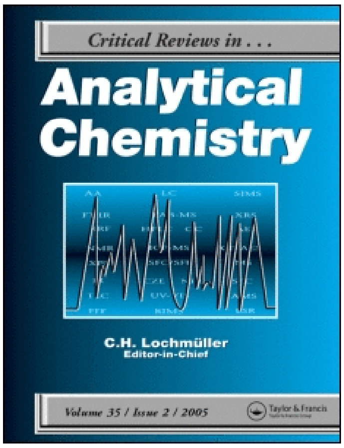

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GAS CHROMATOGRAPHY – MASS SPECTROSCOPY INTERFACIAL SYSTEMS

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I. INTRODUCTION

Some gas chromatographers look upon the mass spectrometer as just another, albeit an expensive, detector for their chromatographs. Mass spectroscopists tend to view the chromatograph as a rather versatile extra inlet system for their spectrometers. Both of these viewpoints are in many ways correct. The mass spectrometer can serve as an excellent, highly sensitive, and selective detector, providing information that would be difficult to obtain by other means.[1] The gas chromatograph also provides a useful function as an inlet system, in that it permits introducing samples either in batches or continuously at carefully controlled rates.

Nevertheless, there can be no doubt that the combined gas chromatograph – mass spectrometer (GC-MS) should be regarded as an instrument in its own right, capable of providing both structural and quantitative information on complex mixtures, and doing so rapidly. Such information could not otherwise be obtained without laborious and time-consuming analyses by conventional chemical techniques.

Gas chromatography (GC) is the most powerful technique available to the analyst for the separation of the constituents of complex volatile mixtures, but its one major disadvantage is that it does not provide a direct identification of the eluting species. Solute identity may be determined chromatographically, but the process is time-consuming and not all of the standards that are requisite in the analysis of a complex mixture may be available for comparison purposes.

Mass spectroscopy (MS) can provide detailed information on the structures of pure compounds by analysis of the molecular ion and fragmentation pattern produced. However, the MS does not necessarily indicate that a sample is impure, and interpretation of the spectra may, therefore, be complicated by overlaid fragmentation patterns. Good spectra may be obtained from about 1 μg of sample, and in certain favorable circumstances adequate spectra may be obtained from samples of nanogram size or less.

The sample requirement of the MS compares very favorably with that of the GC and hence the combination of the two instruments is very attractive. However, there is a major source of incompatibility in the operating pressures of the two instruments, and the crux of successful GC-MS lies with the interface linking the two machines. The interface, or separator, as it is often called, must be capable of effecting the necessary pressure drop from 1 atm to 10^{-5} to 10^{-7} torr, and several such devices have been described (see Section IV).

Combination GC-MS was first attempted by Holmes and Morrell in 1957.[2] They used a direct coupling technique and successfully analyzed the constituents of town gas. In 1959, Gohlke[3] combined a time of flight (T.O.F.) MS directly with a chromatograph and obtained spectra of various aromatic compounds. The experiment was followed using an oscilloscope display made possible by the high scanning speed of the spectrometer (10^4 scans/sec).

In 1963, McFadden et al.[4] illustrated the power of the combined instruments in the analysis of some flavors using capillary columns linked to the MS through a splitter.

Almost simultaneously, in 1964 Ryhage in Sweden[5] and Watson and Biemann in the U.S.[6] described the jet molecular separator and porous glass separator, respectively, for effecting a pressure drop between the two machines by preferential removal of the carrier gas with respect to solute vapors. In succeeding years several other designs of separator have been described, and there is now a wide choice of interface available.

Before considering the construction and performance of the various separators in detail, it will be profitable to consider GC and MS individually, in order to provide an appreciation of their operating parameters. These will highlight the problems that have to be solved in obtaining an efficient combination GC-MS.

II. GAS CHROMATOGRAPHY

Kelly et al.[7] have shown that it is possible for the mass spectrometer to recognize the presence of two different components in a partially resolved pair of chromatographic peaks by repeatedly scanning the column effluent. This process, known as deconvolution, can enhance the separating power of a column if the two species in question give rise to significantly different mass spectra (Figure 1). Should the unresolved peak consist of close structural isomers, such as *o*-, *m*-, and *p*-xylene, the MS will not distinguish between them.

The above example indicates that a primary chromatographic consideration in GC-MS resides in obtaining the most complete separation possible between the components of a mixture before attempting to provide an identification by GC-MS. This in turn means that chromatographic columns of high separating power must be used. Moreover, the choice of stationary phase can be crucial in achieving the necessary separation. It is also necessary to consider the speed of analysis so that valuable instrument time will not be wasted.

The term resolution (R) describes the chromatographic separation achieved between two successive components of a mixture, and when R=1, components are sufficiently well separated to obtain unambiguous spectra.

Resolution is controlled by two factors: (a) column efficiency, and (b) column selectivity.

A. Column Efficiency

Column efficiency is a complex function of several variables that attempts to describe the various band-broadening processes that occur within the column. The quantity generally used to describe column efficiency is h, the height equivalent to a theoretical plate (HETP); columns that are suitable for GC-MS applications have values h in the range 0.1 to 0.5 mm (Table 1). When comparing columns of different types, however, h does not adequately describe the column efficiency,[11] and in this instance it is better to consider the quantity H, the height equivalent to an effective theoretical plate (HEETP) (Table 2).

Various techniques have been described for minimizing h or H, but a discussion of these is outside the scope of this review. The interested reader should consult some of the excellent standard texts on this subject.[8-10]

One factor requires mention at this point because of its direct relevance to GC-MS. This is the stationary-phase loading in the column.

Column efficiency is controlled in part by the quantity of stationary phase present, in so far as it affects the rate at which solute molecules diffuse in solution. For a column to be highly efficient the stationary-phase loading should be low, 0.5 to 1.0% by weight for a packed column. With capillary columns a thin film is all that can be obtained. This requirement imposes a limit on the sample capacity of the column, and hence on the individual amounts of the various components present available to obtain suitable mass spectra.

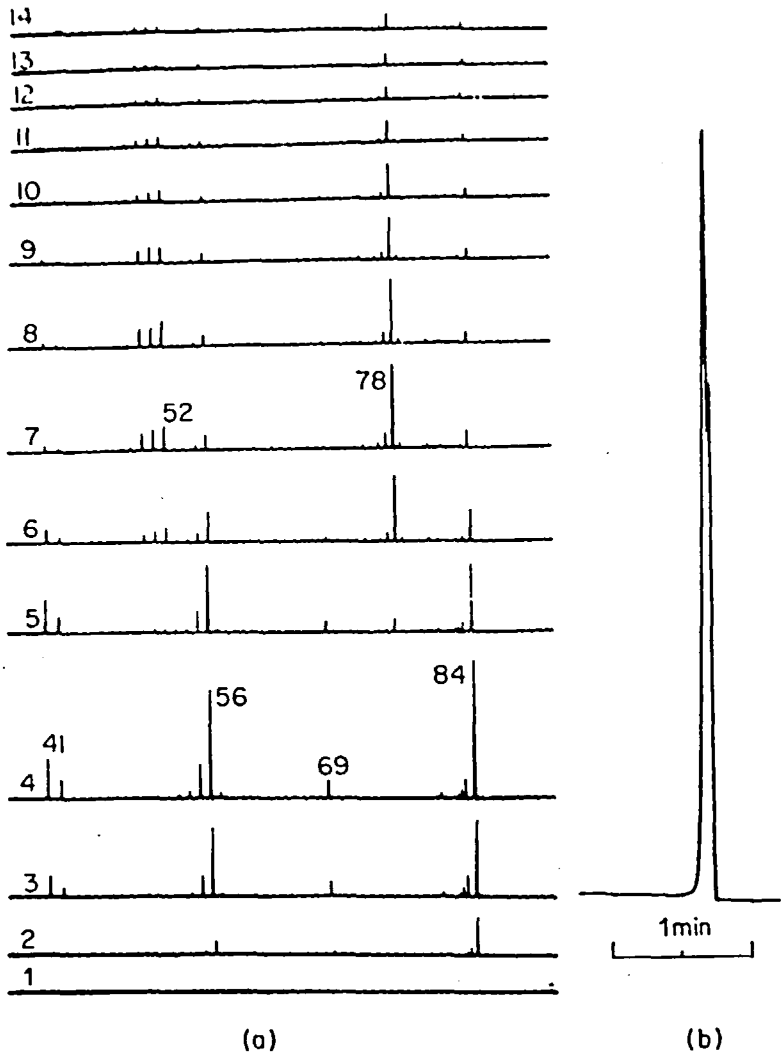

FIGURE 1. (a) 14 successive ½-sec scans during the elution of a 1:1 cyclohexane-benzene mixture (0.1 μl); (b) the chromatogram, from Kelly et al.[7]

For example, if 1 mg of a sample containing 100 components of equal distribution is injected into a packed column, the amount of each of the individual components present is 10 μg, which is more than sufficient to obtain good spectra if an efficient interface is used.

With capillary columns, however, sample sizes are typically in the range of 1 to 50 μg, and therefore each of the individual components will be present in an amount ranging from 10 ng to 0.2 μg. This sample range is close to the limit of sensitivity of the MS, and satisfactory spectra will, therefore, be obtained only if the interface system is highly efficient so that there is no loss of sample in the separator.

The choice of column for GC-MS applications must of necessity be a compromise based upon the complexity of the sample, the resolution required to obtain good spectra, and the time of analysis. Capillary columns have high separating power but low sample capacity associated with high analysis speed. Packed columns can have high separating power and capacity, but the speed of analysis is low.

Probably the best column types for GC-MS applications are the PLOT columns, which are

TABLE 1

Comparison of Column Types

Column type	Abbrev.	Permeability (10^{-7} cm^2)	Phase ratio V_g/V_l	Minimum plate height Hmin cm	Optimum carrier velocity cm/sec	Sample size μg	Carrier-gas flow rate ml/min
Porous cone classical packed (conventional packed)	CP	1-10	4-200	0,05-0,2	5-20	10-1,000	12-50
Thin film bead	B	1.5-15	50-500	0.1- 0.3	10-20	1-100	12-50
Porous layer bead	PLB	1.5-15	50-400	0.05-0.2	20-60	1-100	12-50
Packed capillary	PC	5-40	10-300	0.05-0.2	10-40	1-50	2-6
Classical open tubular (classical capillary)	COT	50-800	100-1,000	0.03-0.2	10-100	1-50	0.5-1.5
Porous-layer open tubular (support coated open tubular)	PLOT SCOT	200-1,000	20-300	0,06-0.2	20-160	1-50	2-6

These data have been abstracted from G. Guichon.[44]

TABLE 2

Comparison of Column Performance for Same Resolution

Column type	Retention time $t_R$sec	Inlet press atm	Column length m	No. of theoretical plates n	No. of theoretical plates N	Particle size d_p,μ	Stationary phase	Column bore mm
CP	200	1.75	9.5	16,000	11,000	100-125	20	cm 3-4
B	4.08	10.7	44	44,000	11,000	80-100	0.15	cm 3-4
PC	7.18	4.5	12	12,000	11,000	100-125	5	0.45
COT[1]	400	1.3	80	100,000	11,000		0.3μ thick	0.25

These data have been abstracted from G. Guichon.[44]

Note: $n = 16\left(\frac{V_R}{\omega}\right)^2$, $N = 16\left(\frac{V_R'}{\omega}\right)^2$ where $V_R' = V_R - Vm$. V_R = retention volume; V_m = gas holdup; and ω = peak width at the intercepts of the tangents to the curve and the baseline.

intermediate in resolving power, sample capacity, and speed of analysis. Nevertheless, it is advisable to consider all types of column by exploratory analyses before reaching a final decision.

B. Column Selectivity

There are some 400 different stationary phases available at the present time, but a large number of these are minor variants of basic types. For GC-MS, the stationary phase must possess certain attributes, the principal one being its involatility (i.e., resistance to bleed). If it is appreciably volatile, an unacceptably high background spectrum will be obtained (Figure 2) and will make it difficult to interpret spectra, particularly if the component is present only to a minor extent.[19]

The choice of stationary phase controls the separation between components and as a convenient rule the "like dissolves like" analogy can provide a basis of selection. The extents to which various solutes are retained by the stationary phase depend on their partition coefficients, which in turn are functions of temperature. Substances that have high partition coefficients will be retained for a long time within the column, and will be eluted as broad bands. The instantaneous concentration of solute vapor in such a band can be too low for the mass spectrometer to produce a satisfactory spectrum, and hence a technique commonly employed in GC-MS is the temperature programming method, where the temperature of the column oven is raised at a controlled rate during the course of a chromatographic separation. Raising the column operating temperature reduces the partition coefficient and the solute is eluted in a sharper band, thus raising the instantaneous concentration. This technique is particularly useful for wide boiling-range samples.

A second technique employed by chromatographers to increase the rate of elution of sample bands is a technique known as "flow-programming."[46] Here the inlet pressure to the column is progressively raised with time, possibly after an initial isobaric period. This causes an increase in the rate of carrier-gas flow through the column, and hence reduces the retention times of eluting components. This technique is particularly useful when chromatographing temperature-sensitive samples. It must be noted, however, that

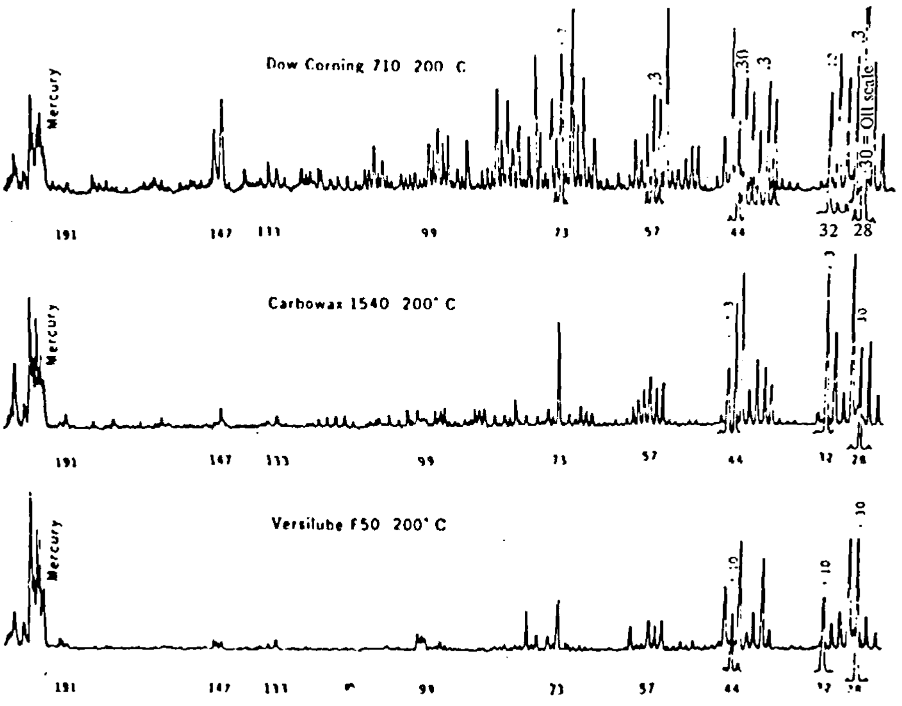

FIGURE 2. Mass spectral patterns of column bleed.[19]

the majority of separator systems are incapable of accommodating large changes in carrier-gas flow rate without significantly reducing the interface yield and enrichment.

A relatively new type of stationary phase that provides bleed-free operation is the chemically bound phase,[12] in which a liquid partitioning medium is bound to a basic matrix by strong chemical bonds. The precise mode of operation of such phases is not yet completely understood but appears to be a mixture of partition and adsorption.[13]

Porous polymer beads have been used with some success, particularly for the analyses of polar substances and of hydrocarbons having low molecular weights. However, with such materials care must be exercised to keep the column operating temperatures below about 120°C.[37]

Table 3 lists various stationary phases in common use at the present time, together with their maximum operating temperatures. The maximum operating temperature is about 20°C below the temperature at which the column has been conditioned for a 48-hr period. As long as this temperature is not exceeded, the column should have a long life and be free from deleterious bleeding.

A simple technique that may be used to assess the maximum operating temperature of a stationary phase, and that is worth following because of the inherent batch-to-batch variability in commercial products, is to take a prepared and conditioned column, and at high detector sensitivity, increase its temperature with time. The onset of column bleeding may be rapidly detected by observing sharp continuous rise in detector response above a given temperature. Operating the column about 25°C below this temperature should give bleed-free operation.

III. MASS SPECTROSCOPY

Organic mass spectroscopy provides information from which the structure of the sample under scrutiny can be elucidated.

Figure 3 is a diagram of the five main parts of the mass spectrometer. Their functions are outlined below.

TABLE 3

Characteristics of Some Stationary Phases

Stationary phase	Application	Conditioning temp. °C	Maximum operating temp. °C
SE-30)poly(dimethyl-siloxane)	General non-polar	375	350
OV-1)	General-polar, Steroids Pesticides	375	350
OV-17(50% phenyl/50% methyl siloxane)	Somewhat polar and selective Aromatics, steroids	350	325
OV-25 (75% phenyl/25% methyl)	Selective for olefins	350	325
OV-210(50% trifluoro-propyl/50% methyl siloxane)	Alcohols, ketones and esters	275	250
OV-225 (cyanopropyl phenylsilicone)	Esters, ketones, alcohols	250	225
Carbowax® 20M(polyethylene oxide)	Alcohols, glycols, esters	225	200
Carbowax® 20M/TPA.	Free fatty acids	250	225
Dexil® 300	Strictly polar	500	475
SP2000 (modified Carbowax® 20M)	Free acids	325	300
Pennwalt® 223	Amines	220	200
Poly-A-103	Barbiturates	300	275

The sample vapor is allowed to flow into the ion source from the sample reservoir through a controlled leak, which maintains the pressure of the system at or below 10^{-5} torr. In GC-MS, the sample reservoir is replaced by the gas chromatograph-interface system. The stream of sample vapor is ionized by an electron beam emanating from a hot cathode, whose energy can be controlled at any value between 5 and 100 eV. At low energy (up to about 10 eV), ionization of the sample molecules is low and usually only the parent ion is observable (molecular weight). As the energy is increased, the sample is fragmented into various ions whose stabilities (and hence intensities) are controlled by the structures of the fragments.

Such ionized species are then removed from the ionization chamber by means of a small potential and focused, by defining slits and electrostatic plates, into a narrow beam. The focused ions are then accelerated through an electrostatic plate held at a large negative potential (up to 8 kV) relative to the ionization chamber and pass through final defining slits or focusing plates into the analyzer section. At this stage each ion has acquired an energy equal to the accelerating voltage, and hence different ions have different characteristic velocities (kinetic energy = $\frac{1}{2}mV^2$).

They now pass at high velocities through a magnetic field and in doing so are deflected from their initial paths in a direction orthogonal to the lines of magnetic flux. The extent to which they are deflected depends upon the momentum of the ion. Only those ions that have the correct momentum will arrive at the ion collector.

There are two modes by which various ions can be focused on the collecting plate. These are magnetic scanning and voltage scanning.

In magnetic scanning, the accelerating voltage is held constant and the magnetic field is varied with time. In voltage scanning, the magnetic field is held constant and the voltage is varied with time. Scanning may be an order of magnitude faster with the second mode of operation, and this mode is in many ways the preferred one, although it has disadvantages, in that mass-discrimination effects may be greater.

The relationship between the charged species detected and the electrostatic and magnetic fields is given by

$$m/_e = H^2R^2/2V \qquad (1)$$

where H is the magnetic field strength, V is the accelerating potential, and R is the radius of curvature of the analyzer tube.

There are many designs of mass spectrometer other than the simple, typical one just outlined, and while they may be much more complex in their operation, nevertheless the basic principles

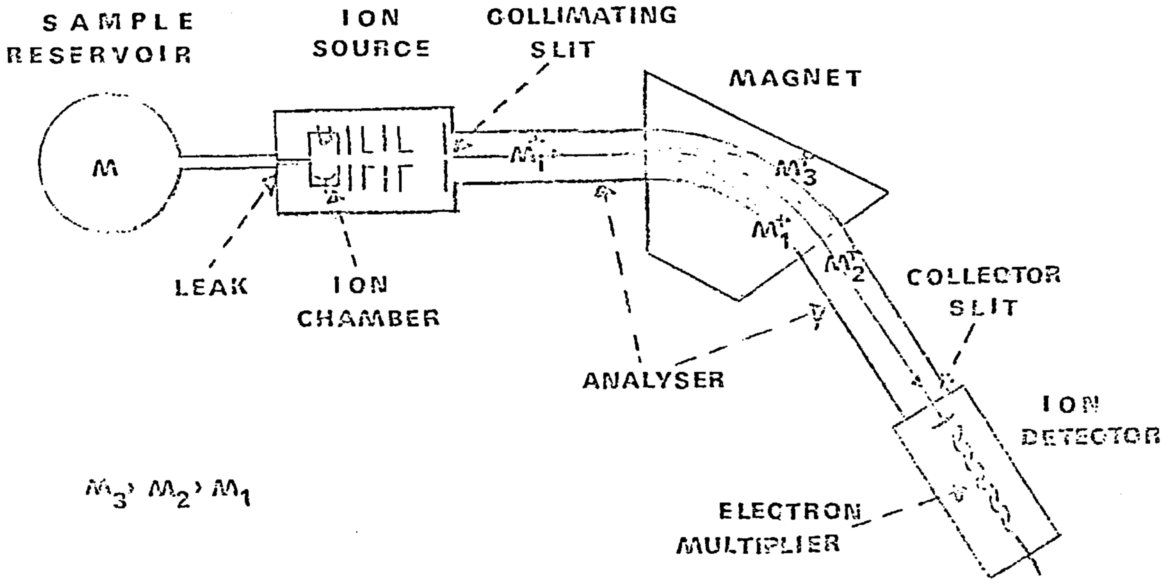

FIGURE 3. Outline of mass spectrometer.

remain the same. An excellent survey of the various types of MS is given in Reference 14.

A. Requirements for a MS Suitable for GC-MS

1. Resolution

There are several ways of defining the resolving power of a mass spectrometer, and this has caused some confusion from time to time. The methods described by the following equations are most popular and in common usage

$$R_X = M/\Delta M_X \tag{2a}$$

$$R_y = M/\Delta My \tag{2b}$$

Equation 2a is the so-called "valley" definition. It expresses resolution in terms of the highest mass at which two consecutive peaks (i.e., peaks at m/e = n and n + 1) of equal height, taken as 100%, exhibit a valley between the peaks of X%, where X is normally 10%. The "peak width" definition, Equation 2b, is calculated from the mass of the peak in atomic mass units M and the peak width at Y% peak height (usually 5%) in the same units.

In practice, the resolutions calculated are effectively equivalent if the values for X and Y are taken as indicated. In many instances, Equation 2b is more convenient, because isolated peaks are often the only ones available for measurement purposes.

Mass spectrometers may be classified into three main categories with respect to resolving power.

Type	Resolution
Low resolution	150-500
Medium resolution	500-2,500
High resolution	2,500-50,000

For general GC-MS applications an MS with a resolving power of 1,000 will prove to be adequate for the large majority of samples. However, it must be appreciated that as the molecular weight of the solute increases, the number of compounds that can have nominally identical apparent parent mass numbers increases as well and can run into many hundreds. Hence it may be necessary to employ high-resolution spectrometers to differentiate between such species.[15]

2. Scanning Speed

The resolution obtainable from an MS depends in part upon the rate at which the spectrum is scanned. A normal mass spectrum is obtained by setting up a constant sample pressure in the ion source from a sample reservoir and scanning at a speed that is appropriate for the spectrometer and the degree of resolution required.

With GC-MS, however, the system is a dynamic one. The sample concentration in the ion source changes as the chromatographic elution band changes and hence the rate of scan is important if the spectra are to be compared with standard spectra obtained by equilibrium methods.

Leemans and McCloskey[16] have demonstrated this effect by considering the spectra obtained from two scanning rates on a sample of bis(trimethylsilyl)sebacate (Figure 4). The first spectrum illustrates the normal spectrum obtained from a fast scan (1.7 sec) at the elution peak maximum, while the second spectrum illustrates the effect of slow scanning (44 sec) on the same peak. The base peak of this compound is the M-15 ion at mass number 331, which spectrum 1 shows correctly while spectrum 2 indicates that it is a minor fragmentation ion. The figure shows that the intensities of the fragmentation ions vary as the instantaneous concentration of the eluate changes under slow scan conditions.

The above example illustrates the necessity for rapid scanning of the spectra so that the ion-source operating pressure remains sensibly constant for the duration of the scan. This is especially important when obtaining spectra from solute bands being eluted from capillary columns, where the duration of a peak may be as short as 1 to 2s. Alternatively, Kennett[17] has described a system where the amplifying system is tied to the total ion-current monitor so that by maintaining a constant total ion current a "true" spectrum is obtained from an elution peak.

Ultra-fast scanning can be deleterious to resolution. McFadden[18] has shown that resolution falls off appreciably as the scanning speed is increased (Figure 5). It would appear, therefore, that scanning speeds should be within the range of 1 to 3 sec per mass decade for low-resolution mass spectra. In view of the above, it would appear that high-resolution GC-MS is impossible to perform. Recent developments in instrumentation, and especially in computer interfaces, have nevertheless made it possible to obtain accurate mass numbers on GC eluates, but such systems are very expensive.

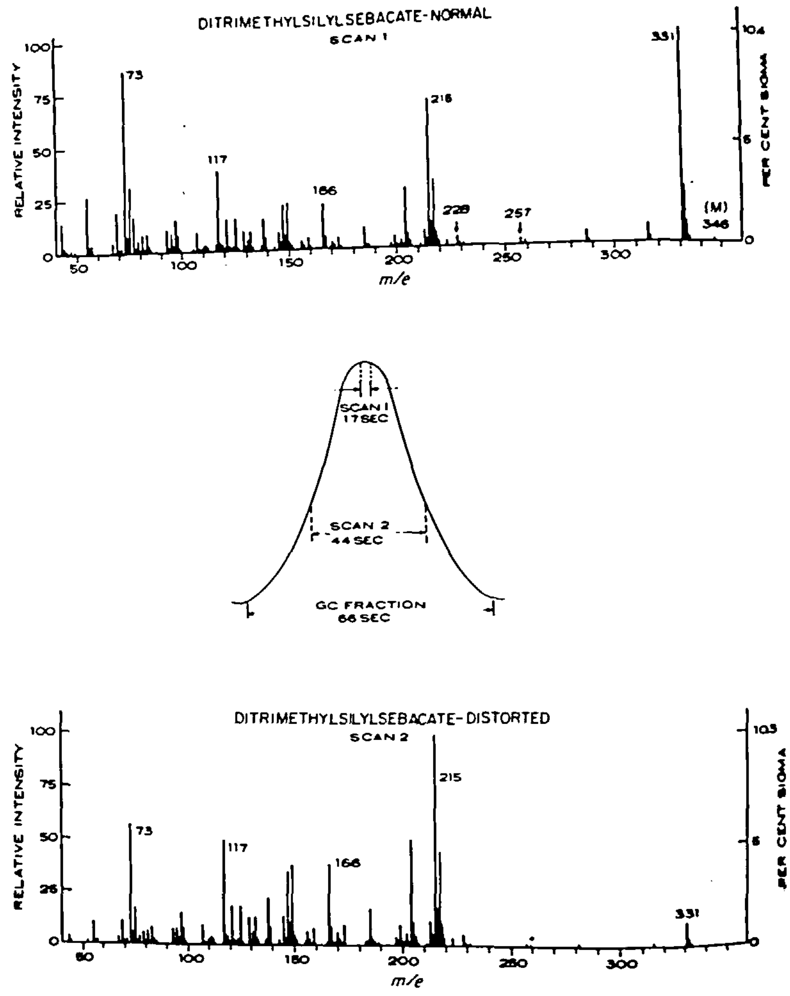

FIGURE 4. Effect of scanning time in relation to sample elution time: top – mass spectrum at nominally constant ion source pressure; bottom – distorted mass spectrum by changing sample pressure during scanning time.[16]

3. Pumping Speed

Mass spectrometers are usually pumped by a mercury or oil diffusion pump backed by a rotary pump. In a vacuum-tight system such a combination will, after out-gassing, produce a vacuum of the order of 10^{-7} to 10^{-8} torr. The time required to achieve such a vacuum depends on the pumping speed of the pumps and the throttling effect of the various connecting pipe-work and valves that are comprised in the total system. Many MS are constructed so that the ion source is pumped separately from the analyzer, the only interconnection between the two parts of the system being the final defining slit that has very low conductance. This type of MS is preferable to use in combination GC-MS, for higher pressures can be tolerated in the ion source than in the analyzer. Thus the last traces of carrier gas may be removed and excess sample pumped away, minimizing contamination of the analyzer.

IV. GC-MS INTERFACES

The performance of the GC-MS depends on the individual performances of its composite parts. The interface between the GC and the MS has a most important role to play and a careful consideration of the factors controlling its efficient operation is necessary to achieve optimum overall performance.

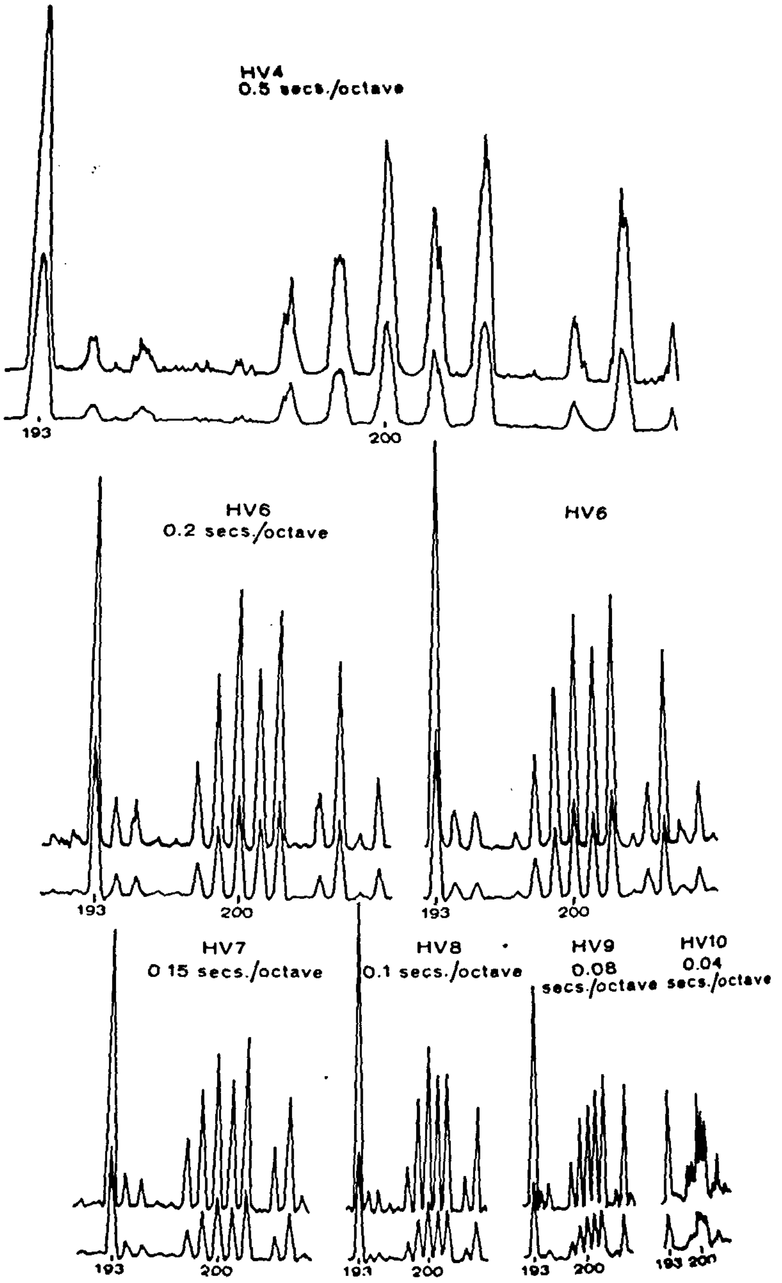

FIGURE 5. Effect of scanning speed on resolution. Hg$^+$ isotopes and other ions.[18]

Various points must be considered for producing the ideal separator, and these are detailed below.

First, it must be capable of reducing the pressure from 1 atm at the column outlet to 10^{-5} torr or less in the ion source of the spectrometer.

Second, it must provide an inert pathway by which solute molecules can be transferred unchanged into the ion source of the mass spectrometer without loss of chromatographic resolution.

Third, it must provide a means of preferentially or selectively removing the carrier gas, while allowing all the sample to pass into the ion source without any appreciable delay or holdup, i.e., increase the sample/carrier gas ratio.

The last factor may be expressed quantitatively in terms of the interface yield Y and the enrichment factor N:

$$Y = Q_{ms}/Q_c \tag{3}$$

$$N = Y \quad GC_c/GC_{ms} = Q_{ms} \times GC_c/Q_c \times GC_{ms} \tag{4}$$

Here Q_{ms} and Q_c are the amounts of sample entering the MS and leaving the column, while GC_{ms} and GC_c are the amounts of carrier gas entering the MS and leaving the column, respectively.

The design of the interface should be such that N is maximized. With certain separators (e.g., the jet and glass effusion), there are practical limits above which significant quantities of the sample are removed as well as the carrier gas. Nothing is to be gained by exceeding these limits.

Table 4 gives information on some of the separators reviewed in this article. Care must be exercised in comparing the data presented, because no definitive procedure is laid down for estimating separator performance. The values of N quoted are not precisely related because their determinations were undertaken using differing solute systems and performed in different ways. Nevertheless, the data presented indicate the orders of magnitude involved.

The choice of separator depends largely upon the type of sample under investigation and the chromatographic conditions necessary for achieving separation – particularly with regard to sample molecular weight and carrier-gas flow rate, which can markedly affect the performance of a given separator. Before considering these points further, it would be preferable to consider the principles by which the various separators operate.

A. The Jet Separator

The jet separator was developed by Ryhage in 1964[20,22] and is based upon the principles established by Becker.[21] The principle of the separation jet is illustrated in Figure 6. The gaseous column effluent, composed of solute molecules in a helium or hydrogen carrier gas, enters the separator through a convergent nozzle N, which terminates in a small orifice d_1. The gas is accelerated through the nozzle and emerges through d_1 as a high-velocity expanding jet. The orifice d_1 is aligned with a second orifice d_3 a short distance, d_2, away. The chamber B in which the two jets are situated is pumped. Because of the lower momentum and greater diffusivity of the carrier gas, it is preferentially deflected from its linear direction of travel and pumped away. Heavier molecules, because of their greater momenta, do not undergo as large deflections and hence pass through d_3 into chamber C. The vapor in C is thus enriched in the heavier component and in Ryhage's adaptation of this separator, C corresponds to the transfer tube leading to the ion source of the MS.

The Ryhage separator for GC-MS work consists of two separation jet assemblies in series. The two-stage system (Figure 7) is capable of accommodating high rates of gas flow. The separator is constructed of stainless steel and is mechanically very strong. It will withstand temperatures in the order of 350°C. The geometry of the system has been thoroughly investigated to optimize its performance,[22] and the following dimensions (in mm) apply:

$$d_1 = 0.1, l_1 = 0.15, d_2 = 0.24, d_3 = 0.24, l_2 = 0.5, d_4 = 0.3$$

The first stage of the separator is pumped by a mechanical pump and the second stage, by an oil-diffusion pump. In a commercial instrument[23] the first stage of the separator is connected directly to the column outlet, which means that the column operates at subambient pressures typically in the range of 300 to 700 torr, depending on the carrier-gas flow rate.

With low rates of carrier-gas flow, <10 ml/min, it usually suffices to operate a single-stage separator;[22] if the double-stage separator is the only one available, make-up gas must be added to ensure adequate performance.[24]

It is therefore apparent that the separator efficiency is flow-dependent. Its performance becomes less efficient as the rate of flow of gas decreases. Enrichment increases as the molecular weight of the solute increases. This type of separator has been used to good effect in the analysis of high-molecular-weight materials (see Section V).

Recently, a single-stage separator has been described that incorporates a control for adjusting the jet separation in situ to accommodate carrier-gas flow rates in the range of 1 to 20 ml/min helium[45] (Figure 8). A further potential advantage of this separator lies in its ability to cope with

Characteristics of Some Molecular Separators

Separator type	Originator	Year	Yield %	Enrichment	Flow rate range ml/min	Delay time sec	Max. operating temp. °C	Remarks	Ref.
Jet double-stage	Ryhage	1964	50	40-86	1-60	None	350	Dependent on mol wt	19
Jet single-stage	Ryhage	–	–	–	1-10	None	350	–	60
Jet variable	Edwards Instuments	1970	20-50	10-55	1-30	None	350	Jet separation can be altered to accommodate varying flows	48
Porous glass	Watson and Biemann	1964	40-60	5-50	1-100	Negligible	250-350	Dependent on seals used Dependent on mol wt	26
Teflon® capillary	Lipsky, Horvath, and McMurray	1965	50	1-5	2-30	Significant 20-30	280	Serious delay time–has to be operated between 250-280°C	33
Silicon membrane double-stage	Llewellyn and Littlejohn	1968	50	10^5	1-50	Variable	250	Dependent upon gas flow and temperature	38
Silicon membrane single-stage	Williams	1969	NA	NA	1-100	Variable	250	Dependent upon gas flow and temperature	39
Porous silver I	Cree	1967	50	2-100	1-50	Negligible	350	Dependent upon mol wt	36
Porous silver II	Blumer	1968	50	4-24	1-10	Negligible	250	–	37
Variable conductance	Brunnee	1969	30	10-60	1-100	Negligible	350	Dependent upon position of disc	44
Silicon coated silver	Teranishi	1969	40	10^5	1-5	Variable	225	–	42
Porous stainless steel	Krueger and McCloskey	1969	40	100	5-30	Slight	360	–	35
Membrane + Silver disc	Grayson and Wolf	1970	50	2-40	5-60	Noticeable	250	–	43
Microporous silver	Grayson and Levey	1971	20-60	2-10	2-7	Negligible	250	Dependent upon solute type and mol wt	50
Palladium	Lovelock, Simmonds, and Shoemake	1970	100	∞	Dependent on length of capillary	Negligible	150mm-350	(Can bring about selective (hydrogenation, and is (subject to poisoning by (sulfur compounds but (regenerable	45
Palladium cell	Lucero	1971	100	∞	Dependent on length of capillary	Negligible	200-250		51

Note:

1. The data quoted in this table are not strictly comparable. Very often the yield and enrichment are dependent upon the solute used and on the carrier-gas flow rate, so that the figures quoted are, of necessity, approximate.
2. NA = Not available.

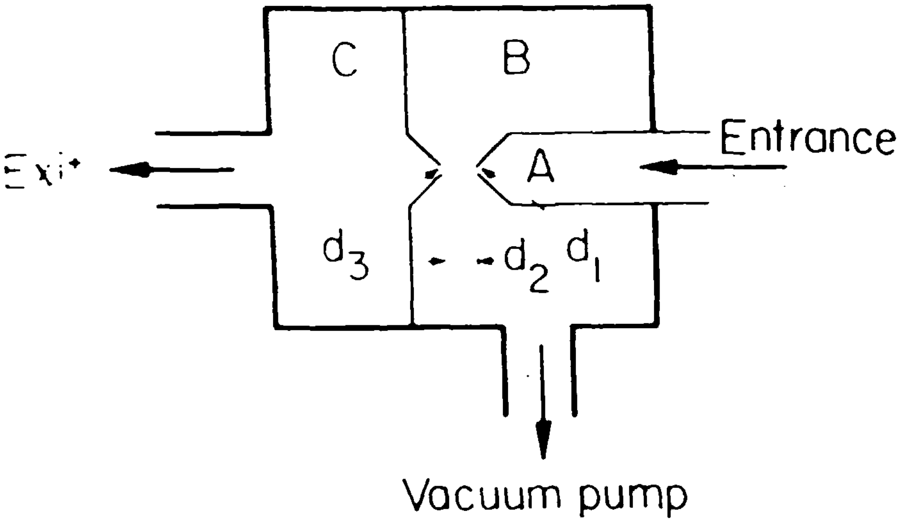

FIGURE 6. Principle of the molecular separator designed by Becker.[21]

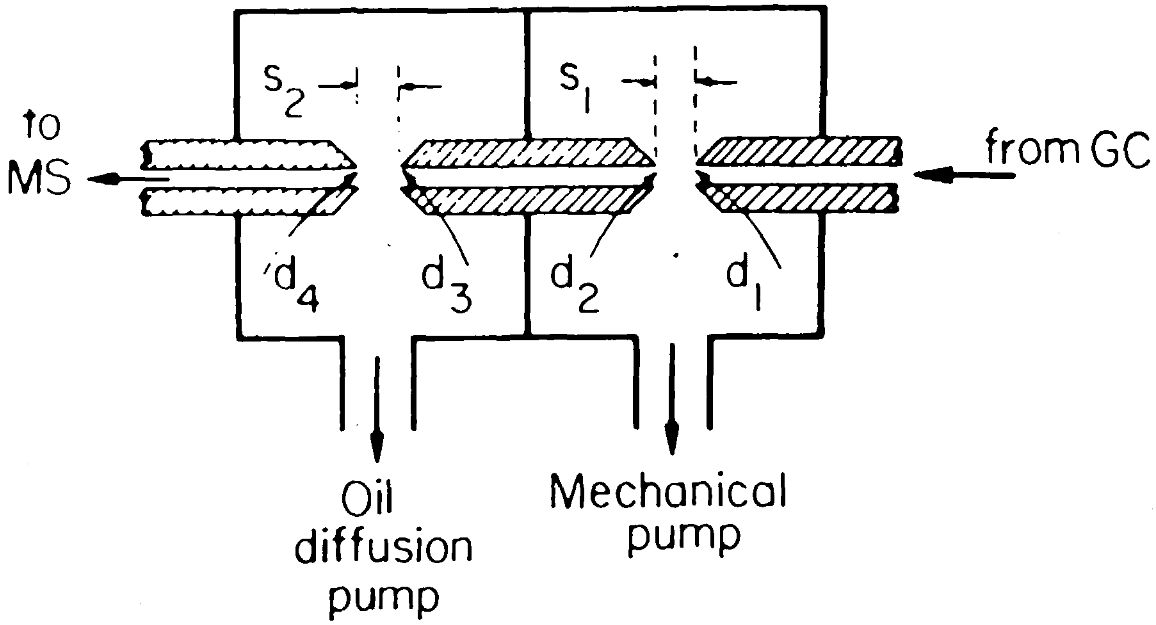

FIGURE 7. Ryhage two-stage jet separator.[22]

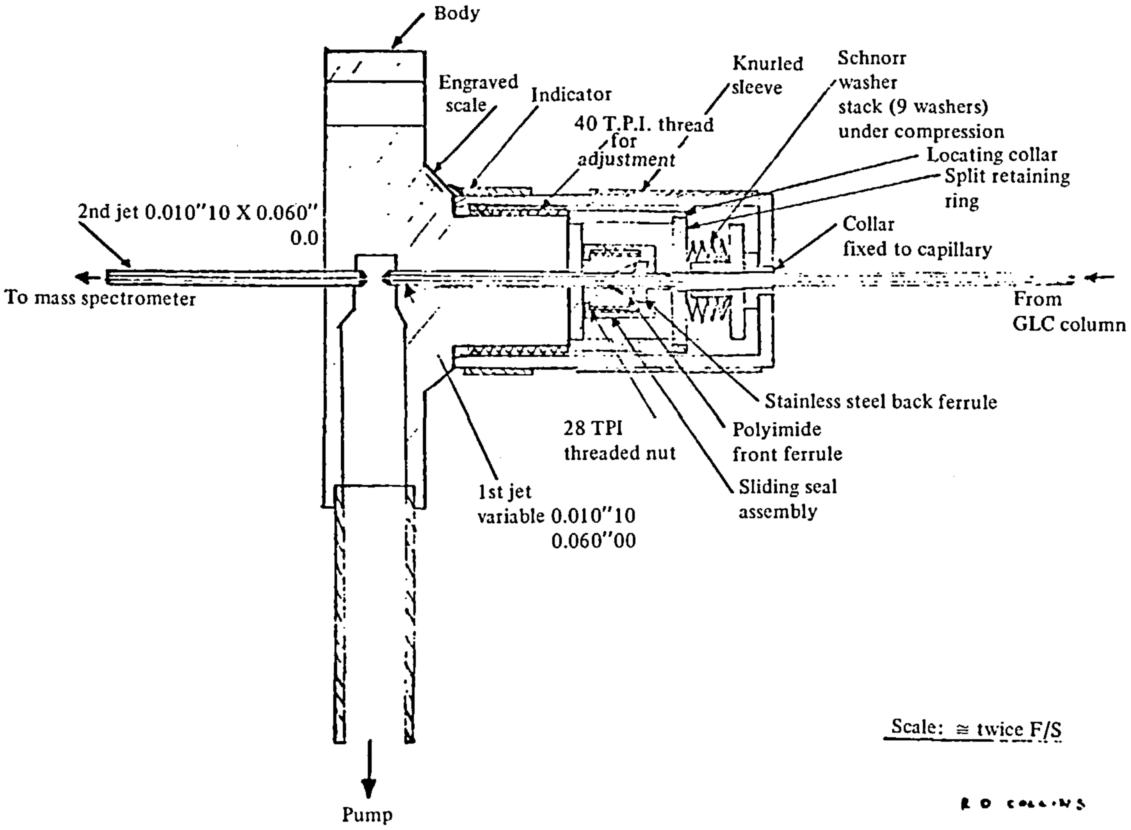

FIGURE 8. Adjustable jet separator.[45]

flow-programmed[46] chromatography in the range quoted. This application could be particularly useful for the transfer of low-molecular-weight compounds, which in the normal jet separator are largely pumped away.

The advantages of the separator are summarized below:

1. Small dimensions
2. Robust
3. Small effective dead volume
4. Little loss in GC performance
5. Good enrichment of sample
6. Low memory
7. Apparently small thermal effect
8. High maximum operating temperature

B. The Porous Glass Separator

The porous glass separator devised by Watson and Biemann in 1964[6] is the first member of a family of separators whose operating principle is the preferential effusion of the carrier gas through a microporous structure. The first Watson-Biemann separator was constructed from a fritted glass tube with a pore size of 5 μ. Restricting capillaries with diameters of 0.1 and 0.12 mm were attached to the ends of the fritted glass tube for throttling the GC exit gases and entrance to the MS, respectively.[6] A modified separator constructed from a glass frit having a pore size of 1.0 μ with entrance and exit capillaries of 0.2 and 0.1 mm diameter, respectively, was developed in 1965.[25] Figure 9 is a diagram of this second separator.

The optimum diameters of entrance and exit capillaries for this separator depend mainly on the pumping speeds of the fore pump and the mass spectrometer. Hence it is difficult to specify precisely the restrictions required. Probably the best method is to collapse the glass capillary (continuously) until optimum enrichment and operating pressures are attained.[25]

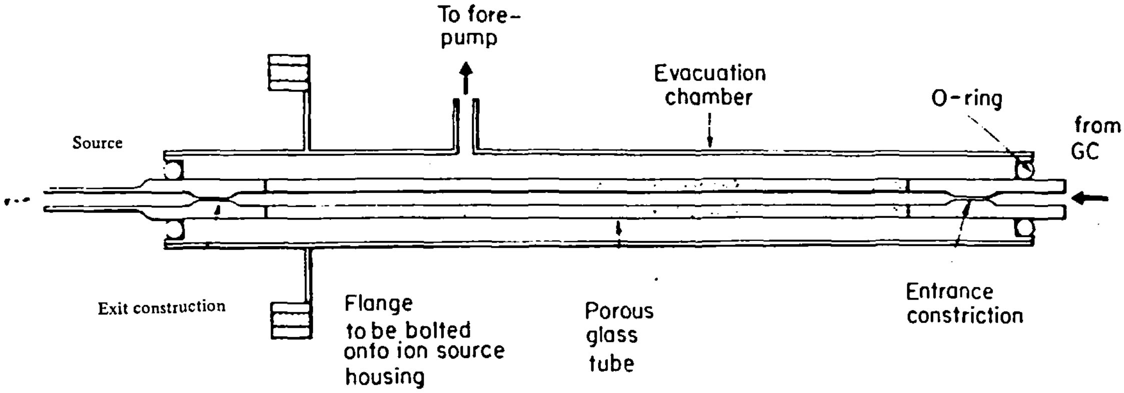

FIGURE 9. Watson-Biemann[25] fritted glass separator.

The entrance constriction controls the flow rate from the GC column and the mean pressure inside the separator. The process of effusion through fine pores occurs under molecular-flow conditions, and hence precise control of the entrance constriction is essential. The exit constriction effects the second pressure drop and controls the operating pressure of the ion source and hence the efficiency of the system.

The enrichment factor of this separator depends on the difference between the molecular weights of the carrier gas and the solute; the greater the difference, the greater the yield. Thus this separator is not to be recommended for the enrichment of low-molecular-weight compounds.

A two-stage design has been used[26] and has shown enrichment factors of about 400 for a solute of molecular weight 250 units. This two-stage model was capable of dealing with rates of carrier-gas flow in the range of 20 to 60 ml/min. For capillary-column effluents the single-stage model is recommended.

The advantage of the Watson-Biemann separator lies in its all-glass construction, which renders it suitable for the transfer of materials that may suffer thermal decomposition or rearrangement on heated metal surfaces. Adsorption of highly polar materials has been noted,[26] but the extent of this may be minimized, if not completely eliminated, by careful treatment of the glass surfaces with organic solvents followed by mineral acid and final treatment, after washing and drying, with a silanizing agent.[27]

In situ silanization has been carried out with some success by injecting 0.1 ml of bis(trimethylsilyl)acetamide into the separator held at 150°C. This technique appears to have no deleterious effect upon the ion source of the spectrometer.[28]

The range of operating temperatures of the Watson-Biemann construction is restricted to about 250°C by the presence of the Viton O-ring seals. A possible improvement used by the author involves the use of glass-to-metal seals.[29]

C. The Teflon® Capillary Separator

Details of this separator were published in 1966 by Lipsky, Horvath, and McMurray;[30] its construction is shown schematically in Figure 10. The separator is of simple design and is easy to construct. It consists of a length (5 to 10 ft) of 0.005-in. Teflon® capillary tube (0.020 in. o.d.) supported in a heated evacuated chamber. A pressure drop is effected at each end of the tube by means of capillary restrictors of 0.010 in. i.d. and 4 ft in length. The temperature of the Teflon® tube is controlled between 270 and 290°C. Care must be taken to ensure that these temperature limits are not exceeded. Below 270°C, the permeation rate for helium falls rapidly until, at 250°C, the capillary is essentially a direct connection between the column outlet and the ion source. Above 290°C the Teflon® starts to soften, and pinhole leaks are formed with complete loss of helium and sample. The change in helium permeation with temperature can be used to advantage to accommodate various carrier gas flows.

In many ways, however, the Teflon® separator is unsatisfactory for general use. Delay times of 20 to 30 seconds can occur between the emergence of the solute from the column and its appearance in

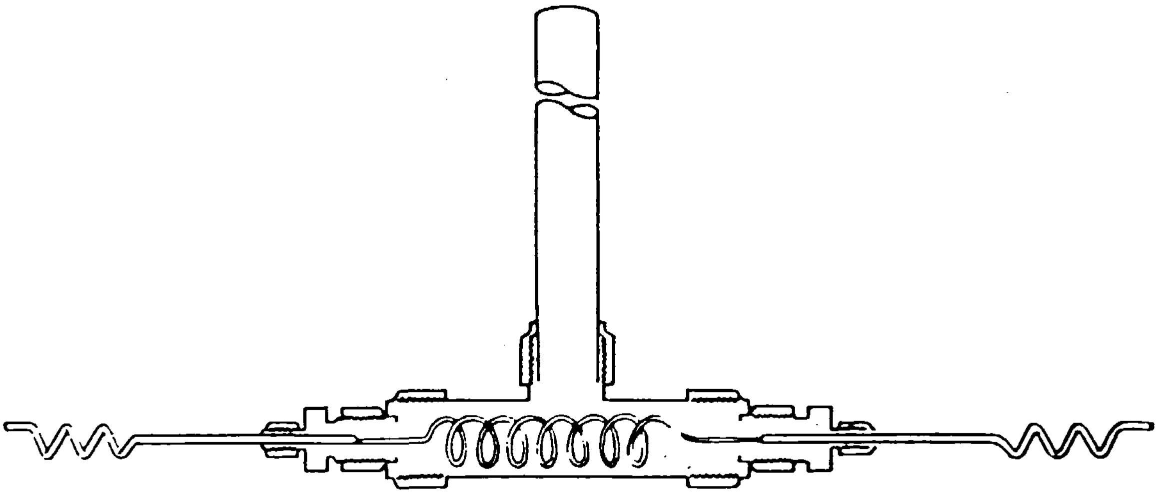

FIGURE 10. The PTFE capillary separator. From lipsky et al.[30]

the spectrometer. Such delay times are unacceptable, particularly with complex mixtures. A further problem arises when reactive compounds, such as silyl halides, are transferred. These can interact with the Teflon® and halogen exchange occurs.[31]

D. The Porous Stainless Steel Separator

Details of this separator were published by Krueger and McCloskey[32] in 1969; a diagram is shown in Figure 11.

This separator is similar in concept to the fritted-glass separator, and it also depends upon preferential effusion of the carrier gas for enrichment. The porous stainless steel tube is 4 in. long, has an o.d. of 1/2 in. and a wall thickness of 1/8 in., and can be obtained in a variety of pore sizes, the smallest being about 0.1 μ. The construction of the separator is such that it is easily demountable for cleaning purposes, and the effective length of the porous tube can easily be changed so that different rates of carrier-gas flow can be accommodated. The inlet restriction is constructed from a length of stainless steel capillary tube; the exit tube has an o.d. of 1/4 in. with a variable constriction in the form of a fine metering valve. It is advisable to silanize the separator (thoroughly) with BSA prior to use.

This separator is of rugged construction, and can readily be made in a laboratory. It requires no critical alignment and can be heated over a wide range of temperatures.

E. The Silver Membrane

Three forms of this separator have been described;[33,34,47] they differ principally in the construction of the interface. All of the forms operate by preferential effusion of the helium carrier gas through the pore structure of the membrane.

1. The form of silver membrane described by Cree[33] utilizes 2 porous silver discs (0.2 μ pore size) separated by a spacer holding the inlet and exit capillaries. This arrangement is clamped between two stainless steel flanges that have concentric pumping ports (Figure 12) and are connected to a mechanical pump.

The entrance and exit capillaries are adjusted so that molecular flow conditions exist in the separator chamber. As would be expected from the separating principle, enrichment and yield increase with increasing molecular weight.

The separator is robust and simple to construct, and it can be readily dismantled for repair or modification. Because it is of all-metal construction, it can be baked to high temperature. It does not show any preferential retardation of olefinic compounds, but little work appears to have been published on this separator.

2. The second form of silver membrane separator was described by Blumer[34] in 1968. It is a very simple construction and may be assembled from pipe fittings normally available in a laboratory (Figure 13). The crosspiece of the T is the

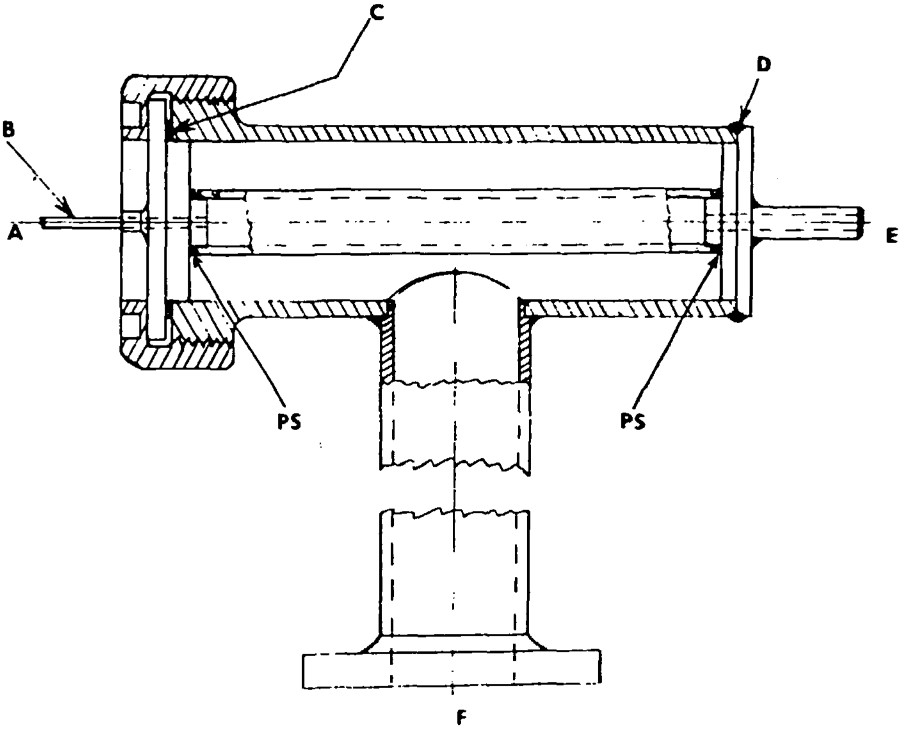

FIGURE 11. The porous stainless steel separator.[32]

direct link between the column and the ion source, and flows are controlled with two metering valves. The stand of the T contains a small silver membrane (pore size 0.3 μ) wedged into position. This separator has been shown to operate satisfactorily with a number of different solute types. Again, no preferential retention of olefinic materials has been noted.

3. Grayson and Levey have recently described a microporous silver separator[47] for use with capillary columns. This separator is of very simple design and quite robust (Figure 14). The area of silver surface exposed to the gas flow is about 25 mm^2 and the separator has an internal volume of only 15 μl. This separator has been shown (by the designers) to perform very satisfactorily with minimal loss in GC resolution and virtually zero time-lag and holdup.

F. The Silicone Rubber Membrane Separator

The first form of this separator was described by Littlejohn and Llewellyn in 1966.[35] A diagram of it is given in Figure 15.

The mechanism of sample enrichment depends upon the preferential solution of organic compounds in the conducting silicone rubber membrane, which forms the interface between the GC and MS. Helium and other inorganic gases are virtually insoluble in the membrane and hence pass over its surface.

The separator described by Llewellyn and Littlejohn was a two-stage device designed so that the column effluent at ambient pressures impinged upon the surface of the first membrane. The organic material passed into solution in the membrane and the depleted carrier gas was allowed to pass out of the separator to a normal GC detector, where residual solute was detected in the normal way. The dissolved organic material diffuses through the membrane to the pumped second stage. The small amount of helium that manages to pass the first interface is thus removed and the remaining sample passes through the second membrane and into the ion source of the MS. The principal disadvantage with this design of interface was the appreciable time-lag involved in passage through two membranes, but for high rates of carrier-gas flow (>20 ml/min) it is to be preferred.

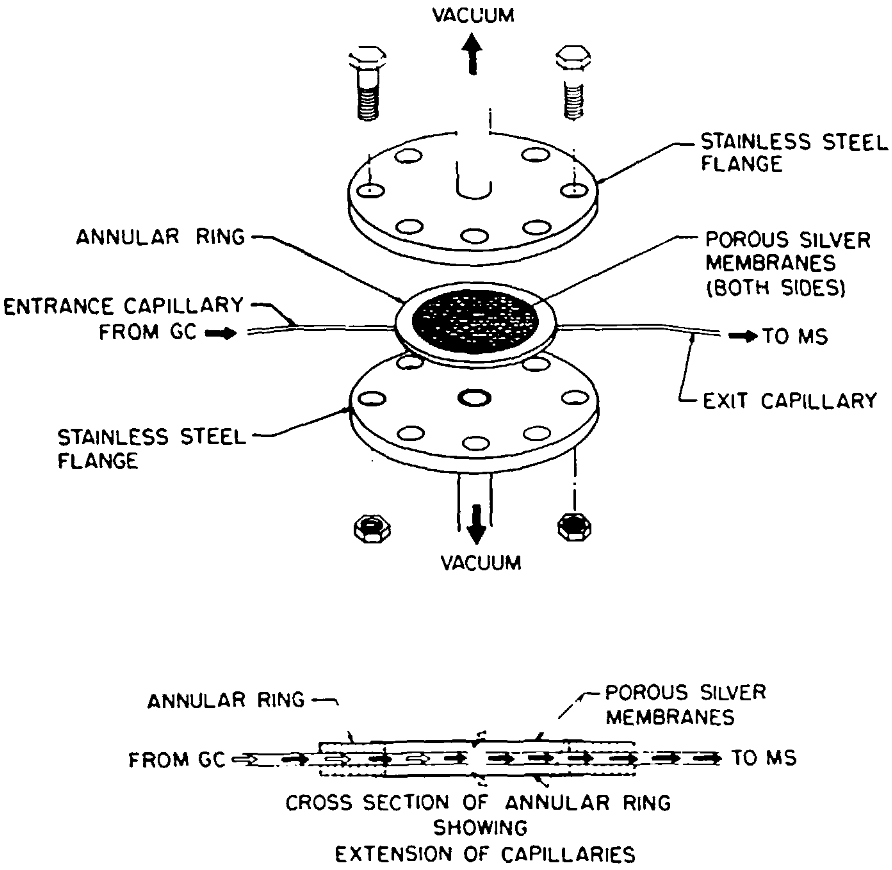

FIGURE 12. The silver disc separator,[33] type 1.

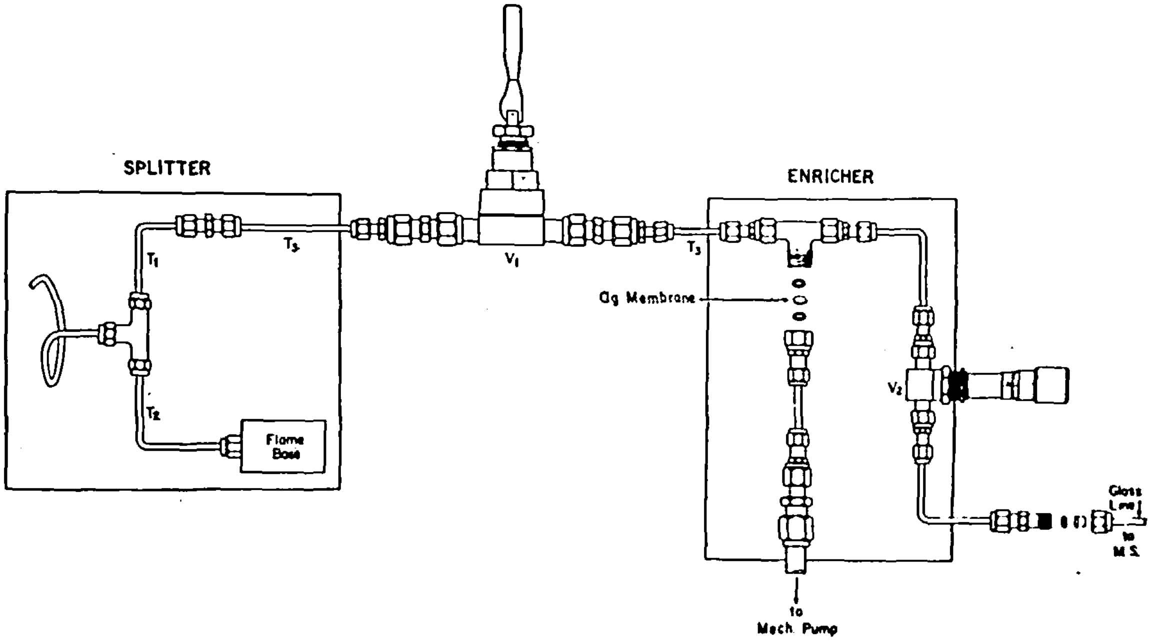

FIGURE 13. The silver separator T,[34] type 2; t_1 = 11 cm, 1/8 in. o.d., 0.047 in. wall tubing packed with 100 to 120 mesh glass beads; t_2 = 3 cm, 1/8 in. o.d., 0.049 in. wall tubing; V_1 = shutoff valve; V_2 = bellows metering valve. Standard couplings and T pieces used throughout.

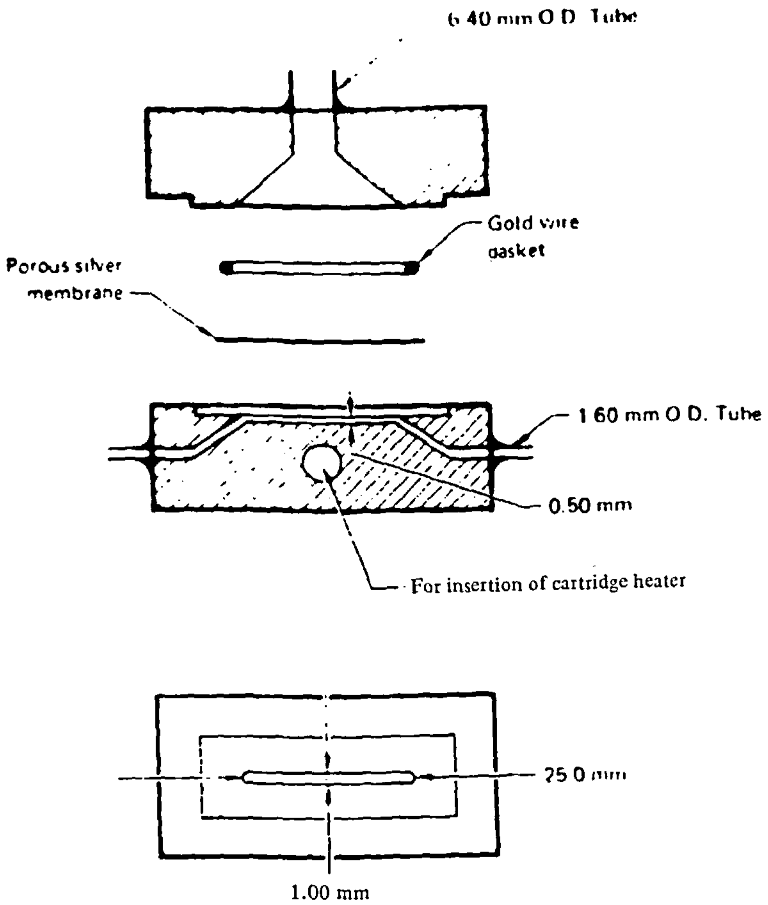

FIGURE 14. Micro-silver membrane separator. From Grayson.[47]

For low carrier-gas flow rates the single-stage separator constructed entirely of glass, described by Williams et al., is to be preferred[36] (Figure 16). With this device a membrane area of only 15 mm^2 is exposed to the GC effluents; sample transmission is high, but varies inversely with the carrier-gas flow rate. This form of membrane separator is to be preferred for the effluents from capillary columns and packed columns of 1/16 in. o.d. Because of its low internal dead volume, little loss in GC resolution was observed and the separator proved to be capable of transferring highly polar materials without loss in performance.

Williams et al. also incorporated in the system a bypass valve for venting unwanted components (such as solvents) away from the spectrometer.

Gough and Simpson[37,38] have constructed a similar type of separator from stainless steel (Figure 17). They have incorporated into the design a simple six-port pneumatically operated valve before the separator so that the unwanted components can be deflected away from the separator and hence the MS (Figure 18).

The effect of temperature upon the separator is to reduce the yield of the device with increasing temperature. Ideally, the membrane should be kept at or below the boiling point of the solute to obtain about 70% transmission.[35] If the temperature is too low, holdup (absorption) and tailing will occur. Hence the ideal situation for the separator is inside the column oven,[36] where it can follow changes in the column oven temperature. However, it is often preferable, especially when undertaking quantitative measurements, to contain the separator under isothermal conditions to prevent changes in ion-source pressure, which, under temperature-programmed conditions, will rise due to the increased permeability of the membrane to the carrier gas.

At high temperatures (250 to 300°C) the membrane will emit organic vapors (which, when

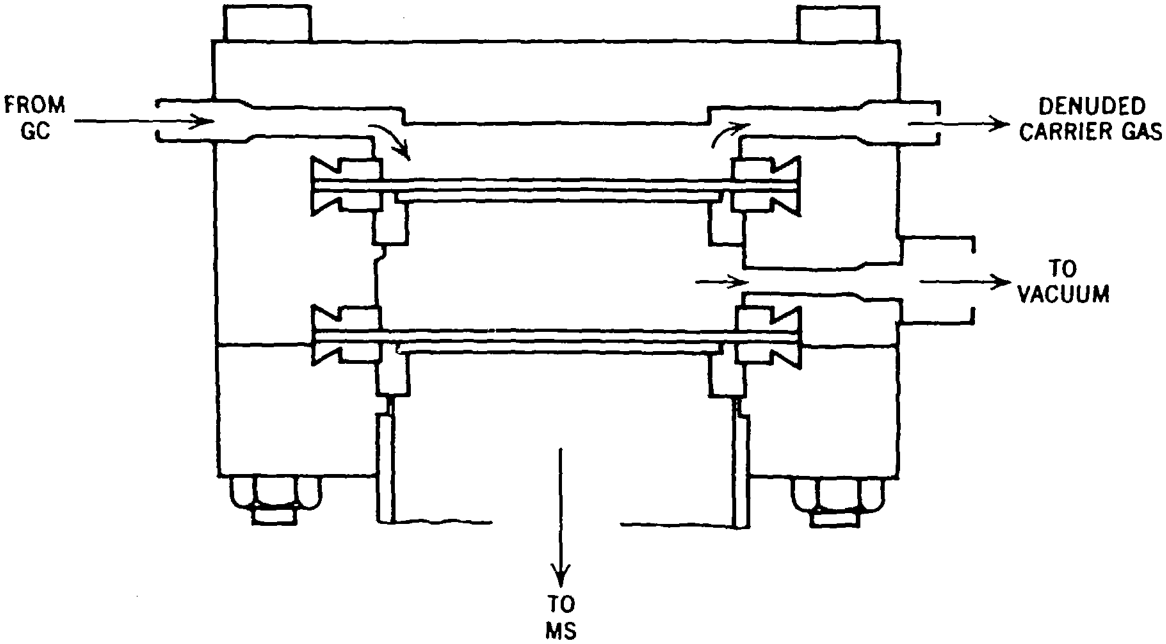

FIGURE 15. Double-stage silicone rubber membrane separator. From Liewellyn.[35]

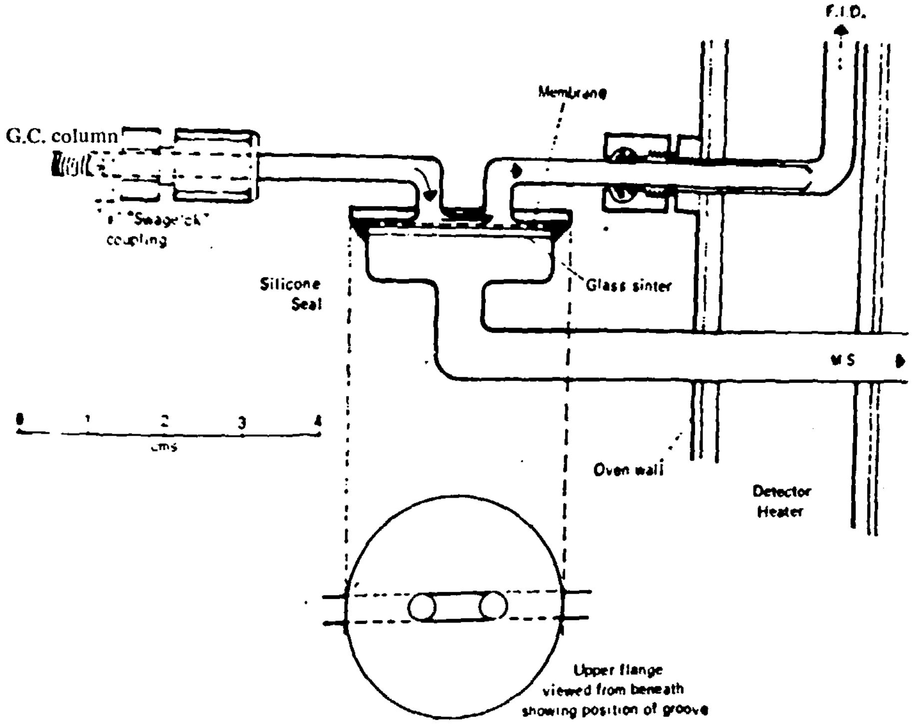

FIGURE 16. All-glass micro-silicone membrane, From Williams et al.[36]

recognized, can provide useful markers in the mass spectrum) and extended operation above 250°C will bring about deterioration in performance. However, this should not detract from the advantages of this particular separator. It is particularly useful, in that it allows the GC column to operate with its outlet at atmospheric pressure over a wide range of rates of flow of gas, and it does not require the use of one particular carrier gas. Furthermore, the design is such that it is readily dismantled so that, if the transmission of organic vapors falls off with time and prolonged use at high temperatures, a new one can be installed with ease.

G. Coated Silver Membranes

A variation on the silicone rubber membrane has been described by Teranishi et al.[39] In this device a porous silver disc 0.002 in. thick with 0.2-μ pores is coated with a solution of 60% phenyl-40% methyl siloxy comonomer, and this is allowed to polymerize on the surface of the silver. The resulting membrane was contained in a suitable holder (Figure 19) and conditioned at 250 to 300°C. Subsequent use of this device indicated good enrichment. Very little bleed of the silicone was noticed at 225°C.

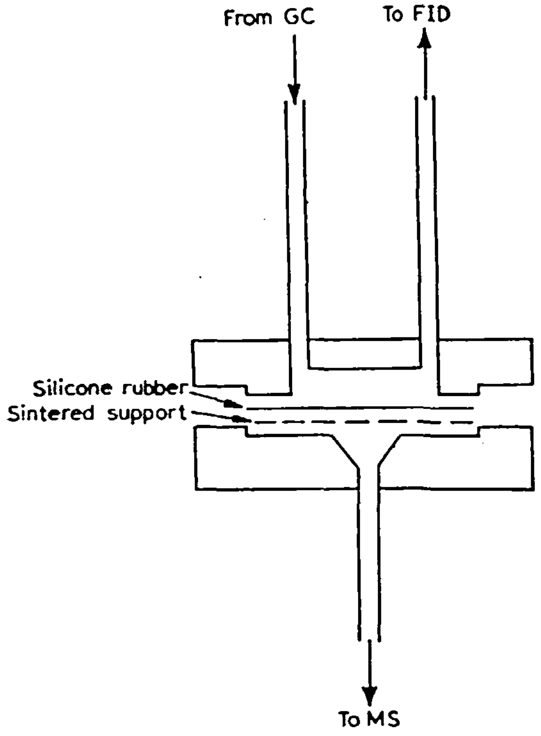

FIGURE 17. Stainless steel micro-silicone membrane separator.[37]

H. The Combined Porous Silver and Silicone Membrane

Grayson and Wolf[40] have recently described an interesting combination which they claim to be useful over a range of carrier-gas flow rates while the GC outlet is maintained at atmospheric pressure.

Figure 20 is a schematic diagram of this device. It consists of a combination of a single-stage silicone membrane described in Section F and the second form of porous silver membrane. The authors describe the operation of this system at various carrier-gas flow rates and temperatures, and they show that the yield varies between 40 and 60% with a sample enrichment between 2 and 40.

I. The Variable Separator

Brunnee et al.[41] described the construction of a simple separator that operates by preferential effusion of the carrier gas. It is of novel design and is shown schematically in Figure 21. The effluent from the chromatograph enters a circular path formed by two concentric knife edges and a coverplate with a very fine screw adjustment to control its distance from the knife edges. With the separator in the "closed" position (i.e., with the coverplate resting on the knife edges), 5% of the gas is pumped away at a flow rate of 1 ml/min; with the separator open, 99.9% is pumped away at a flow rate of 100 ml/min. As would be expected, the separator gives higher yields and greater enrichment with increasing molecular weight.

The flow path in the separator is short and hence problems due to sample decomposition and adsorption on the metal surfaces are minimized. In addition, the separator contributes little to loss in GC resolution. This separator is useful, in that it can accommodate a wide range of rates of flow of carrier gas, and hence any GC column system may be used with advantage. Because of its construction, the separator may be readily dismounted for cleaning purposes, and it may be baked to 350°C. However, the knife edges are somewhat susceptible to damage.

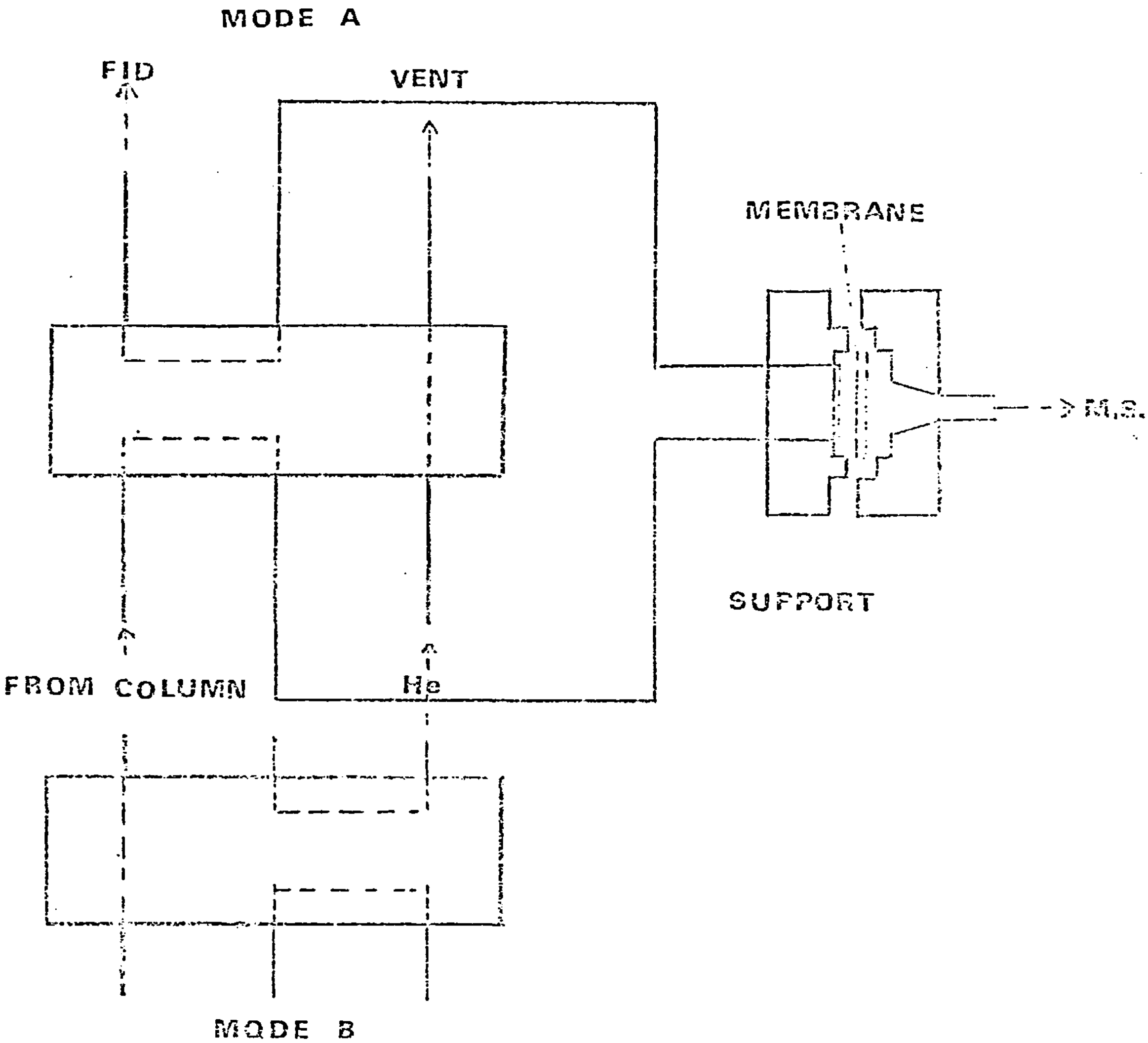

FIGURE 18. Valving system with micro-silicone membrane separator.

J. The Palladium Separator

The separators so far described all suffer from one defect. This is that they operate by *preferential* removal of the carrier gas, and hence sample is also lost. The palladium separator described by Simmonds, Shoemake, and Lovelock[42] does not suffer from this defect, for it operates by the *selective* removal of the carrier gas, hydrogen, through the walls of a palladium/silver or gold alloy. Thus the yield of this separator is 100% and the enrichment factor described by Equation 4 can approach infinity.

The construction of this separator is shown in Figure 22. Provision is made for heating the palladium capillary, either directly by resistive heating or indirectly by winding the capillary around a cartridge heater or by heating the glass envelope. This envelope provides for an atmosphere of air or oxygen flowing at a constant rate over the palladium capillary. At about 200 to 250°C, hydrogen will selectively permeate the palladium alloy and pass through the walls of the tube. The oxygen, or the oxygen in the air, passing over the tube combines with the hydrogen to form water, which is swept away, and theoretically,[43] all the hydrogen may be removed from the column effluent.

The principal disadvantage of this separator lies in the possibility of catalytic reduction of solute molecules. This possibility has been investigated,

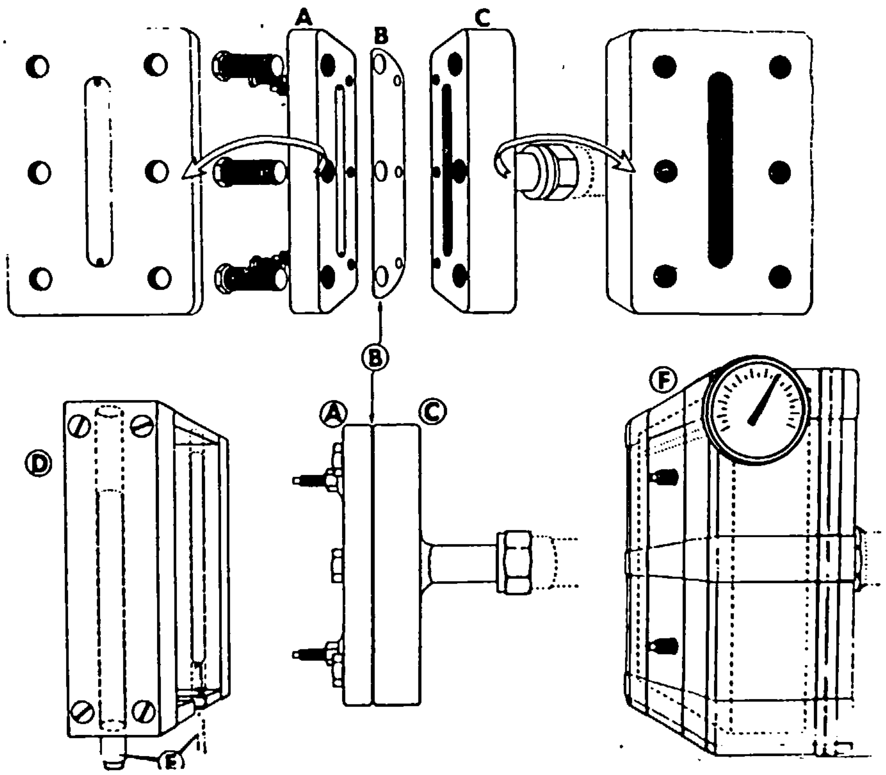

FIGURE 19. Coated silver membrane separator.[39]

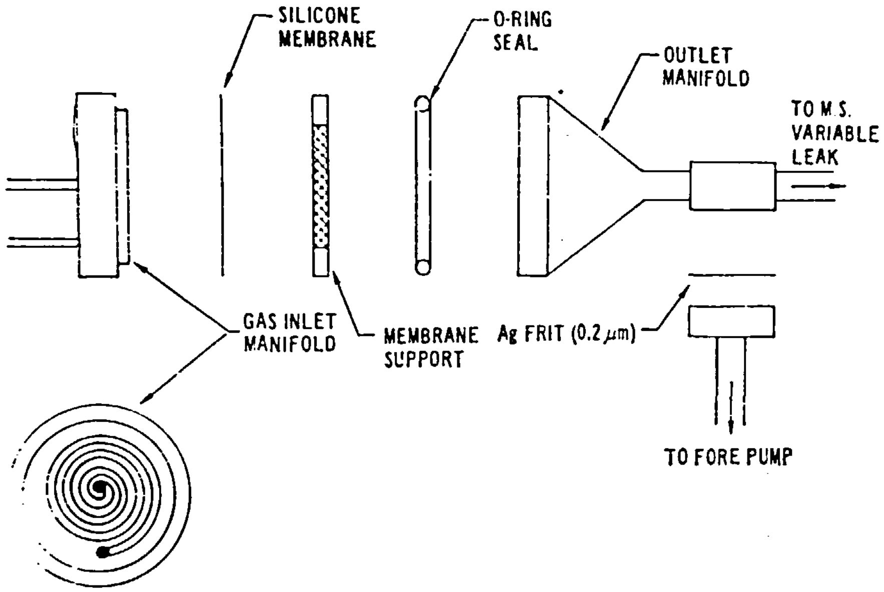

FIGURE 20. Porous silver/silicone membrane separator.[40]

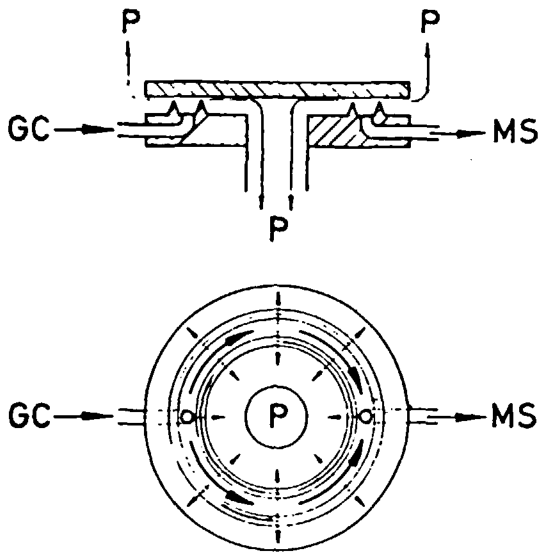

FIGURE 21. Variable separator.[41]

and its realization appears to be highly specific to certain types of unsaturation in the molecule.[42] However, further work is necessary on this point. A second potential disadvantage lies in the poisoning of the palladium surface by sulfur compounds, temporarily allowing hydrogen to break through to the MS. In spite of these disadvantages, the palladium separator is a robust device capable of transferring the entire sample to the ion source of the MS. As such, and with selected compounds that will not be affected catalytically, the separator provides a standard by which the performances of separators of other types may be evaluated.

Lucero[48] has shown that one of the limiting factors with the palladium separator arises from the efficiency and speed with which hydrogen is removed from the outside surface of the palladium tube. In order to provide an environment that will selectively remove hydrogen from the surface, Lucero has developed the electrolytic cell shown in Figures 23A and B, which illustrates the processes that occur in the electrolytic cell separator. The palladium capillary forms the anode of the system and the outer palladium tube forms the cathode. Hydrogen gas passing though the capillary is adsorbed onto the walls of the tube, through which it migrates as a proton and combines with hydroxyl ions derived from the electrolyte, a 66% solution of sodium hydroxide, to form water. On the inner wall of the external tube, water dissociates, and the protons migrate through the external walls to atmosphere. The potential difference of the cell can vary over the range 0.1 to 1.5 V and the cell can be operated up to about 200°C.

V. THE COMBINATION OF THE GC - INTERFACE - MS

There are several techniques employed to provide the necessary combination. The choice depends upon the facilities available in the individual instruments and the separator chosen. These are indicated briefly below for various combinations.

Nondestructive GC detector, MS without total-ion monitor (TIM) – The flow system for this method is illustrated in Figure 24. This method is the least valuable from the point of view of the information provided by the individual systems. Care has to be exercised to ensure that the GC detector will function adequately under conditions that can be subatmospheric. Further, the choice of detector must be such that there is no possibility of the sample components' being altered in character. For example, a thermal conductivity detector could bring about catalytic decomposition or rearrangement of the sample components on the hot wire detecting element. This technique is not recommended if it is possible to use one of the following methods.

Destructive or nondestructive GC detector, MS without total-ion monitor – The block diagram in Figure 25 describes the system employed.

In this case, the column effluent is split into 2 streams, about 90% passing to the MS and 10% passing to the GC detector.

This method of combination provides no information on the sample profile in the ion source of the MS and correlation of the peak identities may be difficult if the conductance ratio of the splitter lines is not known or if the performance of the interface system is unreliable. Nevertheless, this method is to be preferred over that described above.

MS used as a GC detector and component identifier – This system is similar to the first instrument described in this section, except that the MS acts as the detector for the column effluent as well as acting as the "identifier." The disadvantage of this method of combination lies in

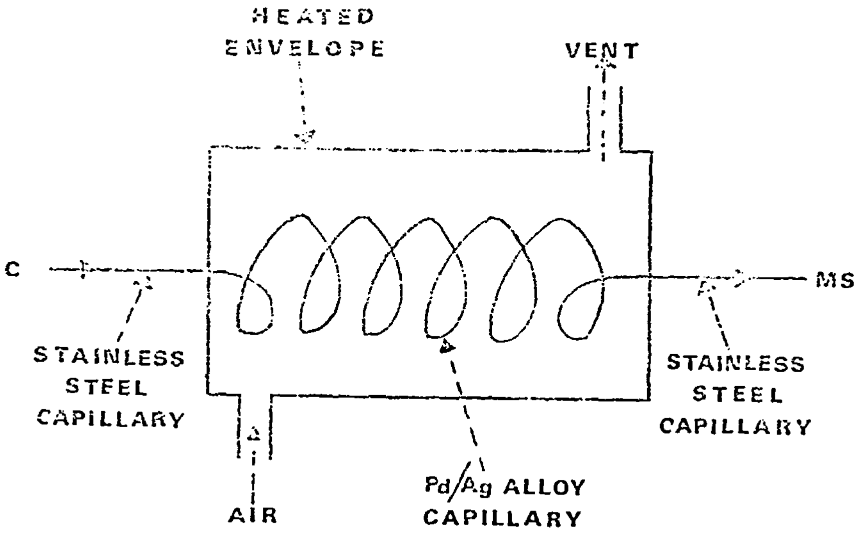

FIGURE 22. Palladium separator.[42]

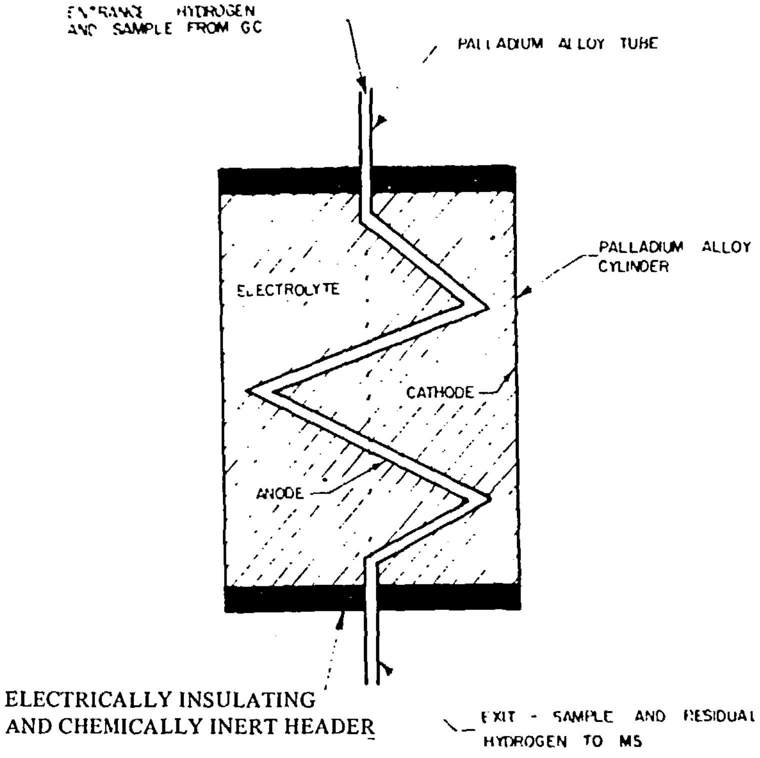

FIGURE 23A. Palladium electrolytic cell.[48]

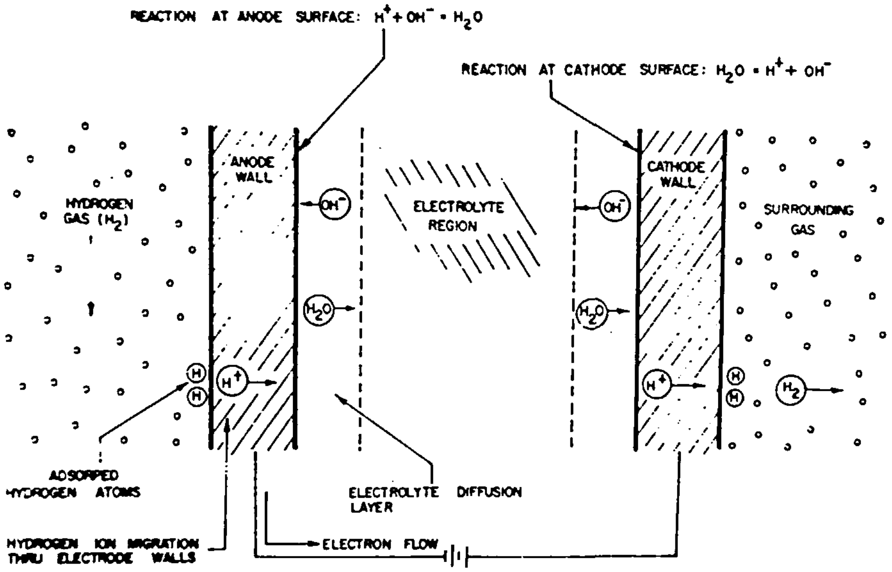

FIGURE 23B. Electrolytic cell reaction.

its inability to determine the extent of any loss in GC resolution brought about by the interface system (see Figure 26).

Combination of GC detector and MS detector/identifier – This system (Figure 27) provides the maximum of information about the analysis being undertaken.

The column effluent is split in a suitable ratio, such as 50:1. The smaller part passes to the GC detector and the larger, to the MS via a suitable separator. The total-ion monitor provides a second GC trace and enables any loss of GC resolution to be detected. Furthermore, the performance of the interface system can be monitored continuously and steps may be taken to modify conditions if required.

It can often be advantageous to include a valve between the interface and the ion source of the MS, in order that the individual instruments can be isolated for other work when not required in combination. It is essential that such a valve possess little if any unswept volume and be capable of holding a high vacuum.

VI. PERFORMANCE OF SEPARATORS

Section IV described the construction of a variety of different systems. In essence there are four different techniques by which the desired pressure drop may be effected:

1. Diffusion (jet type)
2. Effusion (porous membranes)
3. Solution (silicone rubbers)
4. Reaction (palladium)

In this section, the performance of the four types of separators will be discussed, bearing in mind the requirements given at the beginning of Section IV and the modes of operation indicated in Section V.

A. Jet Separators

A study of the literature indicates that, of all the various designs of separators described in Section IV, the jet separator has been the preferred interface for combined GC-MS of complex molecules. This has been due to a number of reasons. The jet separator is an excellent one, possessing minimum effective volume, time lag,

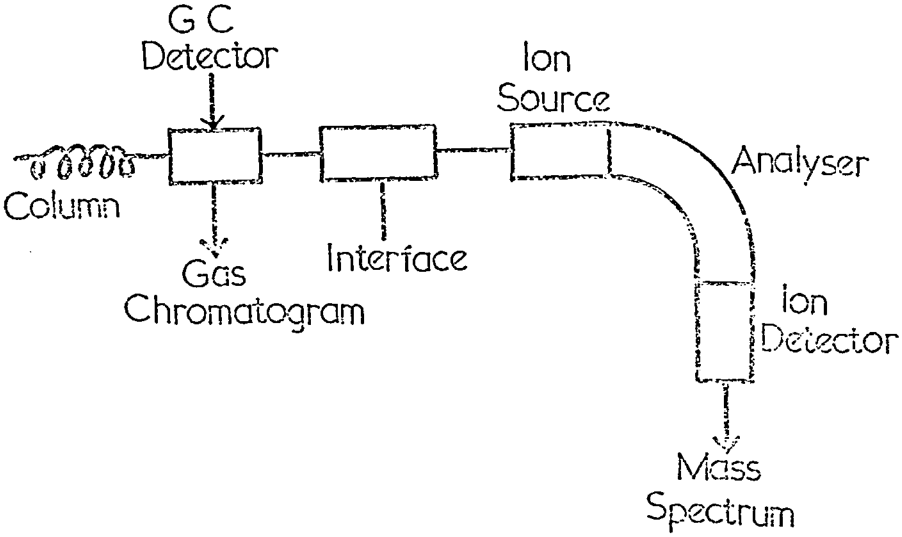

FIGURE 24. Coupling technique no. 1.

exposure to hot metal surfaces (in spite of its all-metal construction), and memory effect, and its efficiency is almost independent of temperature.

For successful operation the gas velocity at the jet must be greater than the velocity of sound, and hence the separator does not function well at low rates of flow of carrier gas (< 5 ml/min). To permit successful operation at such low rates, make-up gas must be employed. For flow rates between 5 and 15 ml of helium per minute, a single-stage separator may be used.[22]

The separator is normally connected directly to the column outlet, which therefore operates at subambient pressures, but it has been shown that this has no deleterious effect on column performance.[49] The presence of the solute in the effluent gas stream is detected by the total-ion monitor in a commercial system.[23]

Separator yield and enrichment vary with the molecular weight of the solute. The separator is ideally suited for the transfer of high-molecular-weight components (>200 mass units). Transfer efficiency starts to deteriorate below this figure, and the separator cannot be recommended for work with compounds of low-molecular-weight (below about 75) present in small amounts (<10 ng).

As indicated earlier, the variable jet separator that allows the jet gap to be changed at will by an external control could extend the range of molecular weights over which this separation mode could be used, and could also prove useful with the flow-programming technique.

In general, the jet type separator is an excellent interface, capable of transferring the column eluate into the ion source of the mass spectrometer quickly and efficiently, with little loss in GC resolution and minimal thermal or catalytic effects.

B. Porous Membrane Separators

The majority of the separators described in Section IV operate by the effusion principle. Enrichment is achieved by the preferential effusion of the carrier gases (usually hydrogen or helium) through the pores of the interface. Hence, as with the jet separator, yield and enrichment vary with the molecular weight of the eluting species. None of these separators operate well with compounds of low molecular weight, particularly at low concentration. The most common form of this separator is the glass frit first introduced by Watson and Biemann, but this is rather inflexible in its mode of operation: it does not cope well with radical changes in the rate of flow of carrier gas. A possible further disadvantage of this type of separator lies in the relatively large surface area, which is, of necessity, exposed to the column effluent. There is a tendency for adsorption to

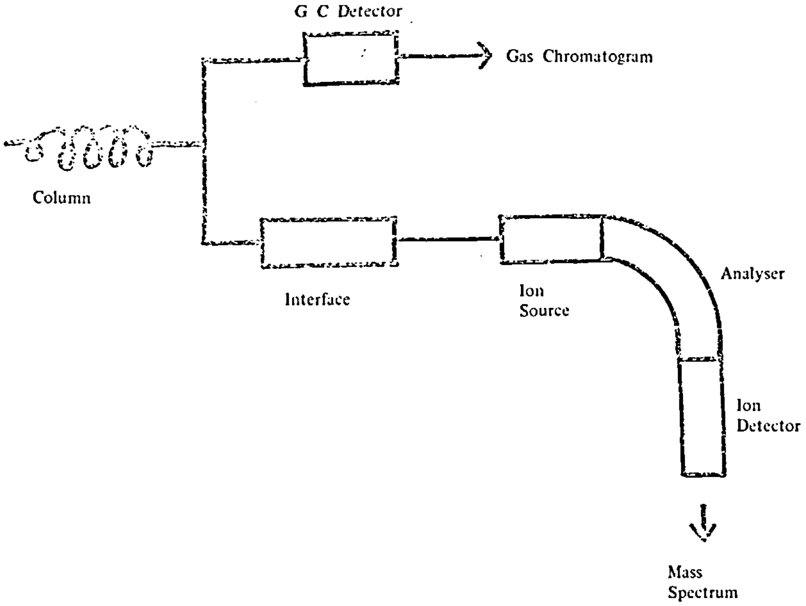

FIGURE 25. Coupling technique no. 2.

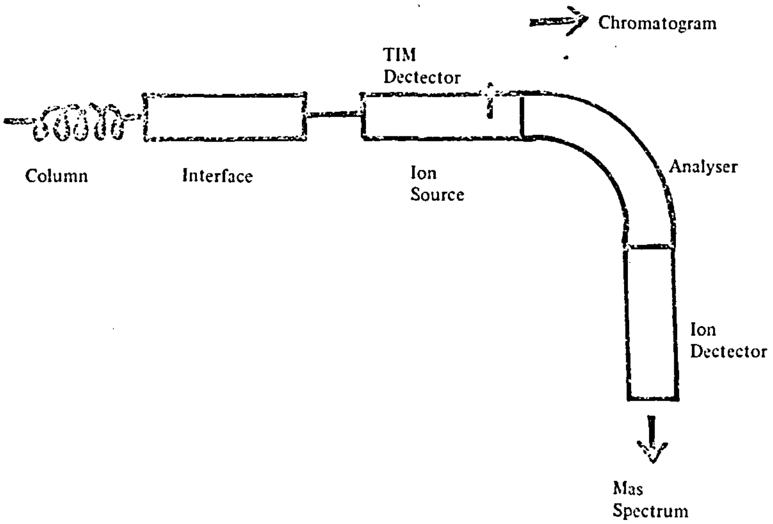

FIGURE 26. Coupling technique no. 3.

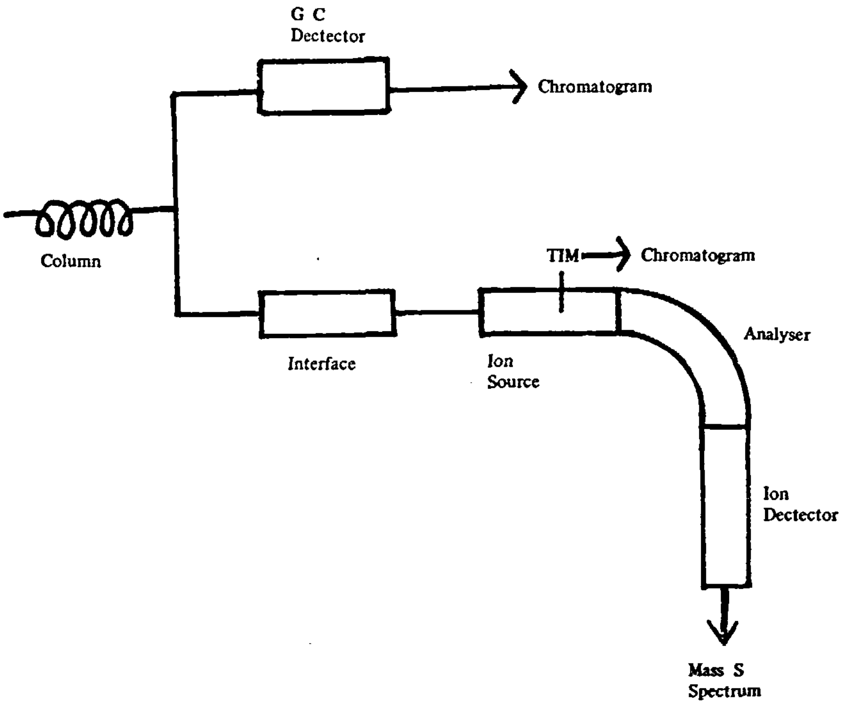

FIGURE 27. Coupling technique no. 4.

occur on these exposed surfaces, with attendant loss in GC resolution and sample holdup. However, this effect can be minimized by thorough silanization of all exposed surfaces.

The microporous silver separator designed by Grayson should be useful as an interface for capillary columns, but at the time of writing, only the original paper describing its construction and some applications is available.[47] The separator is simple to construct and has minimum dead volume; apparently no selective adsorption of olefins has been noticed.

The Brunnee[41] variable effusion separator is potentially more versatile than other effusion separators. Although the construction does not entail the use of a porous membrane, carrier-gas separation does occur by effusion at the narrow gap formed between the concentric knife edges and the adjustable cover plate. The facility of being able to adjust the separation between the cover plate and the knife edges imparts flexibility to the interface and enables it to cope with varying carrier-gas flows. At low rates of flow the interface yield is good (>60% below 4 ml/min) (Figure 28), but the yield diminishes rather rapidly with increasing rate of flow. Schomberg and Henneberg[50] have investigated the performance of this separator and have shown that, if due precautions are taken with respect to dead volumes, column efficiency is unimpaired, and the separator compared favorably with other effusion separators.

C. Solution Separators

All the designs of this form of separator depend upon the selective solution of organic molecules in the membrane followed by permeation through the membrane under the influence of the pressure difference.

Llewellyn and Littlejohn[35] have shown that sample permeation is controlled by the following equation:

$$P = SDA[(P_1 - P_2)/d]t \qquad (5)$$

where S = sample solubility, D = diffusion coefficient, A = exposed surface area, $(P_1\text{-}P_2)$ = pressure difference across the membrane, d = thickness of the membrane, and t = time.

Inevitably, there is a time-lag associated with mass transfer through the membrane that is a function of molecular dimensions and the temperature. The time-lag τ is related to the thickness of the membrane and to the diffusion coefficient by the expression[35]

$$\tau = d^2/6D \qquad (6)$$

In practice, permeation time is of the order of 1 sec, and this will have but a small effect on GC resolution. The separator designed by Williams et al.[36] and modified by Gough and Simpson[37] minimizes the quantity A in Equation 5; both systems can be installed in the GC oven, so that its operating temperature is optimized with respect to the eluting components (about 50°C below the boiling point of the solute).

In spite of the low solubility of inorganic carrier gases in the silicone rubber membrane, a small amount of gas will permeate the membrane. Williams has shown that the ion-source pressure increases with flow rate and temperature.[36] Transfer efficiency also varies with flow rate and temperature.[36] Figures 29 and 30 demonstrate that the amount of solute reaching the ion source decreases with increasing flow rate and operating temperature (due to decreased residence time at the membrane surface and to decreased solubility in the membrane). These data indicate the necessity of operating the interface at the lowest rates of flow and temperatures concomitant with obtaining satisfactory chromatography. If the temperature is too low, unacceptable adsorption and tailing will be experienced.[35]

The effects of increasing molecular weight and polarity on solute-transfer efficiency, holdup, and tailing have been shown to be small up to a molecular weight of about 250. Figures 31, 32, and 33 show FID and TIM traces on series of alkanes, fatty acid esters, and alcohols.[36] While tailing does increase with increasing polarity, it is sufficiently low not to interfere with the spectra obtained. However, the author has not succeeded in transferring materials having molecular weights higher than 300,[51] and this must be recognized as a limitation of this separator.

There can be no doubt as to the potential of the membrane separator. However, a fuller understanding of the mechanism of solute transfer through the membrane could lead not only to the production of membranes of better quality but also to the production of membranes that might be selective or even specific for individual classes of compounds.

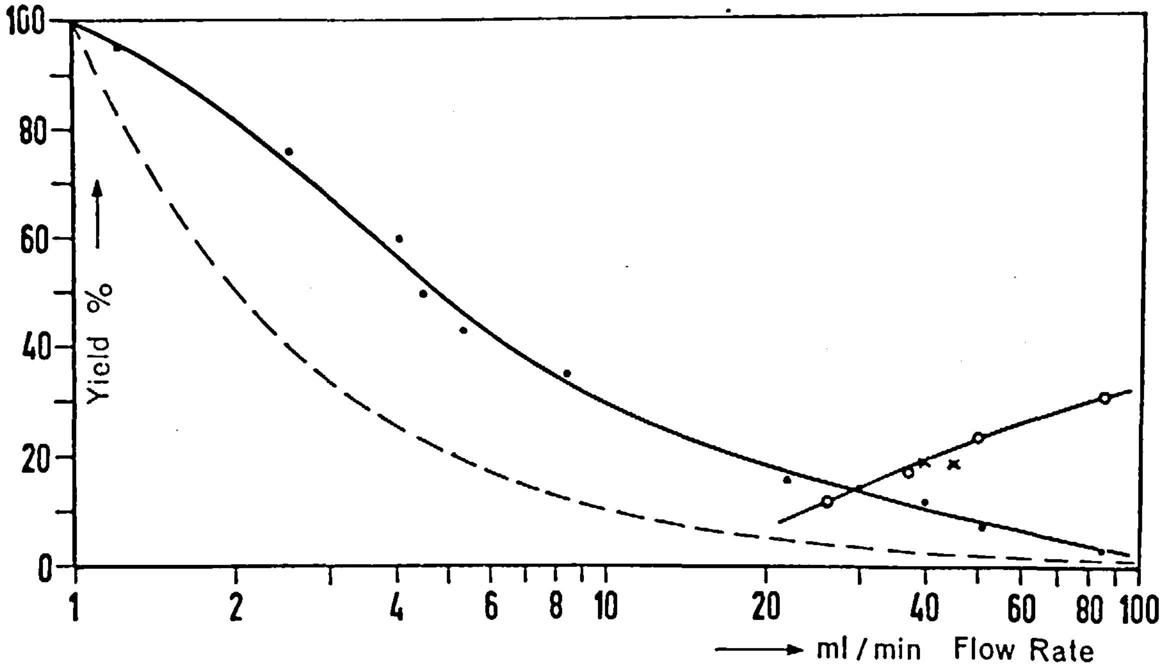

FIGURE 28. Separator yields for sample molecular weight 86 in helium: ——— = variable separator; $\frac{o \quad o}{o \quad o}$ = Watson-Biemann; - - - - = split without enrichment; and X X = values from literature.

D. Reaction Separators

The reaction separator based on the selective removal of hydrogen at a palladium-alloy interface is the only type of separator capable of giving 100% yield of the components with infinite enrichment. The interface is ideally suited for the transfer of trace components, provided that such components will not be reduced by the system.

Lovelock et al.[42] have investigated a wide variety of types of samples and shown that only substances containing activated double bonds are susceptible to reduction. Further work is necessary, however, to delineate precisely when reduction can be expected.

The separator also suffers from the disadvantage that the palladium alloy is poisoned by sulfur compounds and ethyl iodide, causing hydrogen to break through to the ion source. Hydrogen permeation can be restored by regenerating the palladium tube at 500°C for several hours.

The palladium separator is the only interface capable of transferring trace amounts of inorganic gases having low molecular weights to the MS without loss. If its deficiencies are appreciated it should prove to be a most useful interface.

VII. GC-MS APPLICATIONS

There are some 800 papers in the literature describing techniques in combination GC-MS and their applications. A comprehensive list covering the period 1957 to 1970, inclusive, is given in a review by Junk.[52] This bibliography is subdivided into broad classifications of solute type and indicates the separator used in each application.

A very wide variety of different sample types have been analyzed using the technique, ranging from simple mixtures containing about 10 components to highly complex ones containing about 300 components. Figure 34 shows the FID and TIM traces on a complex mixture of cigarette smoke semivolatiles.[53] The separator used in this work was a jet type; comparison of the two traces shows little loss in GC resolution over the entire chromatogram. This example serves to illustrate the inherent power of GC-MS when optimum separator conditions are employed.

For semiroutine applications the identity of many of the components of a given mixture may be known; then GC-MS may be used to monitor the order of elution of the components and to ensure peak homogeneity. It is particularly useful in this respect for the analysis of the products of free-radical reactions.

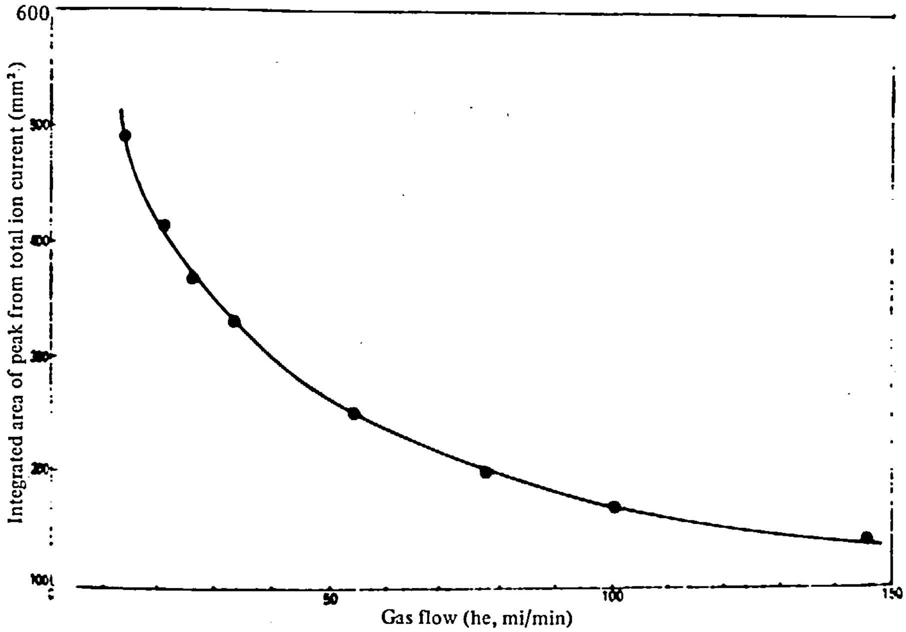

FIGURE 29. Gas flow dependence of solute transfer with micro-silicone rubber membrane separator.[36]

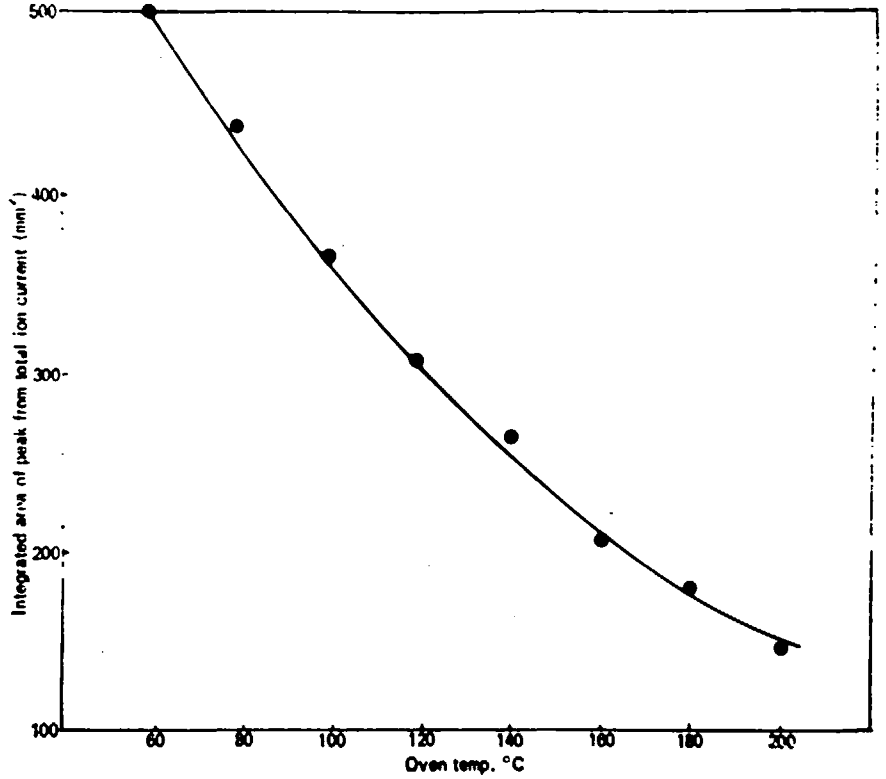

FIGURE 30. Temperature dependence of solute transfer with micro-silicone rubber membrane separator.[36]

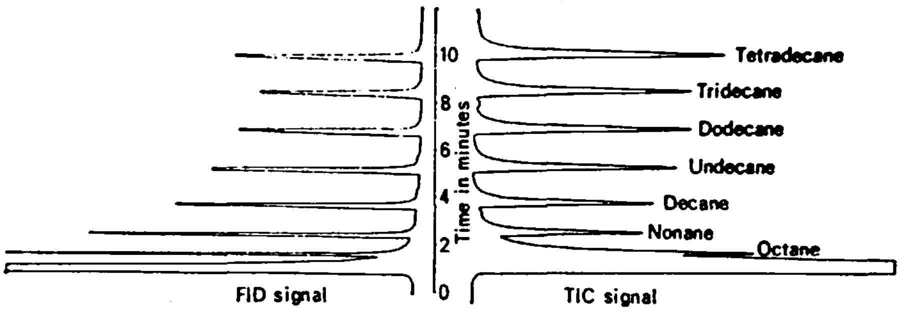

FIGURE 31. FID and TIM traces for N-alkanes with the glass micro-silicone rubber membrane separator.[36]

In addition to the straightforward use of GC-MS for the separation and identification of the constituents of complex mixtures, the combined systems have been used to provide additional information with respect to sample constituents. For example, the mass spectrometer can apparently increase the GC column efficiency by the process of deconvolution. Lindeman and Annis[54] have shown that it is possible to detect the presence of nine different components in a

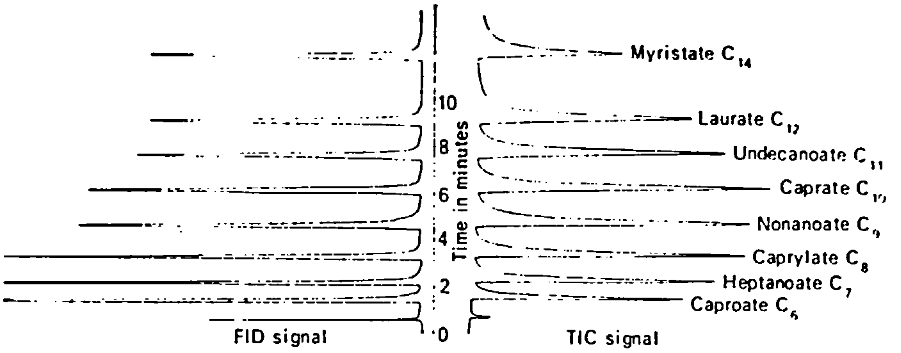

FIGURE 32. FID and TIM traces for fatty acid esters with the glass micro-silicone rubber membrane separator.[36]

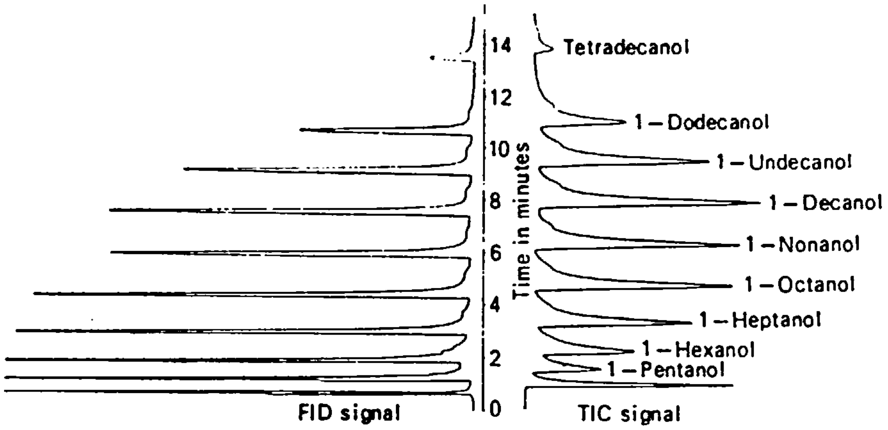

FIGURE 33. FID and TIM traces for n alcohols with the glass micro-silicone rubber membrane separator.[36]

single GC peak (Figure 35). The presence of the various components making up the composite peak is indicated in the mass spectrum by fragment ions unique to each component. From a knowledge of the intensities of the ions present and their abundance in the spectra of the pure components, the individual concentrations of the constituent compounds can be estimated. (In this example it would presumably have been possible to obtain a chromatographic separation of the components in the composite peak by using a capillary column.)

This technique requires some knowledge of the sample being analyzed, and of course is inapplicable if unique fragmentation ions are not present.

VandenHeuvel and Smith[55] have recently shown that a similar technique may be used to improve GC resolution. They employed the GC-multiple-scanning mass spectrometric approach for the resolution of the unresolved GC peak containing protium and deuterium amino acid TMSi derivatives. By successively scanning around the single GC peak, they showed that the fragment ions at m/e 179, 181, 183, and 185, which are characteristic of the 4 differently labeled tyrosines, eluted at different times (Figure 36), thus indicating the following retention time relationship between the isomers, tyrosine d_7 < tyrosine d_5 < tyrosine d_2 < tyrosine. Chromatographic resolution of these components would be very difficult to obtain.

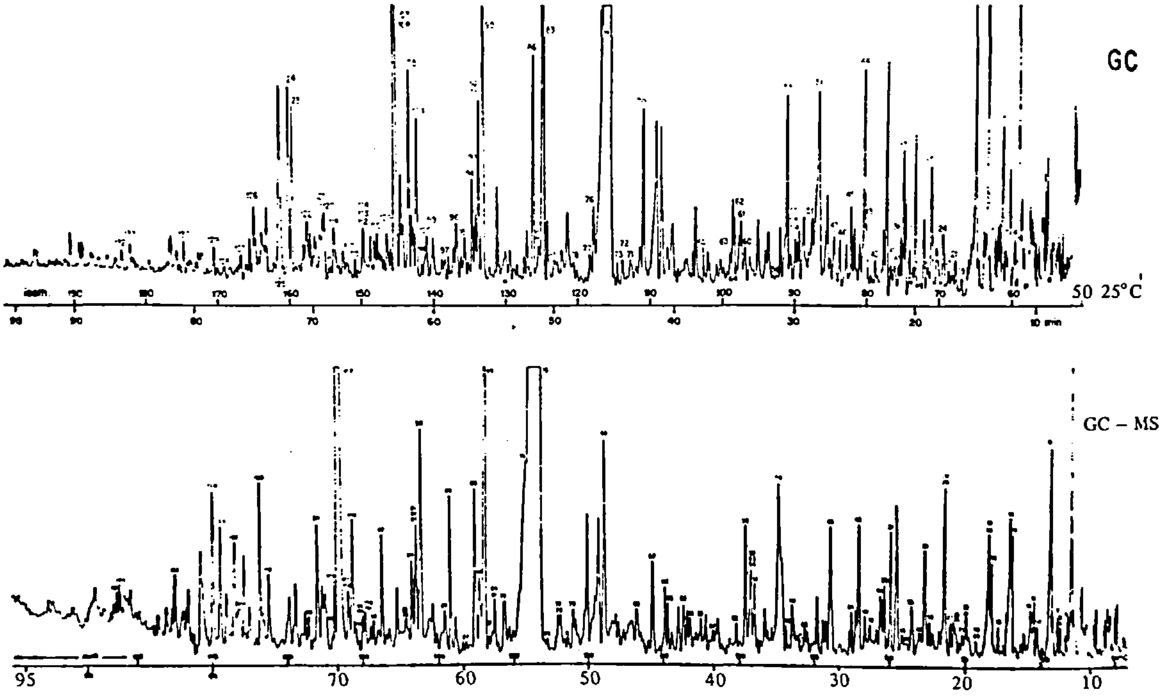

FIGURE 34. FID and TIM chromatograms of cigarette smoke semivolatiles.[53]

Very often, a complete analysis of a complex mixture provides excessive data for reduction in relation to the information required from the analysis. A simple technique reported by McCoy et al.[1] utilizes the MS as a selective detector for the column effluent. Figure 37 shows the form of data presentation. The sample is a high-aromatics-content motor gasoline analyzed on a 300-ft DC 200 capillary column; the effluent is split into two fractions, one fraction passing to a flame ionization detector to give the total chromatogram, the other fraction passing directly into the ion source of a quadrupole analyzer through a 3-ft length of 0.005-in. capillary tube. Scanning voltages are selected so that the spectrometer is stepped from one selected mass number to another. Seven independent channels may be selected at any one time. By operating the mass spectrometer at low ionizing voltage (7 eV), it is made to monitor the distribution of the parent ions of the selected C_6 to C_{12} aromatic hydrocarbons. A similar technique has recently been used by Brooks et al.[56] in the characterization of steroidal drug metabolites.

No reference has been made in this review to the problem of data reduction, which can constitute an important part of GC-MS analyses, particularly with complex mixtures. Several computer systems have been developed to facilitate analysis of the data obtained; the interested reader can find relevant information in References 57-60.

VIII. SUMMARY

Combination GC-MS interfacial systems have now been developed to a stage where it is possible to transfer the components of complex mixtures unchanged and without loss in GC resolution.

It would, however, appear that no one separator is completely satisfactory for all applications, particularly if the solutes under examination are of low molecular weight and present in submicrogram quantities. In the author's opinion the following three interfaces would satisfy all possible requirements:

1. Palladium separator — specifically for low-molecular-weight volatile inorganic compounds and compounds that would not be reduced by the presence of active hydrogen.

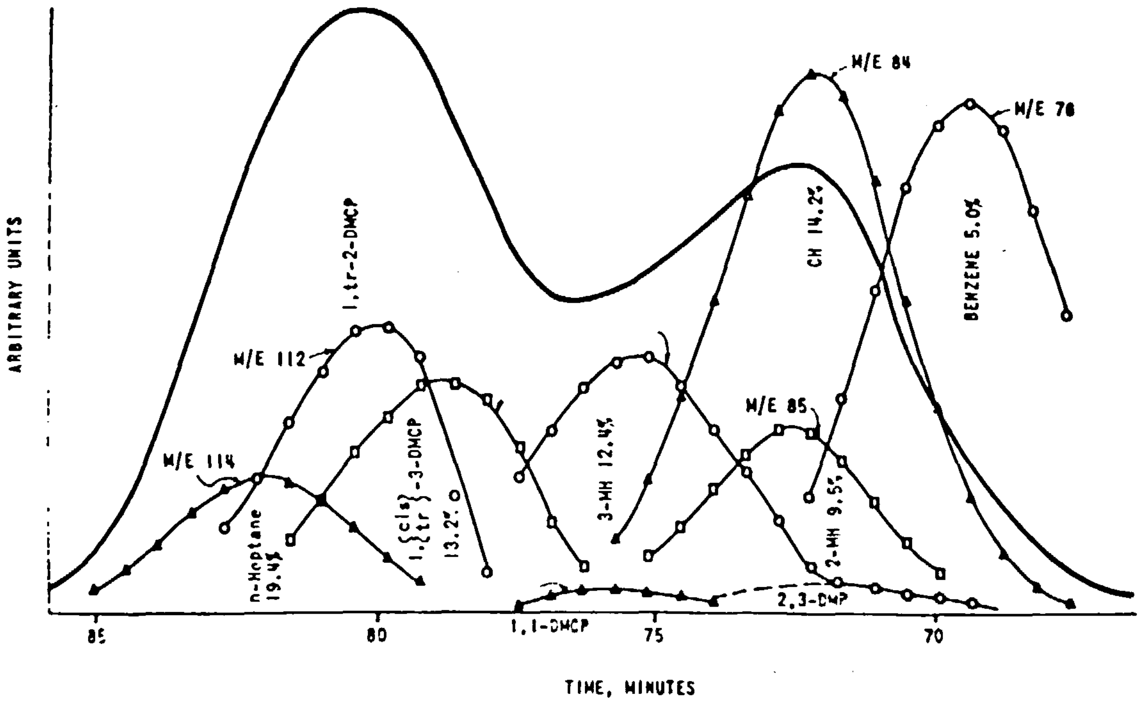

FIGURE 35. Deconvolution of a compound chromatographic peak.[54]

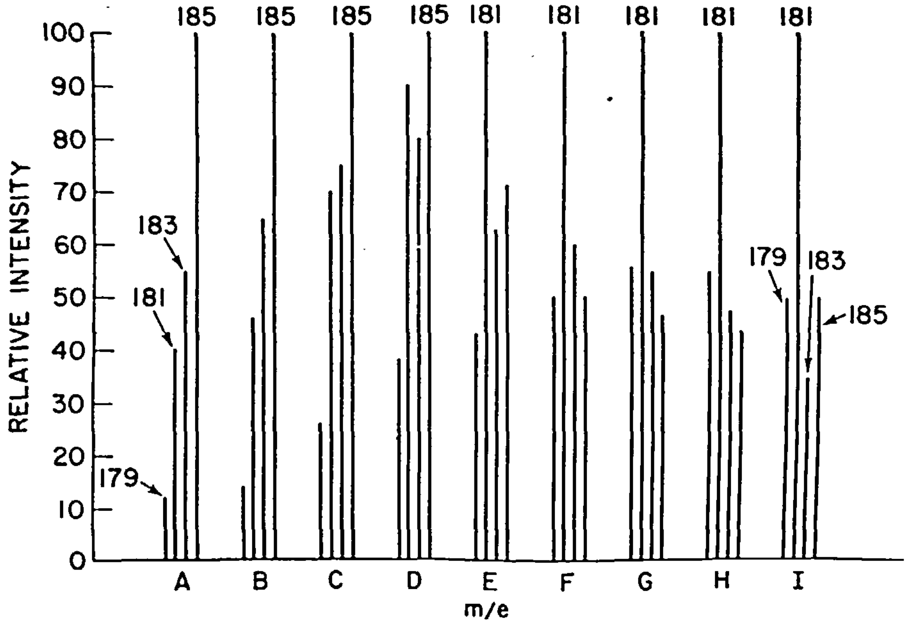

FIGURE 36. Deconvolution by repetitive scanning.[55]

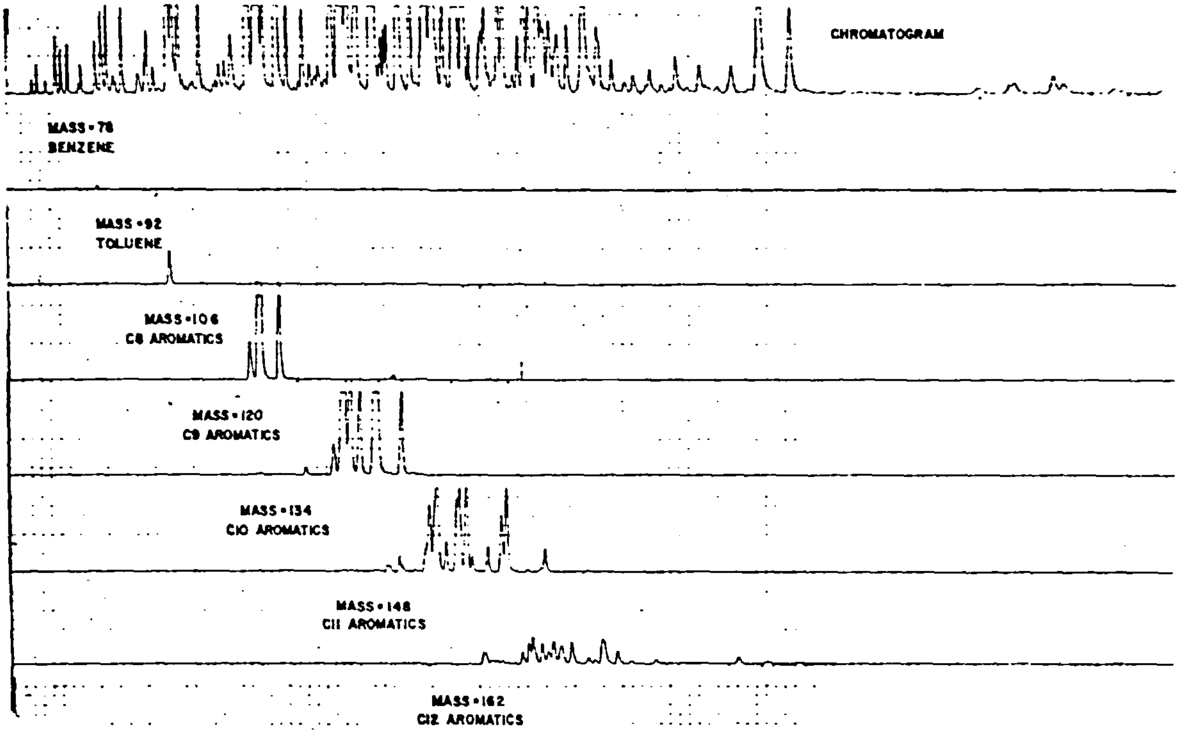

FIGURE 37. The use of the MS as a selective detector for aromatic hydrocarbons.[1]

2. Micro silicone rubber membrane separator for organic compounds up to a molecular weight of 250.

3. Jet separator – single-stage (variable) or double-stage, dependent on carrier-gas flow rate, for molecular weights from 100 upwards.

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