

**Application of a Particle Beam LC/MS Interface to the commercially
available Agilent 5973 Mass Spectrometer**

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Introduction

The particle beam interface as developed by Browner and associates and commercialized by Hewlett-Packard Company (Agilent Technologies, Inc. Palo Alto Ca) has over the years provided a valuable sample inlet technique for the analytical laboratory. However, in recent years, the technique has been overshadowed by newer techniques involving atmospheric pressure ionization. The advent of the Agilent Technologies benchtop model 5973 mass spectrometer with positive EI, positive CI, negative CI ionization modes and a high degree of sensitivity affords an attractive detector for the particle beam interface for liquid chromatography. The industry standard and legally defensible library searchable spectra and search results maintains a niche in the analytical marketplace. A complete benchtop system – mass spectrometer, liquid chromatograph, concurrent data system / controller, the particle beam apparatus as well as data from the system will be discussed.

Instrumentation - Liquid Chromatography and Mass Spectrometry

The mass spectrometer used was an unmodified HP (now Agilent Technologies, Inc.) Model 5973 Mass Selective Detector with 250 L/sec turbomolecular pump. The HP 5973 is a benchtop quadrupole mass spectrometer with mass range of 1.6 to 800 mass units, 10,000 volt HED, and is available with EI or EI/CI capabilities. The liquid chromatograph used was an HP (now Agilent) Model 1090 LC with manual injector, PV5 pumping system and diode array (pn 79880A) detector. The HPLC column used was a Zorbax SB-C18 (Agilent pn 830990-902), narrow bore 2.1 x 150 mm 3.5 micron. The column was preceded by a Security Guard (Phenomenex, Torrance California) KJ0-4282 guard cartridge kit fitted with one SecurityGuard C184x2.0mm cartridge.

Instrumentation – Data System

The LC/MS data system used consisted of a personal computer, mass spec operating software, lc operating software set up to run concurrently and 2 mass spectral libraries. The computer used an Intel (Intel Corporation, Santa Clara California) main board and 450 MHz processor, operating Window 2000 (Microsoft Corp. Redmond Washington). It also had 128 MB RAM memory and 10.5 GB hard drive. The software used for MS control and data analysis was Agilent G1701BA GC/MS Chemstation. The software used for LC control was Agilent G2170AA and G2180AA Multi Technique Chemstation. The two systems were combined on the same Windows 2000 computer by the Eighty-X[®] Mass Spec Upgrade (CSS Analytical Company, Inc. Shawnee Kansas) software conversion. This conversion by CSS allows the software to “co-reside” and provide concurrent control of both mass spec and liquid chromatograph. Two libraries of mass spectral data were used to search with pbm matching. They were the Wiley Registry of Mass Spectral Data 7th Edition, with NIST98 Spectra (John Wiley & Son’s Inc. New York, New York) and the AAFS Forensic Drug Library (American Academy of Forensic Sciences, Colorado Springs, Colorado).

Instrumentation – Supporting Particle Beam Devices

Several supporting devices and fixtures were produced. The first device was a mechanical pump controller, an electrical on/off appliance for securing electrical service to two Edwards E2M18 (BOC Edwards, Wilmington Mass) mechanical rough pumps. A small box with 220 Volt AC inlet jacks and one 220 Volt AC outlet plug also contained a set of 220 Volt circuit-breaker on/off switches, making power connections simple and safe. Both pumps used Fomblin type (PTFE) oil although less expensive Inland type oil could be used if changed and recharged often enough. The particle beam apparatus sat atop a controller box (11”l x 12”w x 9.5”h) which contained the following: a main power on/off switch, KF 25 vacuum fittings (2 each), a fuse holder (2 amp), an digital temperature controller, a temperature on/off switch, a tc vacuum gauge, a nebulization gas regulator, gas inlet connection (Swagelok type) and a 3-way gas controller valve.

	Size (l" x w" x h")	Weight (lbs.)	Electrical Service
LC (HP 1090)	21x28,24	90	110v, 6A
MS (HP 5973)	24x12x16	65	110v, 8A
PC & MONITOR	Typical	Typical	110v, 5A
PB Control Box	11x12x9.5	20	110v, 2A
Pump Controller	7x8x5	2	0
Pumps (ea, x2)	20x8x22	80	110v, 7A 220v, 3.5A

Table 1.

Instrumentation – Particle Beam Apparatus

Helium is directed into the nebulizer at high pressure coaxially around a capillary containing the LC effluent. At the end of the capillary the helium meets the LC effluent and shears the liquid eluting from the tube into droplets forming an aerosol. The aerosol generated at the nebulizer is sprayed into the desolvation chamber where there is a low vacuum (0.25 to 0.5 atm) and a slightly elevated temperature (50-80 C). The droplets in the aerosol have a high surface area and due to the combination of the vacuum and heat the LC mobile phase is evaporated from the droplets. As the LC mobile phase is evaporated, the sample molecules combine to form a particle. The separation of the LC mobile phase from the sample particles is accomplished through the use of a nozzle with a 2-stage skimmer arrangement forming a momentum separator. Each stage of the separator is attached to a vacuum pump so that the vapor molecules with little momentum will be evacuated as they diffuse away from the center hole of the skimmers. The much larger particles have greater momentum and will not diffuse much while passing through the center hole of the skimmers. The momentum separator is attached to the mass spectrometer ion source through a transport tube. Here the molecules will see a drop in pressure from approximately 0.5 torr to 4.5×10^{-5} torr. Because of this pressure drop gas flow will transport the particles to the mass spectrometer ion source.

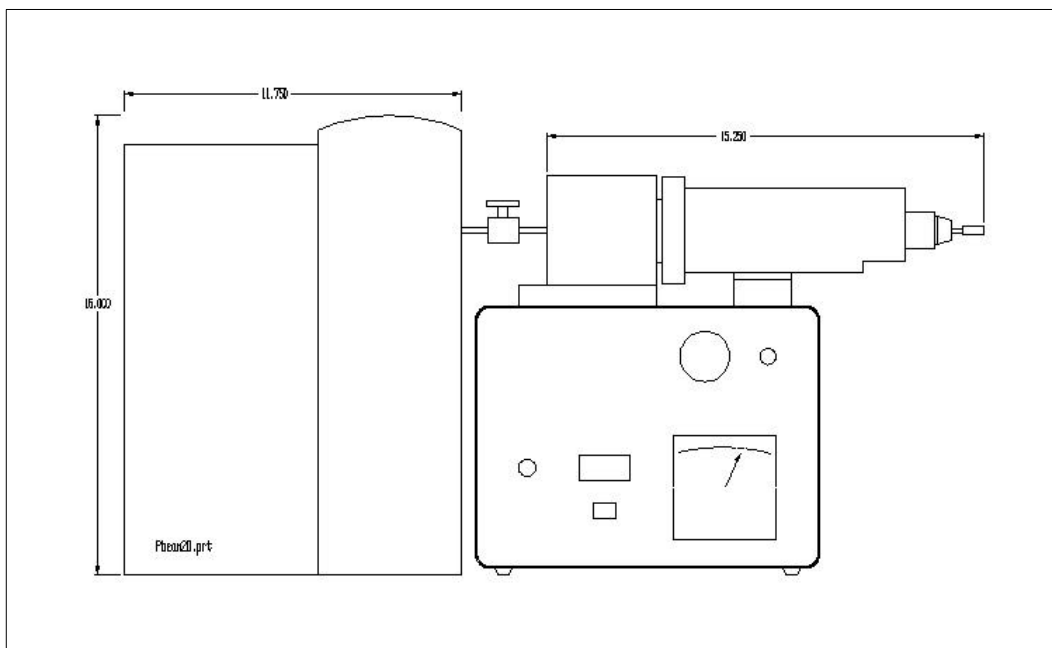


Fig. 1.

Figure 1. Showing line drawing of Particle Beam / Mass Spectrometer system with generalized dimensions. Over all dimensions allow the instrument to fit on a standard laboratory bench taking up less than 30 linear inches of bench. Laboratory bench bases can include "pump cabinets" specially designed to house mechanical rough pumps and associated cables and hoses, allowing for a quieter laboratory.

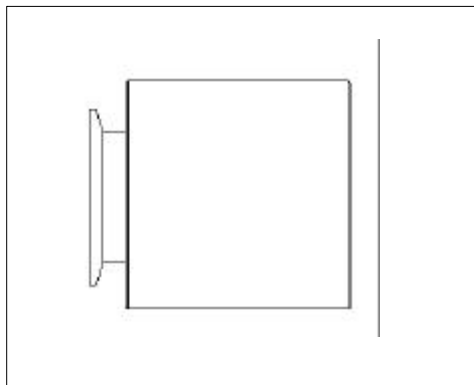


Fig. 3.

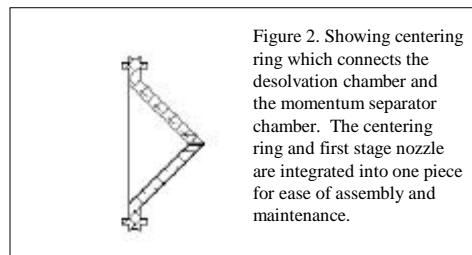


Figure 2. Showing centering ring which connects the desolvation chamber and the momentum separator chamber. The centering ring and first stage nozzle are integrated into one piece for ease of assembly and maintenance.

Fig. 2.

Figure 3. Showing desolvation chamber with integral fitting for KF type flange connection. This unique feature allows easy assembly and break-apart for cleaning.



Fig. 4.

Design features of the Particle Beam / Mass Spectrometer system

- (1) A compact and “bench top” design. See Table 1.
- (2) Utilization of a highly developed and precision manufactured nebulizer assembly.
- (3) A “hot” or “cold” nebulizer mount.
- (4) KF type flange connections between major components. See Figure 3.
- (5) The centering ring for the KF connection is integrated into the first stage nozzle.
- (6) The design utilizes changeable orifices in the nozzle and skimmer.
- (7) Computer Numerically Controlled (CNC) machined parts with precision control of finish with no need for expensive investment casting.
- (8) Unique transport tube and PB/MS isolation valve.
- (9) Digital temperature control of the desolvation chamber.
- (10) Adjustable 2nd stage skimmer, allowing the source pressure of the mass spec to be adjusted over a range of 8×10^{-6} to 5×10^{-5} .

Data and Review of Data

Chromatographic performance and spectra was taken from the particle beam LC/MS and is typical of data from previous commercial instruments. The LC can be adjusted to change chromatographic output. MS parameters (ability to tune) and adjustments to various elements of the particle beam apparatus can be made to produce optimized results. Data shown in figures 6, 7, and 8 respectively are Pseudoephedrine, Sucrose Octaacetate, and Poly Propylene Glycol (PPG).

Figure 6 shows a single 5 ul loop injection of Pseudoephedrine (250 ug/ml), a spectrum and a library match. Figure 8 shows a single on-column injection of PPG using a 2.1 mm x 150 mm LC/MS C-18 column. Figure 7 shows a series of injections of Sucrose Octaacetate. This series of injections illustrates the utility of the instrument to act as an automatic DIP (Direct Insertion Probe) where a sequence of injections can be set up in an liquid chromatograph auto sampler. The instrument method can be set up to automatically produce various reports: TIC, spectra, integration results and library searches allowing for the possibility of “Open Access” mass spectrometry for those molecules not working well with Electrospray Ionization.

Figure 5 further illustrates the utility of the automation aspects of the Particle Beam Instrument. As large amounts of data are generated the data analyst needs to be able to quickly and accurately review the data from an entire sequence, not just for a single sample. Figure 5 is a demo panel taken from the “Quick Review” (Master Enterprises) software showing an entire sequence of data in graphical form. Each dot represents a single sample, with colors representing pass or failure with respect to pre-set limits.

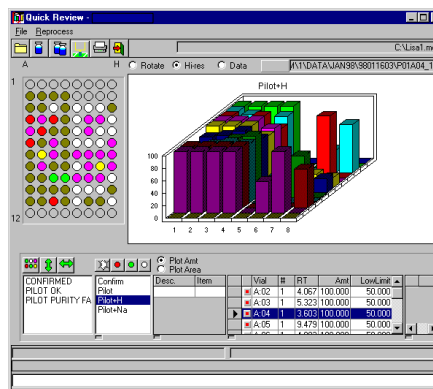


Fig. 5.

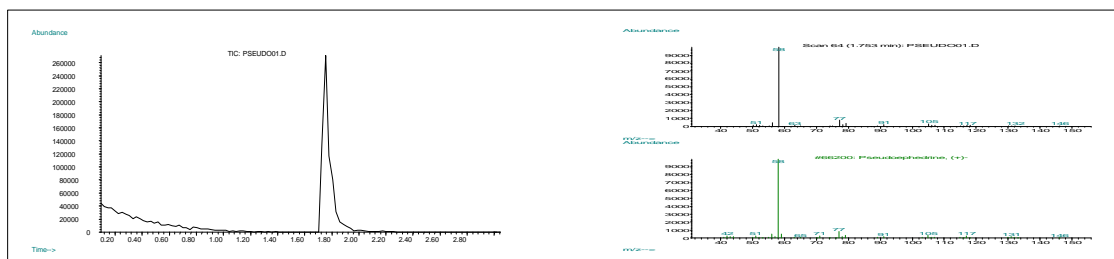


Fig. 6.

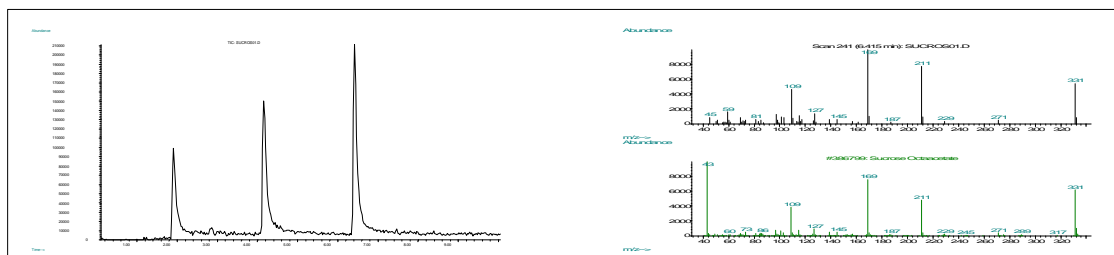


Fig. 7.

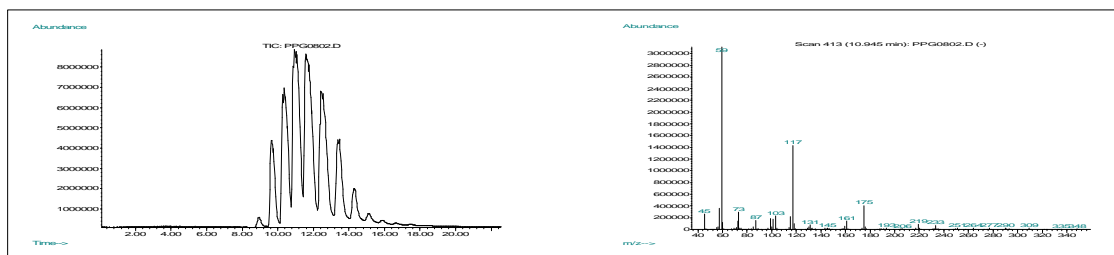


Fig. 8.

Conclusions

The particle beam designed and adapted to the Agilent 5973 Mass Spectrometer indeed can provide a valuable sample inlet technique for the analytical laboratory. Significant benefits of the system produced include the increased sensitivity available from the combination of the re-design of the particle beam apparatus and the Agilent 5973 MS, EI/CI capability of the Agilent 5973 MS, the ruggedness and ease of use of the particle beam technique (long established), the space saving utility and energy conservation of the benchtop system, use of this system as a low cost substitute for the direct insertion probe (open access), and the industry standard and legally defensible library searchable spectra.

The key questions answered during this investigation were: 1. Is the Agilent 5973 Mass Spectrometer, with turbo pump capable of maintaining a sufficient vacuum level under the load of an LC effluent? 2. Can the existing particle beam apparatus of Browner and associates be adapted to the benchtop mass spectrometer? 3. Can significant improvements in mechanical and electrical design be found to improve efficiency and usability? And 4. Can significantly sensitive data be acquired from the improved system? The answer to all of the questions – Yes. Additional work to be done includes investigation of linearity and sensitivity. Recent developments in particle creation and transport suggest the possibility of replacing of the nozzle/skimmer assembly in the momentum separator.

A full reprint of the extended abstract for this poster is available for download at <http://www.cssco.com>