store the samples from an aerosol impactor, a microchemical dispenser to prepare the samples, and a vacuum load lock to introduce the samples into the vacuum chamber. Successful operation of individual components and subsystems has demonstrated (1) the ability to collect aerosol samples suitable for desorption and ionization in a mass spectrometer, (2) the application of matrix using a miniature ink-jet valve, and (3) the creation of vacuum seals adequate to operate the TOF spectrometer.

Continued development is addressing the integration of the complete system, improving MALDI sample preparation techniques to increase sensitivity and wider specificity, increasing aerosol concentration, and locating and incorporating high-efficiency air pumps. We have used commercial hardware (e.g., air pumps) when practical and have developed new technology when necessary, while accommodating advances in commercial sampling systems as they develop. The flexibility of the current system design allows us to adapt to multiple, interchangeable sampling components. Ideally, the system flexibility should allow us to leverage experimental designs in mesomechanics and fluidics as they develop, increasing the overall performance of the system.

REFERENCES

[1] Bryden, W. A., Benson, R. C., Ecelberger, S. A., Phillips, T. E., Cotter, R. J., and Fenselau, C., "The Tiny-TOF Mass Spectrometer for Chemical and Biological Sensing," *Johns Hopkins APL Tech. Dig.* **16**, 296–310 (1995).

[2] Karas, M., Bachmann, D., Bahr, U., and Hillenkamp, F., "Matrix-Assisted Ultraviolet Laser Desorption of Non-Volatile Compounds," *Int. J. Mass Spectrom. Ion Proc.* **78**, 53–68 (1987).

[3] Cotter, R. J., *Time-of-Flight Mass Spectrometry*, American Chemical Society, Washington, DC (1994).

[4] Demirev, P., Westman, A., Reimann, C. T., Håkansson, P., Barofsky, D., et al., "Matrix-Assisted Laser Desorption with Ultra-Short Laser Pulses," *Rapid Comm. Mass Spectrom.* **6**, 187–191 (1992).

[5] Chow, J. C., and Watson, J. G., *Guideline on Speciated Particle Monitoring*, Draft Report 3 for the EPA Office of Air Quality Planning Standards, by the Desert Research Institute, Reno, NV (Aug 1998).

[6] *U.S. Army Test and Evaluation Command Test Operations Procedure, Biological Detectors, Aerosol (BDA)*, TOP-8-2-066, Joint Program Office for Biological Defense, Falls Church, VA (14 Aug 1998).

[7] Lee, K. W., and Ramamurthi, M., "Filter Collection," Chap. 10, in *Aerosol Measurement Principle, Techniques, and Applications*, K. Willeke and P. A. Baron (eds.), Von Nostrand, New York, pp. 179–205 (1993).

[8] Marple, V. A., Rubow, K. L., and Olson, B. A., "Inertial, Gravitational, Centrifugal, and Thermal Collection Techniques," Chap. 11, in *Aerosol Measurement Principle, Techniques, and Applications*, K. Willeke and P. A. Baron (eds.), Von Nostrand, New York pp. 206–232 (1993).

[9] Maddox, R. L., "On an Apparatus for Collecting Atmospheric Particles," *Monthly Microscopical J.*, 286–290 (1 Jun 1870).

[10] Fisher-Klosterman, Inc., Product Bulletin 218-C, 2900 West Broadway, Louisville, KY.

[11] Hering, S. V., "Impactors, Cyclones, and Other Inertial and Gravitational Collectors," in *Air Sampling Instruments for Evaluation of Atmospheric Contaminants*, 8th Ed., American Conference of Governmental Industrial Hygienists, Cincinnati, OH, pp. 279–321 (1995).

[12] Sioutas, C. P., Koutrakis, P., and Burton, R. M., "Development of a Low Cutpoint Slit Virtual Impactor for Sampling Ambient Fine Particles," *J. Aerosol Sci.* **25**(7), 1321–1330 (1994).

[13] In-Tox Products, Product literature, 115 Quincy, NE, Albuquerque, NM.

[14] Grasby Andersen, Product literature, 500 Technology Ct., Smyrna, GA.

[15] Burton, R. M., Howard, J. N., Penley, R. L., Ramsey, P. A., and Clark, T. A., "Field Evaluation of the High-Volume Particle Fractionating Cascade Impactor," *J. Air Pollution Cont. Assoc.* **23**(4), 277–281 (1973).

[16] Dreisewerd, K., Schürenberg, M., Karas, M., and Hillenkamp, F., "Influence of the Laser Intensity and Spot Size on the Desorption of Molecules and Ions on Matrix-Assisted Laser Desorption/Ionization with a Uniform Beam Profile," *Int. J. Mass Spectrom. Ion Proc.* **141**, 127–148, (1995).

[17] Laser Science, Inc., Product literature, Franklin, MA.

[18] Bevis, R. C., and Chait, B. T., "Factors Affecting the Ultraviolet Laser Desorption of Proteins," *Rapid Comm. Mass Spectrom.* **3**(7), 233–237 (1989).

[19] Karas, M., Ingendoh, A., Bahr, U., and Hillenkamp, F., "Ultraviolet-Laser Desorption/Ionization Mass Spectrometry of Femtomolar Amounts of Large Proteins," *Biomed. Environ. Mass Spectrom.* **18**, 841–843 (1989).

[20] Odernheimer, B., "Chemical Process Monitoring by Automated Microsampling on Magnetic Tape and Retrospective On-Site Evaluation," in *Verification of Dual-Use Chemical Weapon Convention: The Case of Thioglycol*, SIPRI Chemical and Biological Warfare Studies, No. 13, S. J. Lundin (ed.), Oxford University Press, Oxford, UK, pp. 69–72 (1991).

[21] Zellweger Analytics, Inc. Modular Multipoint Monitor, Product Catalog No. 970372 (1996).

[22] Cage, B. R., Schreiber, K. T., et al., "Evaluation of Four Bioaerosal Samplers in the Outdoor Environment," in *Proc. 1994 ERDEC Scientific Conf. on Chemical and Biological Defense Research*, pp. 63–72 (15–8 Nov 1994).

[23] Hering, S. V., "Inertial and Gravitational Collectors," in *Air Sampling Instruments for Evaluation of Atmospheric Contaminants, American Conference of Governmental Industrial Hygienists*, 7th Ed., pp. 337–403 (1989).

[24] Rubow, K. L., Lippman, M., et al., in *Air Sampling Instruments for Evaluation of Atmospheric Contaminants, American Conference of Governmental Industrial Hygienists, Part II, Instrumentation*, 8th Ed., pp. 203–368 (1995).

[25] Macher, J. M., Chatigny, M. A., and Burge, H. A., "Sampling Airborne Microorganisms and Allergens," in *Air Sampling Instruments for Evaluation of Atmospheric Contaminants, American Conference of Governmental Industrial Hygienists, Part II, Instrumentation*, 8th Ed., pp. 589–617 (1995).

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