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# DESIGN PROCEDURE FOR PREPARATIVE AND PRODUCTION GAS CHROMATOGRAPHY

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## SUMMARY

A rational design procedure is proposed suitable for both preparative and production chromatography. The procedure is founded on a previously devised model for optimising the column throughput or cost of separated product. Despite their complex interrelationships, the operating parameters can be selected in a systematic sequence that is largely non-iterative. First, the carrier gas, stationary phase and support are selected. Then parameters are determined in the order: column temperature, concentration of solute in injected band, column diameter, particle size of packing, carrier gas velocity, ratio of recycled to injected feed, injection time, column length, and liquid phase loading. Some of the parameters are different for heat-sensitive and thermally stable solutes. The method determines their optimum values by calculation from theory in conjunction with data from analytical scale experiments for the separation concerned.

## INTRODUCTION

Compared with non-chromatographic methods of separation, preparative and production scale chromatography are particularly well suited where high purities are required or separation is difficult[1,2]. As with all methods, however, the design must be optimum if the technique is to be viable. Much of current preparative practice is based on concepts derived from analytical work which are inappropriate; design is also qualitative rather than quantitative. A rational and, where possible, quantitative approach to design is needed for both production and preparative scales of operation. (The distinction between these two scales is essentially a matter of whether economics are important[3].)

Although much has been written on specific aspects of the efficiency of large scale chromatographs there have been singularly few published attempts at systematic design. Hupe's account[4] is considerably more informative than that of Ryan *et al.*[5] but is based on the sub-optimal conditions of narrow, Gaussian bands and a linear partition isotherm. The principles of design and performance of preparative and production gas chromatography (GC) were first analysed comprehensively by

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Conder and co-workers[3,6–9]. The resulting design criteria have been used in designing production scale separations by Shingari[10] and Fruitwala[11]. The criteria have also been broadly confirmed by the experience of Valentin and co-workers in applying a computer model of finite concentration peak shape to model compounds[12] and in extracting over 50 different products from a variety of mixtures[13–16].

In this paper the elements of the previous analysis are put together and developed into a rational design procedure for both preparative and production gas chromatographs.

## THE DESIGN PROCEDURE

We assume that the object of the design is to achieve a specified throughput or product cost at specified levels of purity. We also assume that the options of single- or multi-stage fractionation[14] have already been examined, so that the matter at issue is the design of a single, well defined, separation stage.

The procedure starts with selection of column materials and proceeds to determine, in a set sequence, the optimum column and operating parameters for the separation concerned. The scheme is shown in Fig. 1. Despite their complex interrelationships, the parameters can be selected in a sequence that is essentially non-iterative, except for three principal loops at A, B and C which in principle require iteration, though in practice one cycle normally gives adequate accuracy.

The method of determining parameters is as quantitative as is currently feasible. It is based on an overall optimisation model[3,7–9] which uses available data but is only approximate in matters of detail at present. Consequently at certain points in the design some quantitative judgement is required though based upon qualitative guidelines already established. As experience is gained it will become possible to replace these guidelines by design equations, which at present exist only for some stages of the procedure.

Since the criterion of performance involves the throughput in both production and preparative chromatography[1], the following equation[9] for the throughput, $q_r$, is central to the design procedure:

$$q_r = \frac{rn_f}{n} \cdot \frac{sM_f p_f}{RT} \cdot \frac{\pi d^2 \varepsilon \bar{u}}{4} \tag{1}$$

where

$$s = \frac{\alpha}{6(\alpha + 1)} \text{ for a two-component mixture} \tag{2}$$

$$s = \frac{at_R}{6t_c} \text{ for a multicomponent mixture} \tag{3}$$

In these equations $r$ is the recovery ratio after fraction-cutting and recycling the mixed fraction of the unresolved components (ratio of unrecycled product to injected feed), $\alpha$ is the separation factor, $M_f$ and $p_f$ the molecular weight and vapour pressure of the feed, $T$ column temperature, $d$ column diameter, $\varepsilon$ packing void (inter- and intra-

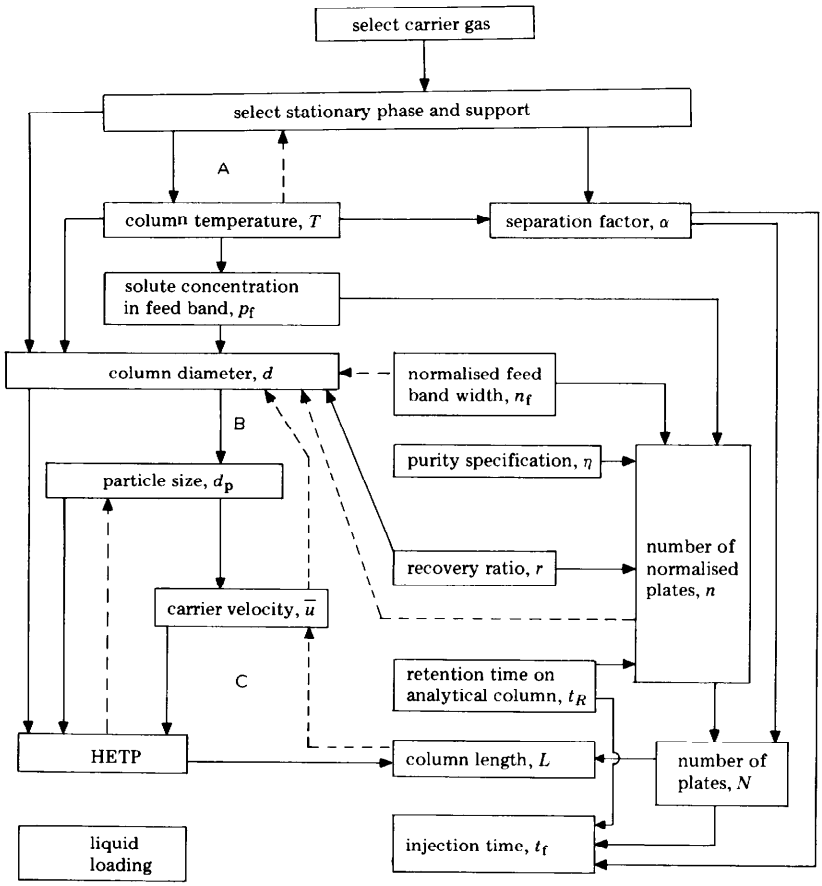


Fig. 1. Flow chart for design of production and preparative gas chromatographs. Feedback is shown by broken lines. A, B and C are principal calculation loops. Calculation loops which are not needed because they arise from weak parameter dependence are omitted.

particle) fraction, $\bar{u}$ the mean ($j$-factor corrected) velocity of the carrier gas, $t_R$ the retention time, $t_c$ the cycle time between successive injections and $a$ is given by

$$a = \frac{2(\alpha - 1)k}{(\alpha + 1)(1 + k)} \tag{4}$$

where $k$ is the mass distribution ratio between liquid and gas phases (capacity factor); $n$ and $n_f$ are normalised plate numbers[7] given by

$$n = Na^2/36 \tag{5}$$
$$n_f = N_f a/6 \tag{6}$$

where $N$ is the number of theoretical plates (measured at infinite sample dilution) in the column and $N_f$ is the number of plates occupied by the width of the injected feed band (sample).

## SELECTION OF MATERIALS

*Carrier gas*

The first step is to choose the carrier gas. Air, though cheap, is generally undesirable as a carrier gas because oxygen tends to age liquid phases which are kept in operation for long periods[17]. Hydrogen is hazardous for large scale work. The choice is principally between nitrogen and helium and depends on cost and on the effect on the height equivalent to a theoretical plate (HETP).

The importance of minimising the HETP was greatly overrated in the past before optimum performance criteria had been adequately analysed. In preparative chromatography the throughput is unaffected by the HETP if the designer is at liberty to choose the column length for optimum performance[3]. In small ( < 1 ft. diameter) production chromatographs, too, the HETP has only a small effect on the performance measured by the ratio, $q_r/G$, of throughput to annual cost. It is only in large production chromatographs that it becomes important to minimise the HETP[3]. In this case, helium is the better carrier gas, since it gives an approximately 3 times higher diffusion coefficient for the solute in the carrier. This gives a lower HETP than nitrogen when operations are conducted at velocities in the region of $\bar{u} = 10$–$15$ cm/sec or more (see *Carrier gas velocity*). In preparative chromatography, if the designer is free to optimise the column length, the HETP is immaterial and the carrier velocity is not dictated by the diffusion coefficient. Nitrogen may then be preferred on account of its lower cost. In small production scale columns the influence of HETP on performance is sufficiently weak to have to be balanced against the cost of the gas, which remains a significant factor even though the gas is recycled: nitrogen may be preferable in countries, such as the U.K., where helium is much more expensive (about seven times more) and helium in areas, such as North America, where it is cheap.

*Stationary phase and solid support*

The criteria for selecting the stationary phase and solid support are described elsewhere[18].

## DETERMINATION OF OPTIMUM PARAMETERS

Once the carrier gas, stationary phase and support have been chosen, the design and operating parameters can be determined. The sequence is as shown in Fig. 1. The method relies on combining theory with small-scale experiments for the particular separation system concerned.

*Column temperature and pressure*

The choice of column temperature is closely linked to the influence of solute concentration on the feed band. Increasing concentration skews and broadens the eluted bands (peaks) and raises the required column length, *i.e.*, raises the required normalised number of plates in the column, $n$, above its infinite dilution value $n^{\infty}$. Writing

$$f = n/n^{\infty} \tag{7}$$

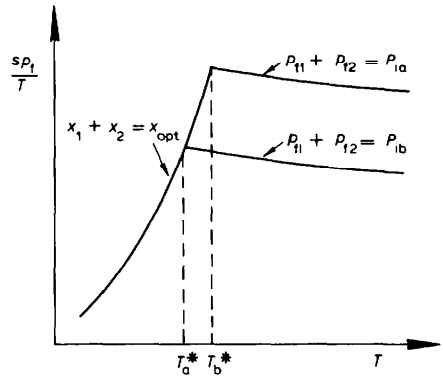


Fig. 2. Plot of ratio $sp_f/T$, to which the throughput is proportional, against column temperature $T$, for two column inlet pressures, $P_{ia}$ and $P_{ib}$. The optimum column temperatures are $T_a^*$ and $T_b^*$. The feed is a binary mixture with partial vapour pressures $p_{f1}$ and $p_{f2}$. Separation factor $\alpha$ is constant. Variation of $\alpha$ with $x$ or $T$ is not normally sufficient to affect the general shape of the plot greatly[8].

and collecting together the temperature- and concentration-dependent factors in eqn. 1 we see that the throughput is maximised by maximising the quotient $sp_f/fT$.

It has been shown[8] that the part of the quotient given by $sp_f/T$ has a maximum at a certain column temperature. The basis of the argument is modified in Fig. 2. The rising part of the curve on the left hand side is governed by the condition that the sum of the mole fractions, $x$, of the solutes in the liquid phase has an approximately constant optimum value, $x_{opt}$, assumed to be between 0.2 and 0.5 (see next section). The curves at the right hand side are governed by the condition that the total partial pressure of feed can never exceed the column inlet pressure, $P_i$. The points of intersection give the optimum temperature $T^*$, which is thus defined as approximately equal to the boiling point of the solute at a pressure $P_i/x_{opt}$. This temperature is 20–60°C above the boiling point at $P_i$ if $x_{opt} = 0.2$–$0.5$. The higher $P_i$ and hence $T^*$, the higher the maximum in $sp_f/T$ and hence throughput.

Valentin and co-workers[14,19] have shown that skewing and broadening of the eluted band is minimised at a temperature equal to the boiling point of the solute at a pressure slightly above $P_o/j$ where $P_o$ is column outlet pressure and $j$ the conventional pressure gradient correction factor. This is for peaks of small concentration; for peaks of a concentration appropriate to production and preparative GC we may deduce from Valentin's graphs[19] that the temperature should be a few degrees higher than this for minimum skewing and broadening, implying a pressure closer to $P_i$. Thus the second component, $1/f$, of the quotient $sp_f/fT$, is maximised by adopting an optimum temperature $T'$ equal to the boiling point of the solute at about, or a little below, the column inlet pressure.

The two optimum temperatures, $T^*$ and $T'$, differ by 20–60°C. It is by no means obvious which of the two is the overall optimum since, as $T$ is raised from $T'$ to $T^*$, the rapid rise in $p_f$ permitted at constant $x$ is offset by a rise in $f$ as the peak becomes more skewed, while $s$ may rise or fall. In many cases, however, the issue is resolved by an additional consideration, the temperature limit of the stationary phase due to column bleed and sometimes thermal decomposition[17]. For long column life appropriate to production GC this limit should be at least 50°C below the recom-

mended limit for analytical work[14,18]. Frequently this will be the requirement which fixes the optimum temperature. The $T^*$ and $T'$ criteria then serve to fix column inlet pressure rather than temperature. However, once $T$ ceases to be a free variable, meeting the $T^*$ criterion by reducing the column pressure confers no benefit over the $T'$ criterion, which accordingly becomes the operative criterion determining inlet pressure.

For example, if the stationary phase has a recommended temperature limit of 270°C and a safety margin of 70°C is required for production scale operation, the maximum allowable temperature is 200°C. Assuming a boiling point rise of 25°C for every doubling of pressure, a feed mixture with a mean normal boiling point of 150°C would therefore be run at an optimum column temperature of 200°C and a column inlet pressure of about $1 \times 2^{50/25} = 4$ atm absolute (applying the $T'$ criterion to the pressure).

On the other hand, in preparative GC where a shorter column life is usually acceptable, the same stationary phase could be operated at up to, say, 250°C. Suppose that the mixture has a mean normal boiling point of 100°C and that the equipment limits column inlet pressure to a maximum of 8 atm absolute. The optimum temperature then lies at some point between $100 + (25 \log_2 8) = 175$°C ($T'$ criterion) and 195–235°C ($T^*$ criterion) and so is not restricted by the temperature limit of the stationary phase. This optimum point may be found by experimental determination of $sp_f/fT$ as a function of temperature between $T'$ and $T^*$. Of the two temperatures, $T^*$ permits a higher partial pressure of feed mixture which can be calculated from the saturation vapour pressure, $p^0$, of the feed. Thus, at $T'$, $p_f \approx p^0(T')\, x_{opt} = P_i x_{opt} =$ 1.6–4 atm (assuming an activity coefficient of 1); at $T^*$, $p_f \approx p^0(T^*)\, x_{opt} = (P_i/x_{opt})\, x_{opt}$ $= 8$ atm.

The examples just given apply to thermally stable solutes. For thermally unstable solutes the optimum temperature is reduced to the maximum permitted by thermal degradation, $T_D$. In this case, again, the loss of the temperature parameter as a free variable leads to the $T'$ criterion, alone, being used to fix the pressure. The optimum column inlet pressure is then reduced to the value at which the mean boiling point of the key components is equal to $T_D$. In effect, this reduction is required to maintain $1/f$ rather than $sp_f/T$, which is greatly reduced anyway by the need to keep $p_f$ sufficiently small to maintain the optimum value of $x$ at the lower temperature $T_D$. Thus, if the normal boiling point is 150°C, $T_D = 175$°C and $x_{opt} = 0.2$–0.5, we have $P_i$ $\approx 1 \times 2^{25/25} = 2$ atm and $p_f \approx p^0(T_D)\, x_{opt} \approx 0.4$–1.0 atm. The total mole fraction of solute mixture in the gas phase at the column inlet is then $y \approx 0.2$–0.5, a value which may be difficult to achieve when evaporating heat-sensitive solutes. If so, it remains, as before, to be determined by experiment whether the option of raising $P_i$ (maintaining $sp_f/T$) is superior to that of lowering $p_f$ (maintaining $1/f$).

If the degradation temperature $T_D$ is low enough the $T'$ criterion may require operation at reduced pressure, as Roz *et al.*[14] have noted.

*Solute concentration in feed band*

For maximum throughput the solute concentration needs to be as high as possible. With thermally stable solutes and stationary phases the solute concentration is ultimately limited by stripping of the stationary phase due to friction with the carrier gas[8]. This limit usually lies between $x_s = 0.93$ and 0.996 where $x$ is the sum of

the mole fractions of all feed components in the liquid phase. (A recent suggestion[14] that $y_s = 0.3$ (mole fraction in gas phase), implying that $x_s \approx 0.3$, seems very low.) The optimum concentration, however, is probably lower than $x_s$ and is determined by the rate of band broadening at high concentrations. This is caused partly by skewing due to the partition isotherm and sorption effect[20] and partly by slower mass transfer in the liquid phase as the solute content and volume of the liquid rise. The result is to increase $f$ and so raise $n$ at a rate which, at high concentrations, becomes faster than the rate of increase of $p_f (\propto x)$. Thus, from eqn. 1 the throughput has a maximum at a mole fraction $x_{opt}$ which, on limited present evidence, probably lies between 0.2 and 0.5, depending mainly on the proportionate contribution of the liquid mass transfer term to the overall HETP: $x_{opt}$ decreases as the contribution increases. The corresponding optimum value of $p_f$ is that required to give $x_{opt}$ at the column temperature already chosen. Hence $y_{opt}$ is calculated.

The optimum $x$ is unaffected by whether the feed mixture is thermally stable. If heat sensitivity requires a column temperature lower than the optimum, it is the gas phase concentration parameter $p_f$, rather than $x$, that is reduced. This causes loss of throughput, as already explained.

*Column diameter*

A preliminary estimate of the column diameter is needed to estimate the plate height, $H$. Less essentially, if the diameter is much over 1 ft., a knowledge of its rough value can be used to correct the optimum value of $n_f = 2.5$, assumed in the next stage of the calculation. Accordingly, a first estimate of the diameter required to achieve the specified throughput is made using eqn. 1 and eqn. 2 or 3 as appropriate, with $n = fn^\infty$, $p_f = yP_i$, $T$ = column temperature chosen, $r = 0.6$, $n_f = 2.5$, $n^\infty = 0.5$ and $f = 1.5$ (for a thermally stable feed) or 2.5 (for a heat sensitive feed) and $\bar{u} = 15$ cm/sec. The values of $f$ and $n^\infty$ are merely "rules of thumb" values of sufficient accuracy for the purpose. The diameter can be re-calculated later once $n = fn^\infty$ is known from the next stages of the calculation.

*Particle size of packing*

The relevant support particle parameters are the average particle size and the spread of size in the packing.

The choice of average particle size is determined by its interrelation with HETP and carrier velocity. HETP generally increases with particle size[21]. In preparative chromatography, however, the throughput is unaffected by the HETP if the designer is free to choose the optimum column length without restrictions such as the size of an existing oven[3]. The particle size does not, therefore, need to be kept small. In fact the throughput may increase somewhat if the HETP is raised by increasing the particle size, as this reduces the relative importance of the liquid phase mass transfer term in the HETP and permits a higher $x_{opt}$ ($\approx 0.5$: see above). In addition, a coarse packing allows a high velocity to be more easily achieved (see below). It is therefore desirable to use the largest particle size permitted by the available column length and the required number of theoretical plates (calculated as described below).

On the production scale, for a given carrier velocity, some gain in performance ($q_r/G$) tends to accrue when the particles are small, especially if the column diameter is large (several feet)[3]. Against this is the fact that larger particles permit a higher

velocity for a given pressure difference and this is beneficial to performance, as seen in the next section. This balance of factors has not been analysed overall but it may be noted that average particle size affects the velocity–pressure difference relationship to a far greater extent than it influences plate height[22]. Given the cost of a high compression ratio in the gas it is likely that the balance of advantage lies with a large particle size, especially for small production scale columns of 1 ft. diameter or less. A particle size of around 30 or 40 mesh is suitable.

The question of the spread of particle size is governed by similar HETP considerations to those which determine the average particle size. There is ample evidence[3,4,23] that the HETP increases rapidly as the packing becomes less uniform. Hence some advantage is gained by making the packing as uniform as possible and having a spread of no more than 5–10 units of mesh size, *e.g.*, particles of 35–40 mesh. In preparative work a narrow spread permits any restriction on column length and hence on HETP to be met with a larger contribution to the HETP from higher $x_{opt}$ and higher carrier velocity. On the production scale it raises $(q_r/G)$ by reducing the HETP.

We conclude that a particle size of, say, 35–40 mesh provides a good initial design assumption for both preparative and production operation.

*Carrier gas velocity*

It can be shown from eqn. 1 that the highest practicable carrier velocity should be used[1,3]. However, since the carrier has to be recycled in production GC, the velocity is limited by the extra cost of a high compression ratio, especially if the particle size is too small. In this case the velocity attainable may depend on the column length determined in the next stage (see below). Experience suggests that a velocity of at least 10–15 cm/sec of nitrogen or helium is practicable[14,18]. The velocity is similar for both gases since their viscosities are similar.

*Feed band width, column length and recovery ratio*

At this stage a previous theoretical treatment[3,7,9] is used to provide a guide, which is then refined by measurements on an analytical scale. This approach is needed because the theory applies only to infinite diluation of the solutes in the stationary phase whereas the solutes are to pass through the column at finite concentrations where the bands are skewed and broadened to a greater or lesser extent. It is emphasized that the theoretical plate height in the column is still defined in terms of infinite dilution conditions and the elution (narrow band) mode of operation. On this definition, the effect of finite concentration skewing and broadening is to cause an increased plate number requirement, not an increased plate height[8,9].

There are three possible approaches to compensating for finite concentration skewing/broadening. One either increases the number of plates (and hence length) of the column while keeping the feed band width the same, or decreases the feed band width while keeping the column length and number of plates unchanged, or compensates on both parameters simultaneously. The three approaches will probably differ little in their resulting throughput or throughput/cost ratio, as can be checked by calculating these parameters, using the equations given in ref. 3, once the design variables have been established. We shall describe the first approach on the assumption that the optimum $N$ is more sensitive to solute concentration than the optimum

$N_f$. The second approach can be derived by analogy and is in fact slightly simpler to apply; it would be the most appropriate method when an existing column of fixed length is to be used. All three approaches make the assumption that the third parameter, the recovery ratio, $r$, obtained after fraction-cutting of the overlapping eluted components, should be held at an optimum value of about 0.6 whatever the solute concentration. This has been proved for bell-shaped peaks[3] and appears to be satisfactory for skewed (high concentration) peaks as well.

At infinite dilution with $\alpha = 1.2$–$1.4$ and $d = 10$–$30$ cm theory predicts that the optimum values of the three parameters are approximately $r = 0.6$, $n_f \approx 2.5$ and $n^\infty = 0.3$–$0.8$[3]. The optimum $n^\infty$ varies with the product purity specification. The available graphs[9] from which $n^\infty$ is determined, however, relate only to two values of the impurity fraction (fractional impurity of one key component in the other component after separation and fraction-cutting), $\eta = 0.02$ and 0.10 (or 0.01 and 0.05 for a multicomponent mixture). They also relate only to component bands of equal mass (though at infinite dilution the mass ratio has no effect[9]). The procedure to be described corrects the optimum value of $n$ not only for the effect of finite concentration but also for different impurity ratios and mass ratios.

Taking $r = 0.6$ and $n_f = 2.5$, *i.e.*, $rn_f = 1.5$, $n^\infty$ is first estimated for the specified impurity fraction $\eta$ from Conder and Shingari's[9] Figs. 8 and 9 if the feed mixture is binary, or Figs. 6 and 7 if multicomponent. About three analytical scale columns are made up with different plate numbers corresponding to, say, $f = 1$, 1.8, 2.6. For example, if the value of $n$ at infinite dilution has been estimated as $n^\infty = 0.5$, then columns are required with $n = fn^\infty = 0.5$, 0.9, 1.3, say. Since the column length, $L$, is given by

$$L = NH = 36\, nH/a^2 = 36\, fn^\infty H/a^2 \tag{8}$$

where $N$ and $H$ are the plate number and plate height at infinite dilution and $a$ is given by eqn. 4, the required column lengths are approximately $L = 18\ H/a^2$, $32\ H/a^2$ and $47\ H/a^2$. $H$ is the analytical-scale plate height and, in calculating $a$, $k/(k+1)$ can be taken as approximately unity. (It is sometimes possible to achieve the same values of $fn^\infty$ with fewer columns by keeping the column length $L$ fixed and simply adjusting the carrier velocity to give the desired plate heights: $H = La^2/18$, $La^2/32$ and $La^2/47$ in the example given.)

The injection time required to give $n_f = 2.5$ is now calculated from the equation[7]

$$t_f = t_R \cdot \frac{N_f}{N} = \frac{at_R n_f}{6\, fn^\infty} = \frac{at_R}{2.4\, n^\infty} \tag{9}$$

where $t_R$ is the retention time on the column of $f = 1$ ($L = 18\ H/a^2$ in the example given) for the key component used to measure $H$. Since $t_R$ for the other columns is proportional to $fn^\infty$, $t_f$ is the same for all the columns when $n_f$ is fixed at 2.5. (If the carrier velocity is not constant $t_f$ is adjusted in inverse proportion to the velocity.) Samples of the key components are injected both individually and as a binary mixture in the proportions in which they are present in the feed specification (binary or multicomponent). The samples are each injected as rectangular feed bands for the

fixed time of injection $t_f$ calculated from eqn. 9. The rate of injection during $t_f$ is controlled to give $y_1 = y_2 = y_{mix}$ equal to the gas-phase mole fraction $y_{opt}$ previously chosen, where $y_{mix}$ is the total mole fraction of the mixture of keys 1 and 2. (This is probably safer than choosing $y_1 + y_2 = y_{mix} = y_{opt}$.) The chromatograms of the separate peaks 1 and 2 are then superimposed at the same peak separation as observed in the mixed chromatogram and cut points are found which give the desired purity specification. The recovery ratio $r$ is determined on each column and plotted against $N (= L/H)$. The number of plates $N$, required to give a recovery ratio of 0.6 at the chosen finite concentration is read from the plot. This is the design value for the large-scale column.

The procedure described is of course only approximate because the chromatogram for the mixture at finite concentration is not exactly the same as the superimposed pure component chromatograms. Nevertheless, it offers an adequate approximation in most cases and provides one of the only two procedures available at present for estimating $f$. The other, profile deconvolution, gives roughly similar results for bands not grossly skewed. The alternative approach of modelling the finite concentration band profiles, though feasible[12], is not routinely practicable because it needs data (diffusion coefficients, partition isotherms) which are not normally available without much time-consuming experimentation. Such models could, however, possibly be employed to derive general predictive relationships for the extent to which $f$ is modified by lack of superimposability of pure component band profiles in the mixture.

The final stage in the calculation requires an estimate of the theoretical plate height $H$ at infinite dilution for the large scale column under design. This value depends greatly on how the column is packed[1] as well as on the column diameter, particle size and carrier velocity already selected[18]. The design parameters are then calculated from the following equations

$$\text{Column length, } L = HN \tag{10}$$

$$\text{Feed injection time, } t_f = t_R \cdot \frac{an_f}{6n} = \frac{15t_R}{aN} \tag{11}$$

where $t_R$ is the retention time on the large scale column and is obtained by simple proportionation from the retention time on the small scale column and the ratios of column lengths and carrier velocities on both columns. The recovery ratio on the designed column will be 0.6 if $H$ proves to be as estimated. If not, it is better to maintain the fractional impurity $\eta$ by adjusting $t_f$ rather than $r$.

At this stage of the design calculation, all the parameters in eqn. 1 have been established. Accordingly the equation can now be used, if necessary, to refine the initial estimate of column diameter required to achieve the desired throughput.

*Liquid phase loading*

The stationary phase loading is not a very critical parameter since it does not affect the throughput[3]. Convenient loadings are 15–25% on pink and white diatomite supports and 5–7% on high density diatomite. In production GC, loadings at the upper end of the ranges may offer some benefit in reducing costs through permitting less frequent packing changes.

## CONCLUSIONS

The design calculations proceed as shown in Fig. 1 and detailed in the text with the following main points:

(1) Choose the stationary phase at least as much for its upper temperature limit as for its selectivity, especially if the feed mixture to be separated is only binary.

(2) Set an operating temperature equal to the mean solute boiling point at a pressure between $P_i$ and $P_i/x_{opt}$, or reverse this criterion to determine $P_i$, depending principally on the thermal stability of both the solute and the stationary phase.

(3) Use coarse particulate packing of narrow mesh spread, *e.g.*, 35–40 mesh.

(4) Choose a carrier velocity of 10–15 cm/sec in production GC, and as high as its influence on $P_i$ and column length permit in preparative GC.

(5) Inject the solute at a partial pressure which will give a liquid phase mole fraction, $x_{opt} = 0.2$–$0.5$.

(6) Use wide feed bands, *i.e.*, long injection times, calculated from eqn. 11. These will typically be measured in minutes or fractions of a minute rather than seconds.

(7) Inject successive samples so that their respective first and last components overlap at the column exit.

(8) Instead of aiming for complete resolution, cut the overlapping fraction with a recovery ratio $r = 0.6$ and recycle it; calculate the necessary column length as described under *Feedband width, column length and recovery ratio.*

An example of the proposed design procedure has recently been described in which it is applied to the separation of geraniol from nerol and α- from β-pinene, both heat-sensitive mixtures[18].

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