Hollow-Fiber Liquid Chromatography

Modules containing from 120 to 27,000 parallel hollow fibers 100 μm in diameter can separate mixtures by reversed phase chromatography. The mixtures separated include aqueous solutions of ketones using alkanes as the stationary phase, and aqueous solutions of the proteins myglobin and cytochrome-c using an octane solution of reversed micelles as the stationary phase. The dispersion observed in these separations is comparable to that predicted from the Aris-Taylor theories. Modules of these fibers promise a lower pressure drop and a greater reproducibility than columns of spheres of equivalent surface area per volume. Such modules can facilitate scale-up of liquid chromatography.

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Introduction

This paper is concerned with the development of large-scale hollow-fiber liquid chromatography. As such, it is part of a new look at separation processes ignited by the spark of biotechnology. Biotechnology requires tremendous purification: a feed containing as little as 10^{-8} g of product/g of feed must often be purified to a final product that is more than 99.99% pure. This purification can be accomplished by known but tedious laboratory methods. Replacing these methods with industrial-scale separations is a current engineering challenge (Belter et al., 1988).

One key laboratory purification method is liquid chromatography. This method uses a packed column of adsorbent particles. In elution chromatography, a pulse of mixed solutes is injected into the bed, and washed through the bed with pure solvent. If different solutes are adsorbed differently, they will be washed out of the bed at different times, and can be collected as purer but more dilute fractions. Alternatively, in frontal chromatography mixed solutes in solution are pumped continuously into one end of the bed until one key solute "breaks through" and begins to come out the other end. The process is then stopped; the bed is washed; and the key adsorbed solute is eluted with a different solvent.

The keys to successful liquid chromatography are the chemistry and the geometry of the adsorbent that fills the packed column (Ladisch et al., 1984; Arnold et al., 1985). The chemistry has been more completely developed than the geometry, a heritage of the past emphasis on chromatography as a laboratory technique. The best available geometry uses small, monodisperse beads, often of hydrogels. The beads are small and monodisperse so that dispersion in the bed is minimized and the separations are improved. These gains extract a high price. The requirement of small particle sizes means that the pressure drops in the bed are high, around 400 psi (30 atm) for a bed only 10 cm deep. The requirement of monodisperse particles means that the bed packing is expensive, about \$1/g, or \$40,000/ft^3. Because this cost is so high, large-scale purifications use larger, less monodisperse particles, typically 100 μm dia. and costing at least \$0.20/g. In addition, the packed beds built for large-scale operation are shaped like pancakes, very shallow but very wide. Such beds seem to offer few economies of scale. In other words, a chromatographic unit that is 10,000 times bigger than the laboratory unit will cost 10,000 times as much.

Hollow-fiber liquid chromatography can be effected in two geometries. First, the fibers can be a form of shallow packed bed, containing affinity ligands and rolled into the shape of a hollow fiber (Brandt et al., 1988; Henis, 1988). In this case, a feed solution is forced across the hollow-fiber wall until solute breaks through into the permeating solution. As such, this form of hollow-fiber chromatography is like adsorption in a very thin packed bed of very large cross-sectional area.

The second geometry for hollow-fiber chromatography is that used here. A stationary phase coats the surface of the hollow fibers, and a mobile phase flows through the fibers' lumen. A peak of mixed solutes, injected into the mobile phase, is eluted as peaks of separated solutes. As a result, this form is a closer parallel to the elution chromatography common in analytical chemistry.

Hollow fibers in this second geometry offer one way to reduce these disadvantages of conventional liquid chromatography (Meyer et al., 1983; Gibbs and Lightfoot, 1986; Beaver, 1987; Lightfoot and Cockren, 1987). The pressure drop in a hollow-fiber bed will be much less, and the hollow fibers are more easily produced in a monodisperse form. Each of these features merits further discussion.

The pressure drop in hollow fibers is much less than that in

packed columns for two reasons. First, hollow fibers have straight streamlines and no form drag. Fluid flows straight through. In contrast, fluid flowing through a bed of spherical particles must constantly turn and twist to avoid the particles. Thus the pressure drop for a packed bed of 30% voids is over 80 times that in a fiber bed. To be sure, the fiber bed has 30% less area per volume, but this can be a small price to pay for a reduced pressure drop.

Second, in some cases, the savings in pressure drop can be larger still. Some hydrogels used for column packing are extremely swollen, and so tend to deform under their own weight. Long columns of these gels can blind, increasing the pressure drop even beyond that expected for flow in a packed bed. As an alternative, gels can be used to fill the pores in the walls of microporous hollow fibers. Now, the stresses of gel mass are supported by the fiber itself, while the gel still provides the chemical selectivity. Hollow fibers seem promising.

We next turn to the case of making monodisperse packing. Monodisperse spheres for chromatographic packing must be obtained by carefully sorting the polydisperse spheres produced by chemical synthesis. This careful sorting is expensive, which is the reason that packing which costs \$1/lb (454 g) in bulk sells for \$1/g as microspheres. Again, the fibers offer a way of avoiding this sorting. These fibers are made by continuous drawing. The success of the drawing depends on the fiber having uniform properties along its entire length. If it does not, it breaks. To be sure, a spool of hollow fiber made today may have a diameter 10% different from a spool made last week. Along one spool, however, the diameter will vary by less than 1%. While variations in fiber diameter and in stationary phase concentration can cause some dispersion, this is commonly less than the Aris-Taylor dispersion caused by flow. Again, hollow fibers seem promising.

At the same time, all this discussion is speculation. Can we really build hollow-fiber modules that are effective chromatographic columns?

Building such effective columns and showing how their behavior can be predicted is the goal of this paper. In seeking this goal we make one major compromise: we use hollow fibers of an internal diameter of about 100 μm. We choose to use these fibers because we are experienced with their properties and fabrication. Such fibers are much larger than the 10 μm dia. spheres preferred for liquid chromatography and so will not give separations directly comparable with the best analytical separations. Still, columns made of these fibers should bring us closer to our goal of evaluating hollow-fiber chromatography.

Experimental Details

All organic chemicals were reagent grade and were used as received. Myoglobin (horse heart type III, nominally 99% pure, Sigma), cytochrome-c (bovine pancrease, 41 units/mg protein, Sigma), and chymotrypsin (horse heart type III, nominally 96% pure, Sigma) were used as received. Water was distilled twice before use.

The basic apparatus, including a detail of the chromatographic column, is shown in Figure 1. Solvent is pumped (FMI Lab Pump model RP-G6) through a pulse dampener (FMI no. PD-60-LF) and an injection valve (Rheodyne type 7010) into the hollow-fiber column. When it comes out of the hollow-fiber column, it passes into a UV–visible detector (Micrometrics model 787). The output of the detector goes to a Macintosh

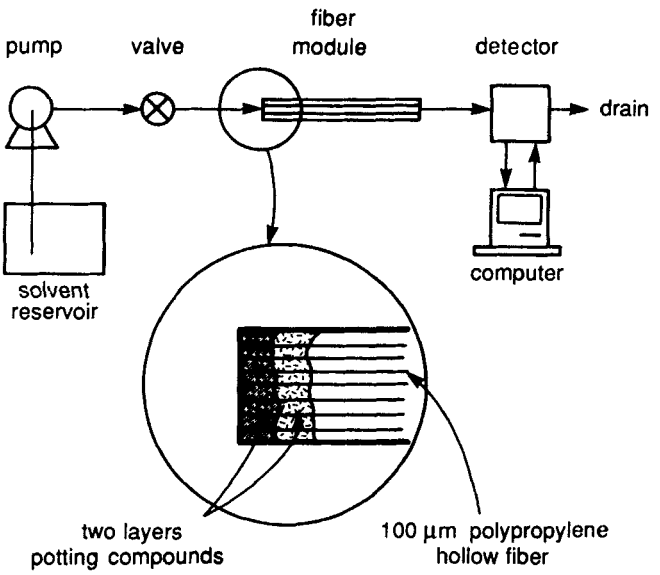

Figure 1. Basic apparatus.
Setup parallels a conventional liquid chromatograph, but with hollow fibers in place of a packed bed

microcomputer. In some of the protein experiments, the single pump and reservoir of solvent is supplemented by a second pump and reservoir attached through a second pulse dampener and a second solvent exchange valve. This allows switching from one solvent to a second.

A variety of hollow-fiber columns were used in the work, but these differed principally in geometry. Most hollow fibers were microporous polypropylene, of nominal 100 or 400 μm ID (Separations Products Div., Hoechst-Celanese, Charlotte, NC). One module was built with 300 μm Teflon fibers (Gortex, Elkton, MD). The fibers were plotted in glass tubes from 6 to 60 cm long, using two layers of epoxy resin. The resin layer at the end of the column (Full-Weld UR-2187, H.B. Fuller, St. Paul, MN) had a superior solvent resistance. The resin layer inside the column (FE-5045, H.B. Fuller, St. Paul, MN), which is bright red, is exceptionally strong. The two layers produce a superior module.

Some experiments were also made with a commercially manufactured module, 22 cm long and 4 cm in dia., containing 27,000 hollow fibers of 100 μm dia. (Cel-Life, Hoechst-Celanese, Charlotte, NC). This module, which is potted with polyurethane, was modified with new end caps that reduce the volume outside the fibers by about 98%. Additional modifications replacing the injection valve with a large slide valve offered no advantage over conventional injection valves.

Some of the chromatographic modules were used directly, with the microporous polypropylene serving as the stationary phase. More frequently, the modules were wetted with mixed solvents as the stationary phase. The five most common choices were dodecanol, 75% dodecanol/25% dodecane, 50% trioctylphosphate/50% dodecane, 5% Aerosol OT in octane, and 5% sodium didodecyl sulfosuccinate in dodecane. The last two solvent mixtures were used only for proteins. In every case, a small volume of solvent mixture to be used as stationary phase was first placed on top of the column. The solvent wicked into the top, wetting the hydrophobic fiber, but not flowing through the fiber. Sometimes the solvent flow was accelerated with com-

pressed nitrogen, but this is not necessary. We recognize that it is important to wet all fibers evenly with the stationary phase. We were able to do so by watching for the change of the fibers from opaque to transparent. Opaque fibers are not water wet, but have air-filled pores. Transparent fibers have pores filled with the stationary organic phase. While this description of the application of the stationary phase may seem incomplete, it is all that we did: the application is self-regulating. The filling seems remarkably constant, and is probably controlled by surface tension.

Our experimental procedure for simple solutes was straightforward. We prepared by weight an aqueous solution of one or more solutes. We injected a sample of this solution into the valve shown in Figure 1, and followed the sample with a stream of pure solvent. We analyzed the solution coming out of the module spectrophotometrically, recording data at 254 nm for the phenols, 265 nm for ketones, and 254 nm for the markers, uracil and blue dextran. The procedure for the proteins, buffered at pH 6 to 7, was similar, but used a wavelength of 400 nm, and a different elution. Because this elution was tedious, we often used water at pH 10 to 11 to accelerate the process.

Results

Low molecular weight solutes

The hollow-fiber chromatographic modules described above can give effective separations both for low molecular weight solutes and for proteins. An example for simple solutes involves an aqueous solution of 2-butanone, 2-pentanone, 4-methyl-2-pentanone, and 2-heptanone injected into a fiber column wet with 50% trioctyl phosphate/50% dodecane. The column contained 420 fibers 60 cm long, of nominal 100 μm ID and 30 μm fiber wall thickness. The mobile phase flowed through the fibers at a linear velocity of 0.10 cm/s.

The concentration profiles exiting the column are shown in Figure 2. As expected, these show different retention times for each ketone, because each ketone has a different partition coefficient in the stationary phase. In particular, 2-butanone has the smallest partition coefficient, and is retained least; 2-heptanone has the largest partition coefficient and is retained most. Still, while this separation is effective, the peaks are broader than those in analytical chromatography, a consequence of the relatively large hollow fibers.

To put these ideas on a more quantitative basis, we first recognize that peaks are conveniently characterized in terms of two parameters: a retention time at which the maximum concentration exits, and a variance of the concentration about this mean. To interpret the retention time, we turn to the simpler forms of chromatographic theory (Karger et al., 1973). The mobile phase's residence time t_0 in the column is given by

$$t_0 = l/v \tag{1}$$

where l is the column length and v is the velocity within the fiber. The retention time for a solute retained by the stationary phase is:

$$t_R = \frac{l}{v}(1 + k') \tag{2}$$

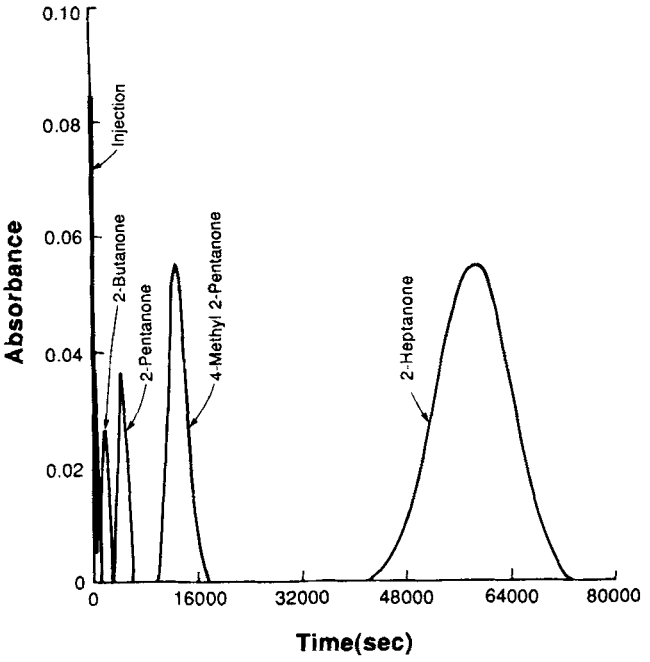

Figure 2. Typical separation.
Column contained 420 hollow fibers, 100 μm dia., 60 cm long, operated in parallel

where k' $(=KV_s/V_M)$ is the product of partition coefficient K and the volume of stationary phase V_S, divided by the volume of the mobile phase V_M. The physical significance of the dimensionless quantity $(1 + k')$ is thus the effective volume of the fiber—including both phases—divided by the actual volume available to the mobile phase.

We find that the retention time varies linearly with l/v for the wide variety of columns given in Table 1. Typical results, obtained as described above, are shown in Figure 3. For the uncoated fiber, the results show a residence time 30% longer than expected. For the coated fibers, the results show much longer retention times, a result of solute partitioning between the mobile and stationary phases.

Other examples of simple solutes, obtained with other modules, are listed in Table 1. The first column in the table gives three numbers describing the column. The first of these is the column length, the second is the number of fibers, and the third is the stationary phase. The second column in the table gives the residence time of the mobile phase in the column, and the third column gives the solute's retention time. The ratio of these times is of course $(1 + k')$, Eqs. 1–2. In all cases, the mobile phase is water and the fibers are 100 μm microporous polypropylene.

The second way in which we can quantitatively characterize curves like those in Figure 2 is by means of the variance of the peaks. If these peaks were truly Gaussian, we could do this in any number of ways; since they are not, we can calculate the variance as the second normalized central moment of each. For the broadly spread peaks characteristic of the 100 μm fibers, this method can be inaccurate, reflecting as a major contribution any small shift in the peak baseline. Nevertheless, we decided to use it here.

Most commonly, the spread of a peak in a cylindrical tube is attributed to Aris-Taylor dispersion, which represents coupling between axial convection and radial diffusion. For uncoated

Table 1. Examples of Reversed-Phase Hollow-Fiber Liquid Chromatography

Column*	Solute	l/v** s	t_R s	σ^2 s^2
60 cm/420/TOP	2-butanone	30	74	1,170
	Methyl-*i*-butanone	30	166	3,400
	2-pentanone	30	176	3,700
	Cyclohexanone	30	139	3,300
	2-heptanone	30	2,200	350,000
	4-heptanone	30	2,400	460,000
61 cm/480/12 OH	*m*-nitrophenol	37	950	121,000
		89	2,300	44,000
	p-nitrophenol	66	1,430	320,000
		140	3,300	900,000
	Uracil	32	43	37
		210	290	2,200
21 cm/480/12 OH	*m*-nitrophenol	10.3	250	14,900
		44	1,070	104,000
	4-heptanone	10.9	430	28,000
		270	10,400	4.2×10^6
	2-pentanone	30	106	4,600
		98	340	23,000
		167	610	68,000
	Phenol	17.6	100	7,000
		26	139	8,300
		76	440	49,000
	o-nitrophenol	30	20	14
		118	79	157
21 cm/480/PP	*m*-nitrophenol	11.6	16.1	16
		42	59	240
60 cm/420/PP	2-pentanone	31	46	56
		56	83	128
21 cm/480/PP	Uracil	16.4	18.8	13.0
		47	52	100
	Blue dextran	11.5	15.6	49
		15.1	20	77
		42	56	460

*First figure is column length l; second figure is number of 100 μm fibers; third figure denotes stationary phase
TOP = 50% trioctylphosphate, 50% dodecane; 12 OH = 75% dodecanol, 25% dodecane; PP = uncoated fiber
**Based on nominal 100 μm dia.

fibers, the variance σ^2 is (Taylor, 1953; Aris, 1956; Cussler, 1984)

$$\sigma^2 = \frac{d^2 l}{96Dv} \tag{3}$$

For fibers coated with a stationary phase, the variance is approximately (Golay, 1958):

$$\sigma^2 = \frac{d^2 l}{96Dv}(1 + 6k' + 11k'^2) + \frac{2\delta^2 lk'}{3D_s v} + \frac{2Dl}{v^3}(1 + k')^2 \tag{4}$$

The first term on the righthand side of this relation represents the generalization of Taylor dispersion. The second term signals the diffusion in the stationary phase, described by the diffusion coefficient D_s, while the third represents axial diffusion. In most circumstances, the first of these three terms is the largest.

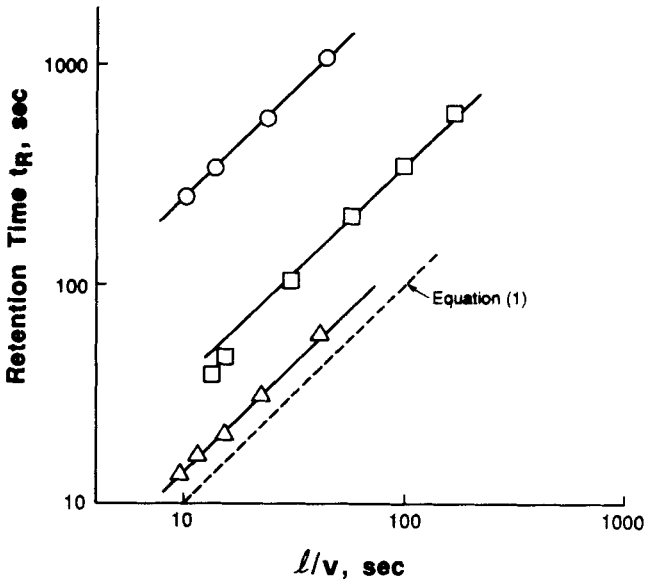

Figure 3. Retention times in hollow-fiber column.
Retention time is directly proportional to column length, inversely proportional to mobile phase velocity
○ *m*-nitrophenol with 12 OH; □ 2-pentanone with 12 OH; △ *m*-nitrophenol with PP; see Table 1

Our results, exemplified by those in Figure 4, do vary with l/v, but not always as predicted by Eq. 4. Additional values for σ^2 are given in the fifth column of Table 1. For uncoated fibers, the variance σ^2 varies more closely with $(l/v)^2$ than with l/v. For coated fibers, which strongly retain the solute, σ^2 is larger and varies more nearly with l/v. These results suggest that extra-column effects are more important for uncoated fibers than for the coated fibers. We explore these points in more detail in the discussion section.

We should mention one additional experiment using these simple systems. We took a tow of 100 μm fibers and froze them

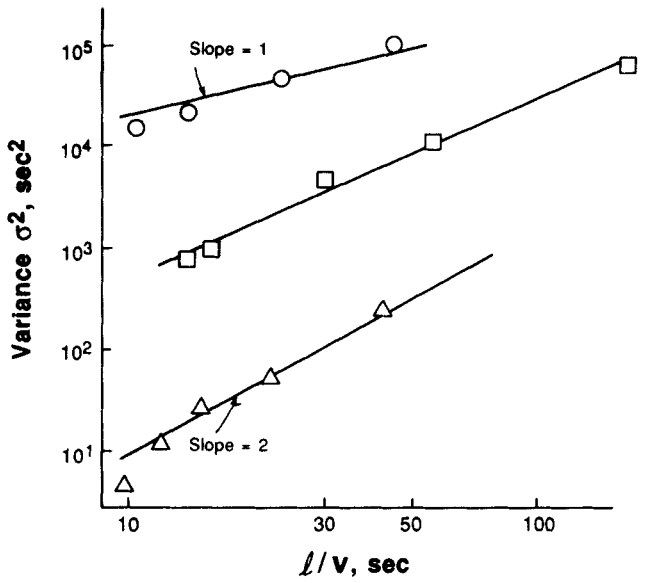

Figure 4. Variance in hollow-fiber columns.
Data obtained with 21 cm constant module length; chemical systems as in Figure 3

in an aqueous polyethylene glycol solution. We then used a microtome to cut rings of fiber 100 μm long. We carefully packed a column with these rings, and used the column for chromatographic experiments paralleling those in Table 1. Reassuringly, we found that t_R and σ^2 are within experimental error of the values found with the fibers. We conclude that the chemistry involved in the fibers is indistinguishable from that in the packed bed.

Proteins

In addition to the results for simple solutes, we made some experiments with protein mixtures. These protein experiments use an aqueous mobile phase, now containing 0.1 M saline and 0.1 M phosphate buffer. They use a solution of reversed micelles (Göklen and Hatton, 1987) as the stationary phase. Two such solutions are used: 0.05 M Aerosol OT (sodium di-2-ethylhexyl sulfosuccinate) in isooctane, and 0.05 M sodium didodecyl sulfosuccinate in dodecane. While the former system has been more completely studied, the latter is much less soluble in the mobile phase.

These protein experiments commonly used the same hollow-fiber modules as those in the earlier studies. One typical result, using a column of 240 fibers 60 cm long, is given in Figure 5. The feed to this column contained 160 μg of total protein, 50% of which was myoglobin and 50% of which was cytochrome-c. The pH in the mobile phase was altered from 6.8 to 10.0 after 4,150 s to elute the cytochrome-c. Had this change in eluent been delayed, the cytochrome would have been retained longer, but the peak shape would have been little changed.

Some protein experiments did not use the modules made for these experiments, but used a slightly modified, commercially available module containing 27,000 fibers 22 cm in length. Results with this module, shown in Figure 6, involve injecting a 10 μL sample containing 16 mg/mL of total protein which is

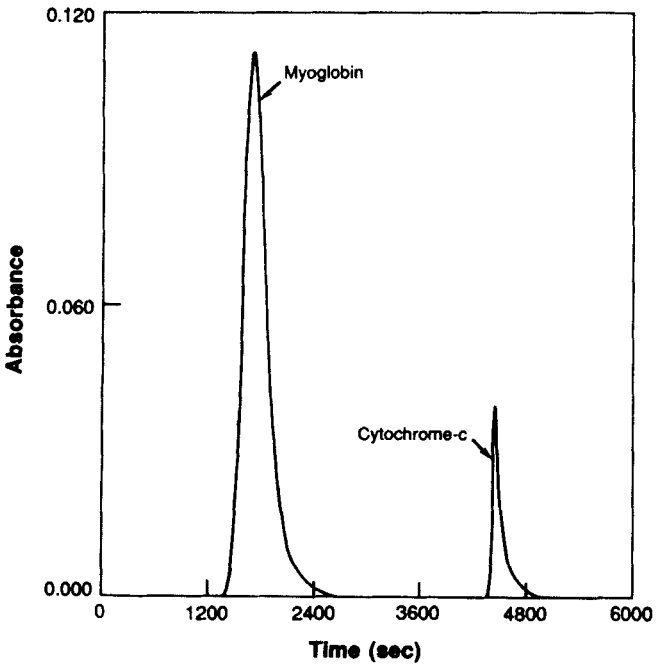

Figure 5. Protein separation in a 240-fiber column.
pH changed from 6.8 to 10.0 after 4,150 s to elute cytochrome-c

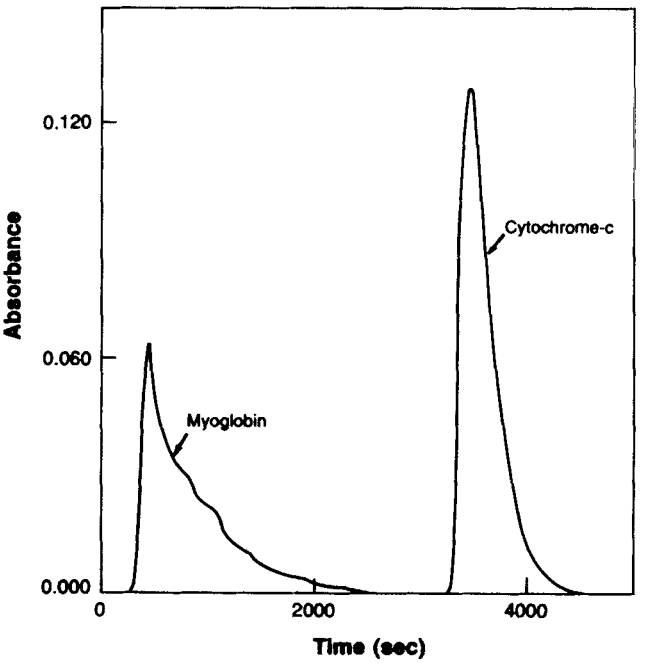

Figure 6. Protein separation in a 27,000-fiber column.
pH changed from 7.0 to 10.0 after 3,000 s to elute cytochrome-c

10% myglobin and 90% cytochrome-c. Again, elution of the cytochrome-c occurred when the pH of the mobile phase was changed from 7.0 to 10.0 after 3,000 s. The retention time of the myoglobin is similar in both the 240-fiber and the 27,000-fiber modules. The retention of cytochrome-c after the pH change is similar in both cases. The standard deviation of, for example, the cytochrome-c is about two times larger for the 27,000-fiber module than for the 240 fibers. Certainly, this increase is undesirable, but it seems small for so many parallel columns. We will return to this point in the discusion that follows.

Discussion

The results given above show that hollow-fiber liquid chromatography can work. The hollow-fiber modules show reproducible separations like those in Figure 2. The microporous polypropylene fibers used here are most easily operated with an aqueous mobile phase and an organic stationary phase. The aqueous phase is excluded from the fibers' pores, but the organic phase easily wets these pores, and is held in place by capillary forces. In this case, hollow-fiber modules are easy to adopt for chromatography.

The results given above imply that hollow-fiber chromatography will be effective at a large, preparative scale. Building larger chromatographs is easy: one simply uses more fibers or modules in parallel. Pressure drop is not severe, for there is little of the form drag that dominates flow in columns packed with small spheres. The form of this pressure drop is especially straightforward because the Reynolds number in the fibers is always less than 5. For cubically arranged fibers, it is given by the Hagen-Poiseuille law (Bird et al., 1960):

$$v(\text{fiber}) = \left(\frac{d^2}{32\mu}\right)\frac{\Delta p}{l} \tag{5}$$

For a packed bed with Reynolds numbers below 10, the pressure drop is found from the Ergun equation

$$v(\text{bed}) = \left[\frac{d^2\epsilon^3}{150\mu(1-\epsilon)^2}\right]\frac{\Delta p}{l} \tag{6}$$

If the fiber diameter equals the packing particle diameter, if the pressure gradients are the same, and if the void fraction ϵ is 0.3, then

$$\frac{v(\text{fiber})}{v(\text{bed})} = 85 \tag{7}$$

The ratio will be still larger if $\Delta p/l$ can be larger in the more rigid fibers.

This advantage, however, can be compromised by the values of the retention time of t_R and the variance σ^2. We need to consider these values more carefully.

We first consider the retention time t_R. From the values for uncoated fibers in Figure 3 and Table 1, we see that t_0 averages 30% larger than l/v. We are not sure why. Turbulence or secondary flows seem unlikely, for the Reynolds number in the fibers is always less than 5. Entrance and exit effects are equally unlikely, for the length/diameter ratio is above 10^3. Partially wet pores are possible, but such pores are inconsistent with a variety of membrane experiments. Solute adsorption on the polypropylene itself is another, more likely possibility, for this would be equivalent to a small volume of stationary phase. This possibility may be supported by the relatively close agreement between t_R and l/v for the marker uracil. However, we have trouble believing in solute adsorption when the difference between t_R and l/v is so nearly constant for the variety of solutes shown.

Another possible cause of the difference between t_R and l/v lies in the fiber diameter. We do not actually measure v; we calculate it from the relation

$$v = \frac{4Q}{n\pi d^2} \tag{8}$$

In this calculation, we have been using the nominal fiber diameter of 100 μm supplied by the manufacturer. If we assume a diameter for the fibers we actually used of 115 μm, we find that t_0 and l/v agree closely for uncoated fiber experiments.

We can make similar estimates of σ^2 by use of Eqs. 3–4. We do best when k' is large. As an example, we consider *m*-nitrophenol in aqueous solution as the mobile phase, moving past a stationary phase of dodecanol/decane at a flow of 0.077 cm^3/s, in a column of 480 fibers 21 cm long—the first value for this column given in Table 1. From Figure 3, k' is 24.3. We estimate that D in the mobile phase is 7×10^{-6} cm^2/s; that D in the stationary phase is 4×10^{-7} cm^2/s; and that the wall thickness δ is 3.0×10^{-5} m (Cussler, 1984). We combine Eq. 8 and the first, most important term of Eq. 4 to find

$$\sigma^2 = \frac{\pi n d^4 l}{Q}\left[\frac{(1 + 6k' + 11k'^2)}{384D} + \frac{2\delta^2 k'}{3D_s}\right]$$

$$= \frac{(480)\pi(21\text{ cm})(0.01\text{ cm})^2}{\left(0.077\ \frac{\text{cm}^3}{\text{s}}\right)} \cdot \left\{\frac{[1 + 6(24.3) + 11(24.3)^2](0.01\text{ cm})^2}{384(6.9 \times 10^{-6}\text{ cm}^2/\text{s})} + \frac{(0.0030\text{ cm})^2(24.3)}{6(4.1 \times 10^{-7}\text{ cm}^2/\text{s})}\right\} = 1.4 \times 10^4$$

The experimental value of σ^2 given for these conditions in Figure 4 is 1.5×10^4 s^2, in reasonable agreement.

The agreement found for the case of strongly adsorbed solutes holds less well for less strongly bound materials, as suggested by replotting the data of Figure 4 in Figure 7. We are not sure why. The most logical explanation is the extracolumn effect caused by the volumes of the feed tubes and the detector. These additional volumes lead to predictions that σ^2 varies with $(l/v)^2$ (Horvath, 1980). Such extracolumn effects become weaker as t_R becomes larger.

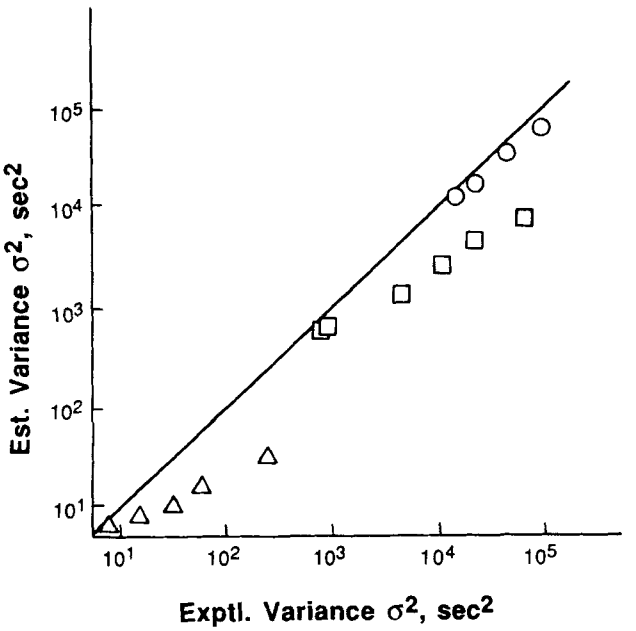

Figure 7. Estimated and experimental variances in hollow fibers.

○ □ △ Chemical systems as in Figure 3

The results for proteins, shown in Figures 5 and 6, show that hollow-fiber reversed micelle chromatography can be effective. More important, they show that scaling-up these systems is straightforward: we can go from 240 fibers to 27,000 fibers without dramatically compromising performance. In particular, Figures 5 and 6 show that the flow through parallel hollow fibers is not subject to significant channeling. Such channeling could be caused by differences in fiber diameter, fiber length, or fiber crimping. Preliminary measurements of fiber diameter and fiber length show only small variations. Accordingly, we are tempted to blame this increase on the slight crimping at the ends of the fibers, a crimping produced when excess potting compound is cut away during module manufacture. Regardless of the origin of this doubled variance, the increase is much less than that expected from past studies of flow in parallel tubes.

We recognize that the preliminary results in this paper are only partially satisfactory. We have shown that hollow-fiber modules can give effective separations, and that the perfor-

mance of these modules can be estimated from existing theory. Still, we have not separated anything of commercial value. Because our values of σ^2 are far above those in analytical separations, we must use smaller diameter hollow fibers to obtain smaller σ^2. We look forward to these challenges.

Acknowledgment

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Notation

d = fiber diameter
D, D_s = solute diffusion coefficient in mobile, stationary phase
k' = equivalent volume divided by volume available to mobile phase
K = partition coefficient
l = column length
n = number of fibers
Δp = pressure drop
Q = volumetric flow
t_0, t_R = residence time of mobile phase, solute
v = mobile phase velocity
V_M, V_S = volume of mobile, stationary phase

Greek letters

δ = fiber wall thickness
ϵ = void fraction
μ = viscosity

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