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USE OF MICROBORE COLUMNS FOR RAPID LIQUID CHROMATOGRAPHIC SEPARATIONS

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SUMMARY

The use of microbore columns for high-speed chromatographic separations is investigated, and apparatus is described that can be used with such columns. Specific details of detector cell construction are given, and photosensor specifications are suggested to provide the necessary fast detector response time. Specifications are also provided for appropriate data acquisition equipment. The performance of microbore columns operated at high mobile phase velocities is examined, and the effect of mobile phase velocity on column efficiency investigated. The precisions of quantitative analysis by peak height and peak area measurements are compared for a microbore column operated at high linear mobile phase velocity. An example of the separation of a seven-component mixture in less than 30 sec is included.

INTRODUCTION

Microbore columns lend themselves particularly well to rapid separations, as very high linear mobile phase velocities can be achieved at relatively low volumetric flow-rates and thus relatively low solvent consumption. Microbore columns require apparatus specially designed to have low extra-column dead volumes, but when such columns are used for high-speed separations, other factors such as amplifier time constant and detector response time also become critical. If the signal from the detector is to be processed by a computer, then the rate of data acquisition is also important. Furthermore, if high mobile phase velocities are to be employed, the detector cell system as a whole must have a low pressure drop across it as well as a low cell volume. A chromatograph for high-speed separations must therefore be uniquely designed.

EXPERIMENTAL

Apparatus design and construction

The chromatographic system used was based on that previously described[1] for microbore columns. A diagram of the apparatus is shown in Fig. 1. A Waters Assoc. M 6000A pump was used, but the frequency generator circuit was disconnected and the stepping motor and drive circuit connected to a Hewlett-Packard (HP) function

generator, Model 3311A. The use of the HP function generator increased the dynamic range of the pump from 0.1–9.9 ml/min to 0.01–20 ml/min. Valco high-pressure valves, modified to provide an injection volume of 0.5 or 0.2 μl, were employed for sample injection and were connected directly to the microbore column in the manner previously described[1]. Column lengths of 10 and 25 cm were examined, and these were connected directly to a LDC detector having a cell that had been specially constructed to tolerate the high linear mobile phase velocities necessary for rapid chromatographic analysis.

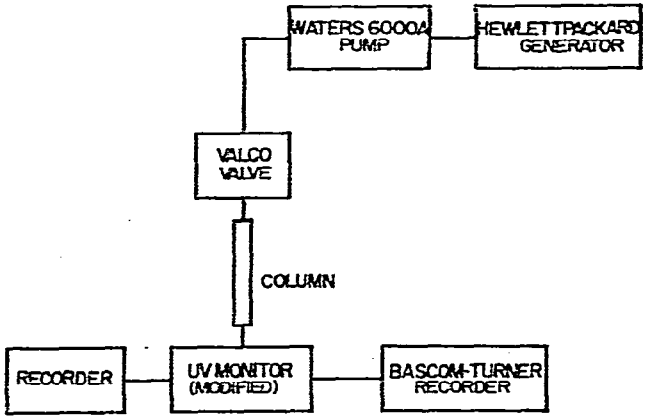

Fig. 1. Block diagram of chromatograph.

The design of the UV detector cell was also based on that previously described[1] but was further modified to permit the microbore column itself to butt directly up to the cell and thus virtually eliminate the necessity for connecting tubes. The reduction of the length of the connecting tubes to a minimum is important[2,3], as the very small internal diameters essential to reduce peak dispersion offer high resistance to mobile phase flow. A diagram of the cell employed is shown in Fig. 2. It consists of a disc of Kel-F, 1.27 cm in diameter and 3 mm thick, which are dimensions that are appropriate to fit the housing of the LDC UV monitor. The discs were truncated 2 mm deep on the top and bottom to produce two flats through which the column entered and the exit tube left. Two holes, 0.8 mm I.D., were drilled symmetrically in the disc, 3.1 mm between centers which constituted the sample and reference cell; the reference cell was left as a hole with no connection, air being used as the reference fluid. Two holes, 3 mm deep, tapped 0-80 NF, terminating 1 mm from the sample cell and 0.5 mm from the face of the disc, were drilled from each flat. The tapped holes were connected to either end of the sample cell by a 0.38 mm I.D. hole 1 mm long. The end of the microbore column was tapped 0-80 NF prior to packing, and, after packing and conditioning, was screwed into the cell block together with a 0.2-μm PTFE frit to prevent the packing from entering the cell. The exit tube consisted of a length of 0.030 in. I.D. stainless-steel tube also tapped and screwed into the cell block. The cell block was mounted in the detector in the normal way using the LDC standard quartz lenses and PTFE washers. The output from the detector was fed to a potentiometric recorder which was used for preliminary monitoring and also to a Bascom-Turner "Intelligent Recorder", Model 8110.

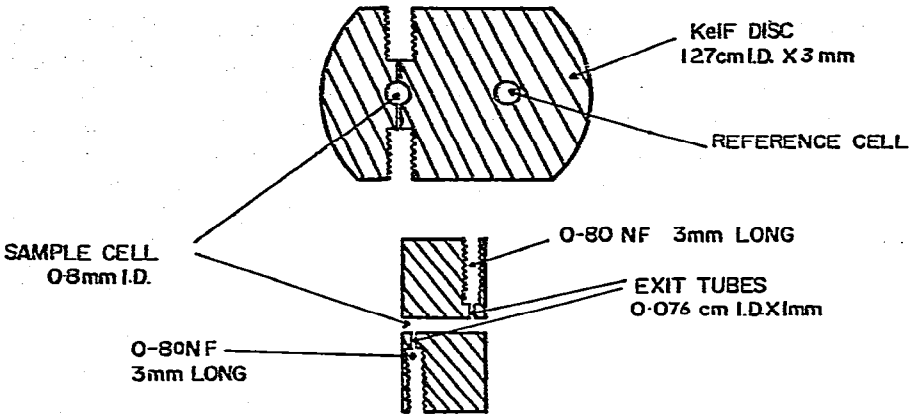

Fig. 2. Low-volume detector cell for fast analysis with microbore columns.

The Bascom-Turner "Intelligent Recorder" was chosen for the following reasons. Rapid chromatographic separations may be achieved in a few seconds; thus the time standard deviation of a peak may be extremely small. For example, a peak eluted in one second having an efficiency of 2000 theoretical plates will have a standard deviation of about 22 msec and thus a total peak width (4 σ) of about 88 msec. Now, if the stored digital data is required to reproduce the peak and at the same time maintain the integrity of its original form, at least 40 data points are required. This necessitates a sampling rate by the data acquisition system of up to 500 data points per second. Generally with standard chromatographic data handling systems, sampling rates are restricted to less than 25 data points a second as a result of employing multi-ranging amplifiers that can provide a wide linear dynamic range for signal output and also by time-sharing the instrument between different chromatographs. If a moderate linear dynamic range of the signal output is tolerated and single channel operation employed, then the sample rate can be increased. Employing this approach, the Bascom-Turner recorder has been designed to achieve sampling rates of up to 500 data points per second for single channel operation and maintain an adequate linear dynamic range. The recorder has a capacity of 3500 data readings which at the maximum data acquisition rate of 500 points per second provides a chromatographic time of 7 sec. Conversely, for very slow chromatographic developments the rate of data acquisition can be reduced and the "Intelligent Recorder", sampling at its minimum rate of 1 every thousand seconds, can acquire data for nearly a thousand hours. However, when operating the Bascom-Turner recorder at its fast sampling rates, it can be an ideal instrument for monitoring high-speed chromatographic separations.

Response time of photosensor

There are two further factors that can render the apparent efficiencies obtained from a chromatographic column less than the true efficiencies available when operated at high linear mobile phase velocities. These factors are the response time of the photosensor and the time constant of the amplifier and/or its associated electronics. It has been shown[3,4] that such electronic characteristics can cause significant band broadening. In the LDC UV monitor, however, there is no amplifier and the electronic

circuit consists of a simple bridge circuit from which the out-of-balance signal is appropriately attenuated and fed to a suitable recorder. In the output circuit of the bridge, however, there is included an appropriate capacity resistance network for smoothing purposes, which introduces a significant time constant. When the normal LDC photosensor and bridge circuit were employed, these capacitors were disconnected to eliminate this artificially introduced time constant. However, the more important source of band dispersion in the electronic circuitry lies in the slow response of the photosensor. In the normal LDC UV detector, a cadmium sulfide photoresistor is employed, which under fairly good illumination has a reasonably rapid response to changes in signal strength. At low light intensities, however, similar to that occurring under liquid chromatographic detecting conditions, the photosensor has a very slow response and can cause serious band spreading. The time constant of the cadmium sulfide photosensor was experimentally measured in the following manner. A switch was incorporated in the circuit of the low pressure mercury lamp which provided the UV light at 254 nm, and with full illumination the output was fed to the Bascom-Turner recorder, which was adjusted to receive a signal of −100 to +100 mV and to sample the signal at 20-msec intervals. After a steady baseline had been achieved, the mercury lamp was switched off and the decay curve was recorded. The signal was then reproduced on the *XY* recorder as a *Yt* plot which is shown in Fig. 3. The curve actually measured shows very significant a.c. noise, which was smoothed by a 5-point smoothing routine available in the Bascom-Turner software, and the smooth curve is also shown in Fig. 3 superimposed on the signal curve. The smoothed curve is also shown expanded to full scale, together with the logarithm of this expanded curve. From the slope of the linear portion of the logarithmic curve, the time constant was calculated in the usual manner and found to be approximately 2.5 sec (ref. 3). A time constant of this magnitude is completely unacceptable in high-speed liquid chromatographic systems where, as will be shown later, a complete chromatogram could be obtained in a period commensurate with that of the time constant of the sensor.

In order to reduce the effect of the time constant of the photosensor, the cadmium sulfide photoresistor was removed and a photomultiplier, IP-28, was substi-

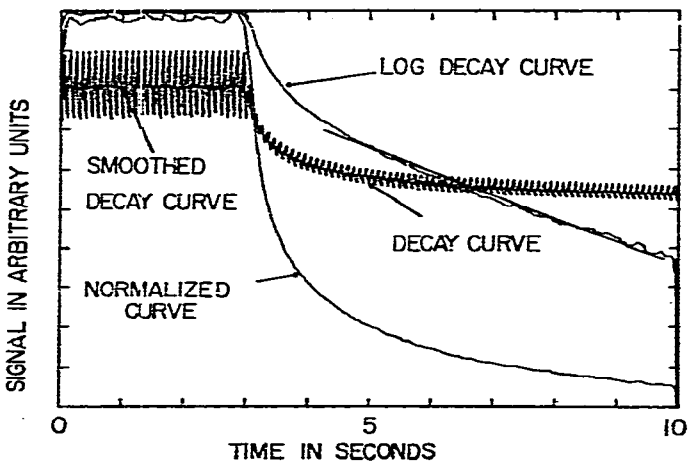

Fig. 3. Response curves of cadmium sulphide photoresistor.

tuted. Any photosensor having a fast response would have been satisfactory, but an IP-28 photomultiplier was readily available. A suitable light-tight housing had to be constructed over the cell to ensure stability. The original cell housing was used to hold the modified microcell, and the bolts for the attachment of the cadmium sulfide photosensor were used to secure the photomultiplier and its light-tight housing. The photomultiplier was supplied with 650-V d.c. derived from a stabilized power supply (Hewlett-Packard, Model 6516A). The output from the photomultiplier was taken across the 1.2-MΩ resistance and fed directly to the Bascom-Turner recorder set at an input range of −10 to +10 V.

The mercury lamp was switched on and allowed to come to equilibrium. The recorder was set to acquire data every 6 msec and the output from the photocell was recorded. The mercury lamp was then switched off. The results of this experiment are shown in Fig. 4. It is seen that the output from the photomultiplier was exceedingly noisy and that the 60-Hz noise pick-up on the circuit was clearly visible. This was shown not to come from the power supply to the photomultiplier, as little noise appeared on the trace when the UV lamp was switched off. The raw signal was smoothed by several five-point curve smoothing procedures, and the smoothed curve is also shown in Fig. 4. The logarithmic function was not produced, as due to the necessary smoothing procedures needed to eliminate the a.c. noise, no sensible data for the time constant of the photomultiplier could be obtained. It was fairly obvious that the time constant was very small, and thus the speed of the response of the photomultiplier would be more than adequate for high-speed chromatographic separations with contemporary column systems. There remained, however, the serious problem of noise from the UV lamp which needed to be at least reduced, if not eliminated. Unless the a.c. noise was eliminated, the smoothing procedure carried out on a curve to permit the calculation of the time constant of the system, or even column efficiencies, introduced artificial delays and rendered such calculations meaningless.

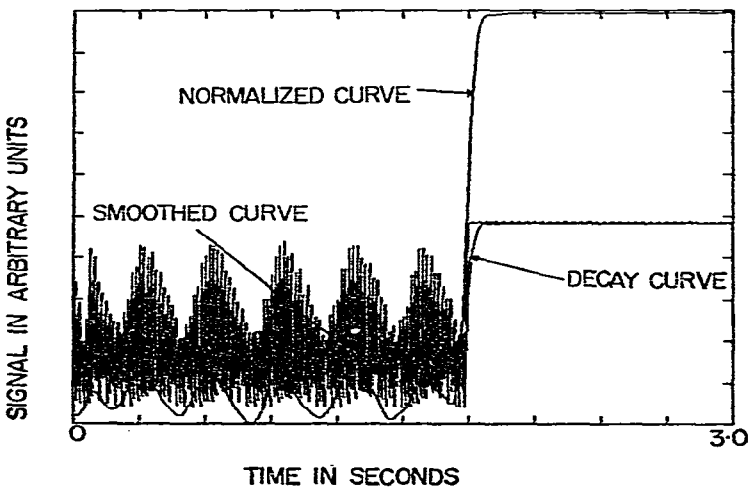

Fig. 4. Response curves for photomultiplier IP-28.

Under normal operating conditions the LDC low-pressure mercury lamp is connected to a 60-V a.c. supply through a choke and a normal discharge lamp starter. After the filaments have been heated, the starter opens circuits and the back EMF from the choke initiates the discharge. The lamp then continues to operate under a.c. conditions, which accounts for the 60-Hz noise measured by the photomultiplier. To prevent a.c. interference, the lamp had to be operated in the d.c. mode, and an 80-V supply was obtained from a Hewlett-Packard 6166A stabilized d.c. power supply. A diode was connected to the positive terminal of the supply, which was in turn connected to the 2.5-Henry choke and the 4-W low-pressure mercury arc lamp. The diode protected the power supply from any back EMF from the choke. The starter was replaced by a simple switch. 80 V were applied to the lamp with the switch closed, which provided a current of 200 mA. After allowing the filaments to heat, the switch was opened and the discharge current adjusted to 110 mA. Using this power supply, the previous experiment was repeated to determine the response time of the photomultiplier. In this experiment data was acquired every 2 msec, and data collection initiated with the lamp on. The lamp was then turned off and the resulting record is shown in Fig. 5. It is seen that the a.c. noise from the lamp had virtually been eliminated, as the small ripple shown is present with the lamp off as well as with the lamp on. In Fig. 5 the expanded curve and the log curves are shown, and from the slope of the log curve the time constant of the overall system was found to be about 40 msec. As a result of improved detector specifications and improved column technology, the performance of liquid chromatography columns is steadily improving. However, cell volumes of about 1 μl and electronic time constants of the order of 40 msec or less should, as stated previously, be quite adequate to cope with contemporary column technology.

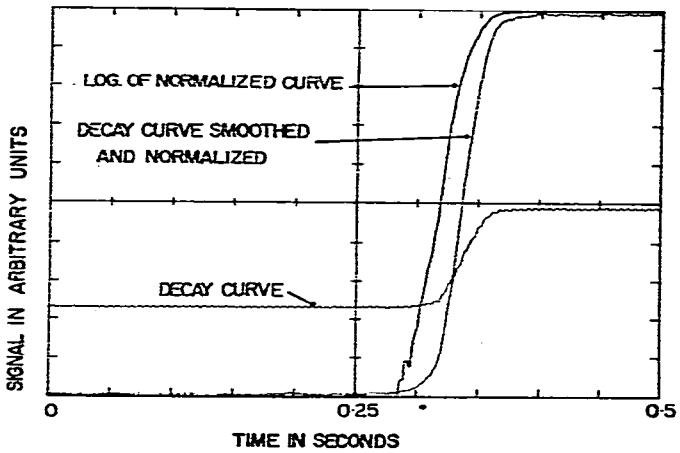

Fig. 5. Response curves for photomultiplier IP-28 used with a stabilized low-pressure mercury lamp.

Determination of the HETP curves for short microbore columns operated at high linear mobile phase velocities

In the first instance, columns 10 cm in length, 1 mm I.D., were examined, and these were packed using the procedure previously described[1] employing a precolumn

of equivalent length. One column was packed with 20-μm Partisil and the other with 5-μm Partisil. A mobile phase consisting of 5% isopropanol in heptane was used, and the solutes chosen were benzene and benzyl alcohol, eluted at the dead volume and at a k' value of 1.8, respectively. Linear mobile phase velocities ranging from 1 mm to 10 cm/sec were used, the linear velocities being calculated from the ratio of the column length to the retention time of benzene. The HETP was taken as the ratio of column length to the column efficiency measured in theoretical plates. The column efficiency was taken as the square of the ratio of the retention distance to half the peak width measured at 0.6065 of the peak height. The column packed with Partisil 20 was first examined using the standard cadmium sulfide photoconductor as the sensing element. The rate of data acquisition was adjusted to suit each mobile phase velocity used. The results are shown for the two solutes in the upper two curves of Fig. 6. The HETP axis is logarithmic, and it is seen that the HETP increases very rapidly at high linear mobile phase velocities. It is also seen that the HETP for the first eluted solute, benzene, is higher than that for benzyl alcohol, clearly demonstrating that the early, fast-moving peak is suffering extra-column dispersion due to the slow response of the photoconductor.

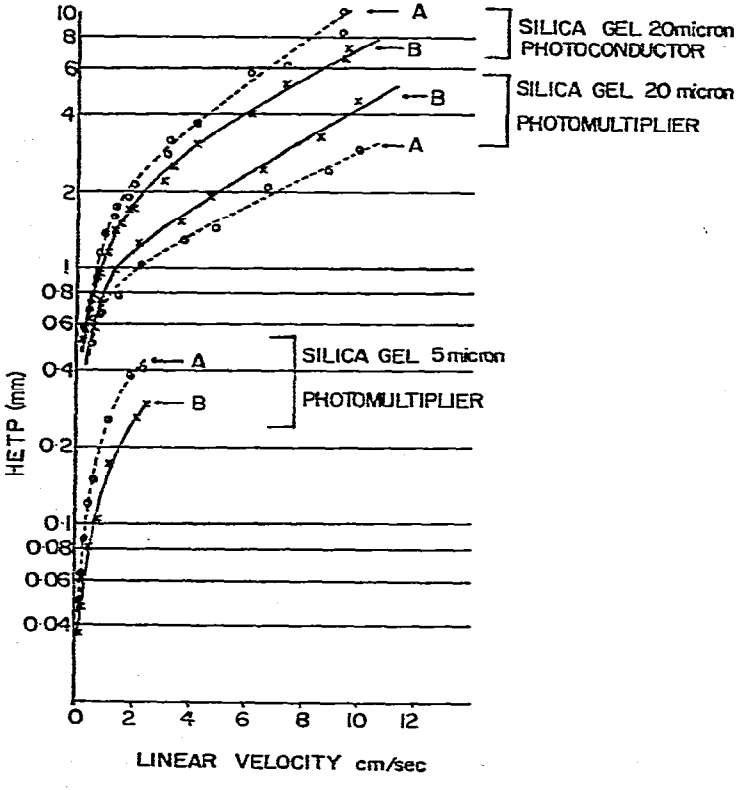

Fig. 6. HETP curves from short microbore columns. Column, 10 cm × 1 mm I.D.; solvent, 2-propanol–*n*-heptane (5:95); sample volume, 0.2 μl; sample mass, 2 μg. A = Benzene; B = benzyl alcohol.

The HETP for the same column was then determined for the same solutes employing the same operating conditions using the photomultiplier as a detecting system, and the Bascom-Turner recorder again set at an acquisition rate appropriate to the mobile phase flow-rate. The results obtained are shown in Fig. 6 as the two curves in the center. It is seen that the HETP for benzene has been reduced by a factor of three and that for benzyl alcohol by about a factor of two. This reduction of HETP and increasing column efficiency is solely due to the more rapid response of the photomultiplier sensor. It should also be noted that the HETP for the dead volume peak, benzene, is now lower than that for benzyl alcohol, indicating that the extra-column band dispersion is now insignificant relative to the normal dispersion of the peak. In each of the two sets of HETP curves, the velocities of about 10 cm/sec were obtained at pressures of about 3000 p.s.i. The lower curves in Fig. 6 were obtained from the 10-cm microbore column packed with 5-μm Partisil. It is seen that much higher efficiencies and lower HETP values are obtained, which would be expected from the reduced particle diameter. However, it is seen that a pressure of 6000 p.s.i. now only produces a linear mobile phase velocity of 2 cm/sec. It should also be noted that benzene, the first eluted peak, has again a higher HETP and a lower efficiency than benzyl alcohol. This means that due to the low value of the peak volume standard deviation and the small period of the peak time standard deviation, the extra-column effects are again becoming significant and are providing apparent efficiencies for benzene which are significantly below the true value. The volume and time standard deviations of benzene at a velocity of 2 cm/sec eluted from the column packed with 5-μm Partisil are 4 μl and 250 msec, respectively.

The HETP of a column 25 cm long was then investigated. It was packed with 20-μm Partisil employing a precolumn 10 cm in length. The same mobile phase, 5% of isopropanol in heptane, was used, and an HETP curve was obtained over a velocity range of 4 mm to 12 cm/sec. Pressures up to the maximum of 6000 p.s.i. were used to obtain these velocities. The HETP curves obtained in this experiment are shown as the upper two curves in Fig. 7. It is seen that again the efficiency decreases and the HETP increases rapidly at the higher linear mobile phase velocities. It is also seen that benzene, the first eluted peak, has a much lower HETP and also a much higher efficiency than the benzyl alcohol, which is eluted at a k' of approximately 1.8. One of the major causes of band dispersion at higher linear mobile phase velocities is due to the high resistance to mass transfer in the mobile phase. This is inversely proportional to the diffusivity in the mobile phase and is directly proportional to the viscosity of the mobile phase. It follows that when operating at high linear mobile phase velocities, mobile phases of low viscosity should be employed or alternatively the separation carried out at higher temperatures. The viscosity of heptane and isopropanol are 0.44 and 2.86 cP at 15°, respectively, and thus the weighted viscosity of the mobile phase containing 5% of isopropanol in heptane is 0.56 cP. To reduce the viscosity of the mobile phase, it would be desirable to employ pentane (viscosity 0.245 cP at 15°) as the hydrocarbon solvent and to obtain an appropriate polarity, replace isopropanol by methanol (viscosity 0.56 cP at 15°). However, pentane boils at 36° and thus tends to cause vapor lock in the pump. An equal mixture of pentane and hexane (viscosity 0.328 cP at 15° and boiling point 69° containing 3% methanol was employed. Such a mobile phase has a weighed viscosity of 0.30 cP at 15°, almost half that of the heptane–isopropanol solvent mixture and due to the relatively high boil-

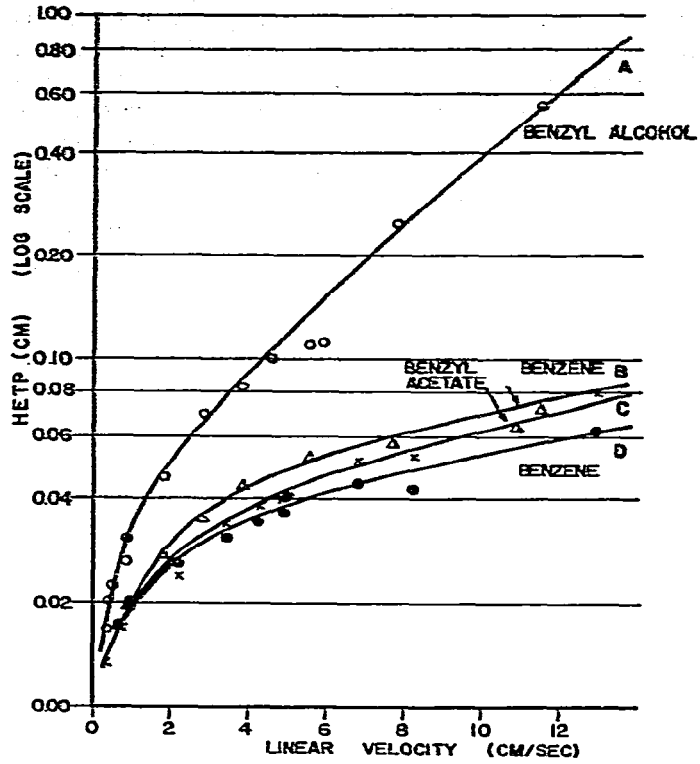

Fig. 7. HETP curves for microbore column, 25 cm long. Solvents: A and B, isopropanol–heptane (5:95); C and D, 3% methanol in pentane–hexane (1:1).

ing point of the hexane would suppress the vapor pressure of pentane and thus reduce the volatility problems in the pump.

The lower two curves in Fig. 7 are for benzene and benzyl acetate. Benzyl alcohol was not employed as the solute, as it has too high a k' value when a mobile phase composition of 3% methanol in the pentane–hexane mixture is employed. Benzyl acetate, the alternative solute, had a k' value of 0.5, which although lower than the k' of benzyl alcohol, is sufficiently well retained to indicate the beneficial effect of using the lower viscosity mobile phase at high linear mobile phase velocities. It is seen from the lower curves in Fig. 7 that the efficiency for benzene has been increased by about 25% at high linear mobile velocities and that the efficiency of the benzyl acetate retained at a k' value of 0.5 is very close to that of benzene but slightly higher. It is clear that even under the carefully controlled operating conditions and specially modified apparatus, when employing high linear mobile phase velocities, the first eluted peak is still suffering from significant extra-column dispersion. Using mobile phase velocities of 12 cm/sec, a separation of benzene and benzyl acetate is achieved in just over 2.5 sec. A chromatogram obtained from this separation is shown in Fig. 8. The time base is expanded so that the integrity of the peak shape is clearly shown. It is seen that even when the column is operated at a mobile phase velocity of 12 cm/sec, excellent peak shapes are obtained. It is interesting to speculate whether the

tails at the base of most peaks obtained in liquid chromatography chromatograms are due to slow recovery of the detector photocell to its base level of illumination. It should also be pointed out that mobile phase velocities of 12 cm/sec are even high for gas chromatography, and it follows that the practical operating parameters for liquid chromatography will merge into the range of those of gas chromatography, provided the apparatus is designed correctly. As a consequence, rapid separations can be obtained in similar time periods in each technique. Obviously, the separation of benzene and benzyl acetate in 3 sec is of academic interest only, but the separation of more complex mixtures in perhaps 30 sec is of real practical value. Such rapid separations could render liquid chromatography viable for process monitoring even where the time constant of the plant process was relatively small.

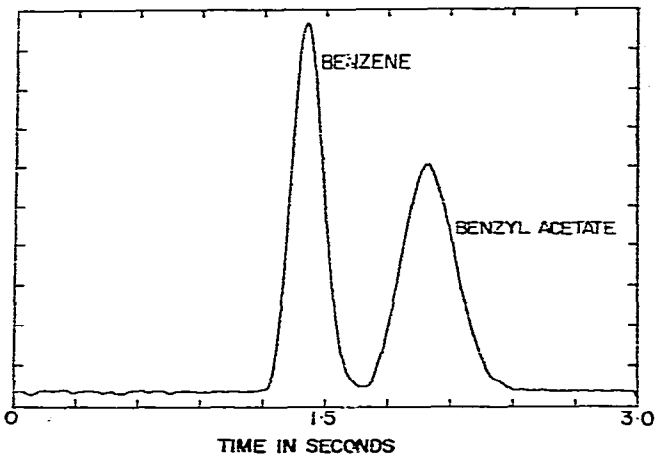

Fig. 8. Separation of benzene and benzyl acetate on a microbore column in 2.5 sec. Column, 25 cm × 1 mm I.D., Partisil 20; solvent, 3% methanol in pentane–hexane (1:1); flow velocity, 12 cm/sec.

Quantitative analysis using microbore columns at high linear mobile phase velocities

The 25-cm column packed with Partisil 20 was employed in conjunction with the solvent mixture consisting of 3% methanol in pentane–hexane (50:50) mixture. The sample consisted of 1% solution of each of phenylundecane (1), benzene (2), benzyl acetate (3), acetophenone (4), dimethylbenzylcarbinol (5), α-phenylethyl alcohol (6), and benzyl alcohol (7). A sample volume of 0.2 μl was used, and a linear mobile phase velocity of 8 cm/sec. The data acquisition rate was one sample every 60 msec. Five replicate samples were placed on the column, and the chromatograms recorded. An example of one of the chromatograms obtained is shown in Fig. 9. The recorder has an integration program to give the integral form of the chromatogram if so desired, and this is also shown in Fig. 9. It is seen that a good separation of the seven components is obtained in about 30 sec, and the integral curves are well defined so that the step heights can easily be measured. In the first instance the peak heights were measured on each chromatogram, and the empirical percentage composition calculated by normalization of the peak heights. The results are shown in Table I. It is seen that the standard deviation for each peak is relatively small and that good

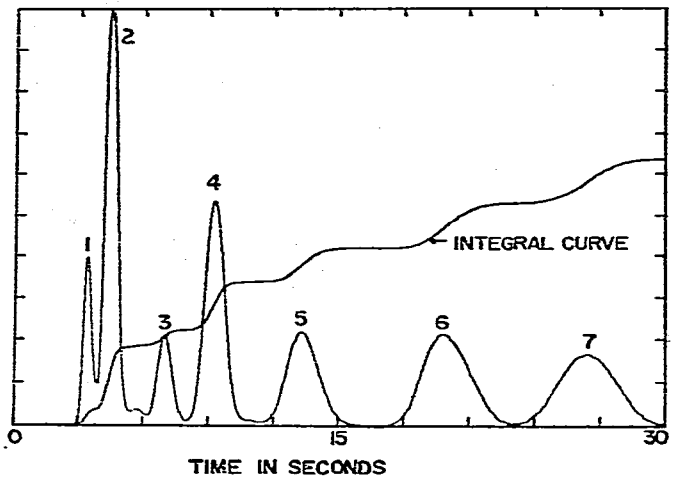

Fig. 9. Separation of a 7-component mixture on a microbore column in 30 sec. Column, 25 cm × 1 mm I.D., Partisil 20; solvent, 3% methanol in pentane–hexane (50:50); flow-velocity, 8 cm/sec. Peaks: 1 = 1-phenylundecane; 2 = benzene; 3 = benzyl acetate; 4 = acetophenone; 5 = dimethylphenylcarbinol; 6 = α-phenylethyl alcohol; 7 = benzyl alcohol.

analytical results are obtained. The maximum standard deviation occurs in the component present at the highest level, which is to be expected.

The step heights of the integral curve were also measured and the empirical composition of the mixture determined by normalization of each peak area. The results obtained are shown in Table II. It is seen, however, that the standard deviation for each component determined by normalization of peak areas is significantly greater than for peak heights. It follows that when carrying out quantitative analysis at high linear mobile phase velocities, normalization of peak heights will give better precision than peak areas. This has been noted before[5] where analyses have been carried out at much slower linear mobile phase velocities and appear to result from the use of a concentration dependent detecting device.

TABLE I

ANALYSIS OF PEAK HEIGHT

Run	*Peak height percentages*						
	*1**	*2*	*3*	*4*	*5*	*6*	*7*
1	14.6	36.7	7.5	19.6	7.9	7.6	6.1
2	14.2	38.7	7.2	19.3	7.5	7.2	5.9
3	14.5	37.4	7.3	19.5	7.7	7.6	6.0
4	14.6	37.0	7.5	19.6	7.7	7.6	6.0
5	14.5	37.3	7.4	19.6	7.8	7.4	6.0
Mean	14.5	37.4	7.4	19.5	7.7	7.5	6.0
σ	0.16	0.77	0.13	0.13	0.15	0.18	0.07

* 1 = Phenylundecane; 2 = benzene; 3 = benzyl acetate; 4 = acetophenone; 5 = dimethylbenzylcarbinol; 6 = α-phenylethyl alcohol; 7 = benzyl alcohol.

TABLE II

ANALYSIS BY PEAK AREA

Run	*Integral height percentages*						
	*1**	*2*	*3*	*4*	*5*	*6*	*7*
1	6.0	23.5	6.7	18.6	12.4	17.3	15.5
2	6.1	22.7	5.7	17.9	12.7	17.9	17.0
3	5.7	23.0	5.2	18.3	12.2	17.8	17.8
4	6.0	22.8	5.2	18.1	12.5	18.2	17.2
5	5.7	21.9	5.7	17.8	12.5	18.6	17.8
Mean	5.9	22.8	5.7	18.1	12.5	18.0	17.0
σ	0.19	0.58	0.61	0.32	0.18	0.48	0.99

* 1 = Phenylundecane; 2 = benzene; 3 = benzyl acetate; 4 = acetophenone; 5 = dimethylbenzylcarbinol; 6 = α-phenylethyl alcohol; 7 = benzyl alcohol.

CONCLUSIONS

The technique of liquid chromatography can provide extremely rapid separations and linear mobile phase velocities similar to those used in high-speed gas chromatographic separations can be employed. The high-speed separations demonstrated in this paper do not compare with the gas chromatography separations of Desty and Goldup[6] or Scott and Cummings[7], described in 1960, but these workers employed capillary columns, which have unique properties that render themselves readily to exceptionally fast chromatographic separations. The results given in this paper, however, compare equally to the high-speed separations obtained from packed gas chromatographic columns. Gas chromatographic columns generally provide efficiencies of 500–600 plates/ft. at the optimum gas velocities of 2–3 cm/sec. This is equivalent to 1500 to 1800 plates/m. Operating at high mobile phase velocities of 10 or 12 cm/sec, these efficiencies will fall to 400 or 500 plates/ft., equivalent to 1200 to 1500 plates/m. Referring to Fig. 7, it is seen that at mobile phase velocities of 12 cm/sec, efficiencies of about 1600 plates/m are obtainable from liquid chromatographic columns. It follows that the operating parameters of packed gas and packed liquid chromatographic columns can be very similar. However, due to the high viscosity of the mobile phase used in liquid chromatography, much higher inlet pressures are necessary. To achieve comparable performance between the two techniques, liquid chromatographic apparatus and columns have to take a particular form and have special specifications. To the best of the authors' knowledge, separations at the speeds shown in this paper have not been approached with widebore packed liquid chromatographic columns, and it may well be that such speeds can only be achieved using microbore columns. Certainly the only practical procedure for high-speed separations would be to use microbore columns, otherwise for continuous operation at high linear mobile phase velocities the consumption of solvent would be enormous. The apparatus used with the microbore columns also has to be specially designed. Extra-column dead volumes must be reduced to a minimum both at the injection end of the column and at the detector. The connection between column and injector and column and detector cell must be kept to a minimum, and the detector cell itself must be less than 1 μl in volume. Furthermore, the geometry of the cell[1] must also be carefully designed

to meet the required minimum dispersion and have specific radius to length ratios[3]. Instrument peak dispersion must also be minimized by maintaining low photosensor response times and minimal electronic time constants. In this paper the photosensor chosen was a photomultiplier which, as has been shown, can have a response time of about 40 msec. A solid state sensor could be used equally well, provided that at low light intensities the response of the device was equally fast. Improved detector design not only permits separation with microbore columns at high mobile phase velocities, but also generally improves the performance of normal wider bore packed columns, as has been shown previously[1]. The results shown in that original publication on microbore columns would have been further improved if, at that time, the response time of the photosensor and the amplified time constant had been also reduced. At the present time detector and injector design lag woefully behind column technology. It is hoped that detector manufacturers will not wantonly disregard the demands of the improved modern column technology but eventually be persuaded to manufacture and provide detectors with minimal volume and fast response to match the progress taking place in other areas of liquid chromatography.

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