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Computer Simulation (Based on a Linear-Elution-Strength Approximation) as an Aid for Optimizing Separations by Programmed-Temperature Gas Chromatography

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If the dependence of retention on temperature is specified for the various components of a sample in isothermal gas chromatography (GC), it is possible to predict retention, bandwidth, and resolution for programmed-temperature GC separations as a function of experimental conditions. The use of a linear-elution-strength (LES) approximation for isothermal retention allows these predictions to be carried out more easily and conveniently, in turn facilitating rapid simulations with a personal computer. This approach to GC method development appears promising, especially if segmented-temperature programs are used. The LES approximation also provides added insight into how different factors affect separation in programmed-temperature GC.

A rigorous treatment of programmed-temperature GC separation has existed for several years, as summarized by Harris and Habgood (*1*) and used by Dose (ref 2; see also other citations of ref 2) for the computer simulation of GC separation as a function of experimental conditions. Dose (*3*) further demonstrated that computer simulation can be a valuable tool in the systematic optimization of these separations, varying (for example) the initial temperature and programming rate. Several studies (*3-10*) suggest that band spacing (values of the separation factor α) and resolution can often be varied by changing either (a) the separation temperature in isothermal GC or (b) the programming rate and/or starting temperature in temperature-programmed GC. By analogy with liquid chromatographic separations based on gradient elution (*11-14*), this suggests the use of segmented-temperature programs as a potentially useful tool for maximizing overall sample resolution in GC separations.

Our understanding of programmed-temperature GC is limited by the inherent complexity of the equations (*1*) that describe these separations. This has also prevented the wider use of computer simulation (as in refs 2 and 3) for GC method development. Thus, the application of computer simulation requires an initial knowledge of the dependence of (isothermal) sample retention on temperature. This information is most conveniently obtained (as described here) from two experimental runs using programmed-temperature GC, rather than a larger number of time-consuming isothermal runs—as has been required in previous attempts at the computer simulation of programmed-temperature GC.

Furthermore, previous attempts at computer simulation (e.g., ref 2) have used numerical integration for the solution of the rigorous equations that describe separation as a function of experimental conditions. This approach results in calculation times of 10-30 s/chromatogram when using a personal computer (*2*, *15*). These relatively slow computation times can be inconvenient when a large number of simulations are required to determine optimum final conditions (see ref 3 and the discussion of our Figure 6).

In the present study we describe an approximate treatment of programmed-temperature GC that overcomes the various problems cited above. This so-called LES approximation is similar to the linear-solvent-strength (LSS) treatment for gradient elution in liquid chromatography (*16*, *17*); it allows a comparable simplification of the various relationships be-

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tween separation and experimental conditions. The LES model also provides a basis for the development of faster computer-simulation software for GC, including accurate predictions of separation based on segmented temperature programs.

EXPERIMENTAL SECTION

Equipment. The gas chromatograph was an HP5890A (Hewlett-Packard, Avondale, PA) equipped with a split/splitless injection port and flame ionization detector. The system makes use of Hewlett-Packard's INET system network for control of the H3396A integrator and HP7672A autoinjector. Most injections were performed manually.

Column. A nonpolar column (DB-5, J & W Scientific, Folsom, CA) was used in the present study. The column was 30 m long and 0.025 cm in diameter, with a film thickness of 0.25 μm. A flow rate of 1 mL/min was used in all of the present studies.

Sample. The "phenol test mixture" is a mixture of 11 phenols: 2,4,6-trichlorophenol, 4-chloro-3-methylphenol, 2-chlorophenol, 2,4-dichlorophenol, 2,4-dimethylphenol, 2-nitrophenol, 4-nitrophenol, 2,4-dinitrophenol, 2-methyl-4,6-dinitrophenol, pentachlorophenol, and phenol (Supelco, Bellefonte, PA).

Procedures and Calculations. Replicate runs were carried out during the present study to determine the reproducibility of reported retention times: ±0.2% (1 SD). Capacity factors k' were determined from measurements of retention time t_R in isothermal separations: $k' = (t_R - t_0)/t_0$. Values of the column dead time t_0 (air-peak measurement) varied with temperature: at 100, 120, 140, 160, and 180 °C, values of t_0 were 1.96, 2.12, 2.28, 2.45, and 2.58 min, respectively (these temperature-dependent values of t_0 were used in the calculation of the k' values plotted in Figure 1). An average value of t_0 = 2.1 min was used in the computer simulations described here; the accuracy of computer predictions was relatively insensitive to the exact value of t_0 assumed.

Bandwidths $W_{1/2}$ were measured at half-height; base-line bandwidths W were calculated as $1.70W_{1/2}$. An average plate number N = 100 000 was measured from one isothermal run ($N = 16[t_R/W]^2$), and this value was assumed for all solutes and experimental conditions (isothermal or temperature programmed) in subsequent computer simulations.

Software. The computer program (DRYLAB GC, LC Resources, Lafayette, CA) described here is written for use with an IBM-compatible personal computer having a math coprocessor; it provides approximate predictions of separation, with each simulation (total sample) requiring less than 0.1 s of computing time. All references to computer simulation in the following text refer to predictions based on DRYLAB GC.

THEORY

The isothermal retention of a solute i in a GC column of phase ratio β can be assumed to be given by (*2*)

$$-T \ln k_i = -(\Delta H_{v,i}/R) + T[(\Delta S_{v,i}) + \ln \beta] \quad (1)$$

or

$$\log k_i = A + B/T \quad (2)$$

T is the column temperature (kelvin), k_i is the capacity factor of the solute i, and $\Delta H_{v,i}$ and $\Delta S_{v,i}$ are the enthalpy and entropy of vaporization of i from the stationary phase to the mobile phase. Values of $\Delta H_{v,i}$, $\Delta S_{v,i}$, A, and B are usually assumed to be temperature independent. The retention time t_R of solute i in a temperature-programmed GC separation is given (*1*) by

$$1 = \int_0^{t_R} dt/[t_0(1 + k_i)] \quad (3)$$

t is the time from injection of the sample and the start of the temperature program, and t_0 is the column dead time. For linear or segmented temperature programs (the topic of this paper), eq 3 (with k_i given by eq 2) cannot be solved explicitly, leading in turn to a number of practical complications.

The LES Approximation. A situation similar to that for programmed-temperature GC exists for gradient elution in liquid chromatography (LC), where retention time t_g is given by

$$1 = \int_0^{(t_g - t_0)} dt/(t_0 k_i) \quad (3a)$$

k_i refers to the isocratic capacity factor for a given mobile phase and solute i. In the case of gradient elution, a considerable simplification results by assuming an LSS gradient, such that

$$\log k_i = \log k_0 - b(t/t_0) \quad (4)$$

k_0 is the value of k_i at the start of separation. For reversed-phase systems and linear gradients, this requires that k_i be related to the mobile phase composition ϕ as

$$\log k_i \approx \log k_w - S\phi \quad (5)$$

k_w is the value of k_i for water as the mobile phase, ϕ is the volume fraction of organic solvent in the mobile phase, and S is a constant for a given solute i. Equation 5 is an empirical relationship that is approximately valid for typical reversed-phase separations (*18–20*). Nevertheless the use of this approximation leads to greatly simplified (but reliable) relationships between separation and experimental conditions (*11, 14, 17, 18, 20, 21*).

An approximation similar to eq 5 for gradient elution can be assumed for temperature-programmed GC:

$$\log k' = A' - ST \quad (6)$$

which leads to an LES system (as defined by eq 4) for GC carried out with a linear temperature program. The programming-steepness parameter b (eq 4 for GC) is given by

$$b = t_0 \Delta T S/t_P \quad (7)$$

ΔT is the change in temperature during the separation (equal to the final temperature T_f minus the initial temperature T_0), and t_P is the program time.

In ref 18 it was noted that plots of log k' vs %B for reversed-phase HPLC exhibit maximum deviations from linear behavior (values of Δ', see Table X of ref 18) of 13%—without an important effect on the accuracy of computer simulation. The corresponding error in eq 6 (Δ') for GC systems where eq 2 is obeyed is typically about 7%, suggesting that the LES approximation will yield errors no worse than those found for predictions of gradient elution separation based on eq 5.

The present computer-simulation program (DryLab GC) includes two additional approximations: (a) the variation in pressure between the column inlet and outlet is ignored, and (b) the dependence of t_0 on column temperature is not taken into account (pressure and t_0 are assumed constant). The use of computer simulation for GC method development does not require extreme precision in predictions of separation, however; resolution values within ±10% and retention times within ±5% are adequate.

LES Relationships. The prediction of temperature-programmed GC separation as a function of experimental conditions requires certain explicit equations that can be derived from eq 3, 6, and 7. Solute retention time for a linear temperature program is given as

$$t_R = (t_0/2.3b) \ln [e^{2.3b}(k_0 + 1) - k_0] \quad (8)$$

For the case of segmented-temperature programs, an equation is also required for the fractional migration r of the solute along the column during a given segment. A derivation similar to that for the case of gradient elution (eqs 23a–c of ref 16) yields

$$r = (1/2.3b) \ln [(e^{2.3bt/t_0} + k_0)/(k_0 + 1)] \quad (9)$$

The base-line bandwidth W (4σ, min) at elution is given by

$$W = 4t_0(1 + k_e)N^{-1/2} \quad (10)$$

k_e refers to the value of k_i at elution, and N is the column plate number. Values of k_e can be calculated from eq 2, and the temperature T_e at elution, which is given by

$$T_e = T_0 + (t_R/t_P)(T_f/T_0) \quad (11)$$

for a linear temperature program:

$$T = T_0 + (t/t_P)(T_f - T_0) \quad (12)$$

The resolution of any two adjacent bands 1 and 2 in the chromatogram is

$$R_s = 2(t_2 - t_1)/(W_1 + W_2) \quad (13)$$

t_1 and t_2 refer to values of t_R for bands 1 and 2, and W_1 and W_2 are the corresponding bandwidths.

Isothermal Predictions from Gradient Data. If experimental data from two temperature-programmed runs are used to predict isothermal separation, significant errors in retention can arise from the excessive extrapolation of eq 6 outside the temperature range covered by the two experimental runs used to initiate computer simulation (see later discussion of Figure 5). A similar problem is encountered in computer simulations for gradient elution (*19, 20*). These GC errors can be minimized by using values of A' and S to predict values of A and B in eq 2. The latter relationship can then be used to predict isothermal retention.

This approach begins with eq 6, and values of A' and S derived as above. For one of the two input runs and a given solute, the "average" k' value ($\bar{k}$) during elution of the band is estimated in an analogous manner as for the case of gradient elution (*18*); $\bar{k}$ corresponds to the k' value when the band has eluted halfway through the column. For GC this value of k_i ($\bar{k}$) can be obtained from eq 9 by (a) setting $r = 0.5$ and solving for t, (b) determining $\bar{T} = T$ at time t, and (c) using eq 6 to calculate $k_i = \bar{k}$ at the column midpoint. A similar procedure is applicable for the same solute in the second input run (different programming rate or value of t_P), yielding a second set of values of $\bar{T}$ and $\bar{k}$ that can be used with eq 2 to solve for values of A and B.

RESULTS AND DISCUSSION

Computer Simulation. The computer-simulation program used in the present study is based on the preceding LES-derived relationships. Beginning with two experimental temperature-programmed runs having different times t_P and other conditions the same, values of b and k_0 for each solute i are derived by a numerical solution of eq 8 (see the similar treatment of gradient elution in ref 22). Equations 6 and 7 plus the starting experimental conditions then allow the calculation of corresponding values of S and A' (eq 6), which permits the prediction of separation as a function of different experimental conditions: T_0, T_f, t_P, temperature-program shape, and N. Values of N are assumed to be the same for all solutes in the sample and for all separation conditions (isothermal or temperature programmed).

Accuracy of Computer Simulation: Retention Time. Experimental data for both programmed and isothermal runs were collected for a range of separation conditions to evaluate the accuracy of predicted retention times. The isothermal data are summarized as k' vs $1/T$ in Figure 1. All subsequent computer simulations were based on the same two experimental runs for input (50–250 °C, program rates of 4 and 12 °C/min).

Table I compares predicted and experimental retention times for several different separation conditions (both temperature programmed and isothermal) and gives average errors in retention time and *retention-time differences* for adjacent bands; the latter are proportional to resolution (eq 13). Table II summarizes similar data for a larger number of experimental runs; the average error is ±5.1% for predicted retention times and ±7.2% for retention-time differences.

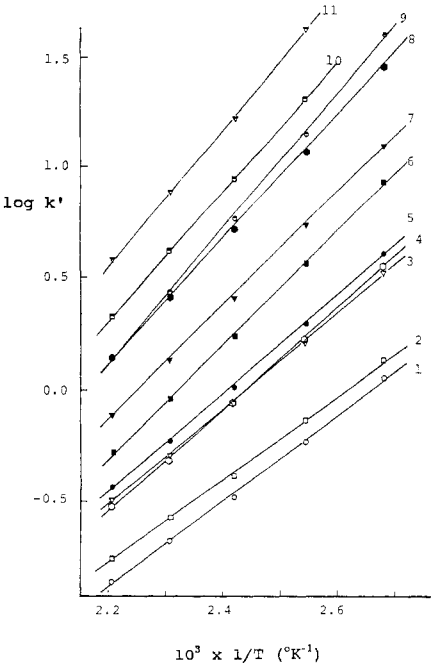


Figure 1. Isothermal retention vs temperature for the phenol mixture.

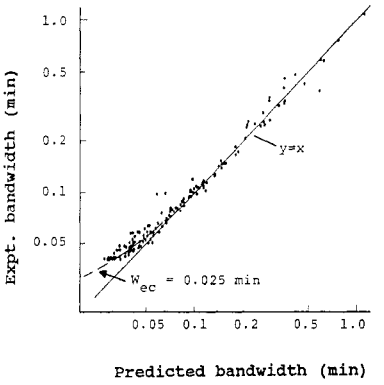


Figure 2. Experimental vs predicted bandwidths for the phenol mixture and separation conditions of Table II. No correction for extra-column effects.

Accuracy of Computer Simulation: Bandwidths. Figure 2 shows a log–log plot of predicted vs experimental values of W for the various runs summarized in Tables I and II; the solid curve in Figure 2 is the line for $y = x$. Although the overall agreement between experimental and predicted bandwidths is reasonably good (±13% average), experimental bandwidths are consistently larger than predicted when $W < 0.05$ min. These errors in predicted values of W for narrow bands could arise from either (a) extra-column contributions to band broadening or (b) an increase in the plate number N as k' increases. Either possibility is plausible (*2, 23*); we have chosen to treat the combined effect as an extra-column contribution to W, so that

$$W_{expt}^2 = W_{calc}^2 + W_{ec}^2 \quad (14)$$

Here W_{expt} is the observed (experimental) bandwidth, W_{calc} is the expected value (from computer simulation), and W_{ec} is an "effective" contribution from extra-column sources.

The present software allows a value of W_{ec} for the GC system to be entered, based upon preliminary observations of predicted vs experimental bandwidths as a function of W. The data of Figure 2 suggest a value of $W_{ec} = 0.025$ min,

Table I. Comparison of Experimental vs Computer-Simulated Retention Times for Phenol Mixture (Conditions as in Experimental Section except as Noted)

			retention times for other run conditions,[c] min									
	input data[b] 50–250 °C		100–250 °C				150–250 °C		isothermal runs			
			6 °C/min		12 °C/min		2 °C/min		100 °C		180 °C	
band[a]	run 1	run 2	expt	calc	expt	calc	expt	calc	expt	calc	expt	calc
#1	9.24	5.83	3.63	3.64	3.33	3.24	2.68	2.43	4.20	4.39	2.54	2.34
2	9.61	6.10	3.92	3.94	3.56	3.47	2.81	2.56	4.61	4.82	2.62	2.44
3	14.70	8.12	5.74	5.92	4.75	4.76	3.47	3.28	8.45	8.96	2.95	2.79
4	15.24	8.19	5.74	5.96	4.75	4.74	3.39	3.21	8.80	9.41	2.89	2.70
5	15.99	8.58	6.24	6.48	5.09	5.09	3.67	3.52	9.93	10.6	3.05	2.89
6	20.39	10.06	8.20	8.56	6.21	6.25	4.50	4.60	18.8	20.2	3.41	3.29
7	22.66	11.02	9.65	10.0	7.09	7.15	5.52	5.86	26.3	28.0	3.95	3.96
8	27.65	12.79	12.7	13.0	8.73	8.78	8.12	8.95	58.0	61.5	5.32	5.61
9	28.49	12.94	13.0	13.4	8.84	8.90	8.37	9.31	80.3	76.8	5.32	5.68
10	31.11	14.03	14.9	13.3	9.92	9.97	10.9	12.0	*d*	107	6.98	7.66
11	35.39	15.62	17.8	18.1	11.5	11.5	15.5	16.8	*d*	204	10.6	12.1
error[e]												
retention time, min			+0.18 ± 0.11		+0.02 ± 0.04		+0.49 ± 0.34		±1.36 ± 0.97		±0.15 ± 0.49	
retention time, %			±2.8		±0.6		±7.4		±5.4		±4.7	
resolution, min (%)			+0.05 ± 0.05 (±6.1%)		+0.01 ± 0.04 (±4.5%)		+0.11 ± 0.12 (±7.6%)		+0.34 ± 0.60 (±1.7%)		+0.09 ± 0.11 (±17.5%)	

[a] Bands numbered as in Figure 1. [b] Run 1 is 4 °C/min and run 2 is 12 °C/min. [c] Initial and final temperatures shown with programming rates. [d] Bands did not elute within 90 min. [e] Errors in retention time (min) are expressed as the average error ±1 standard deviation from the latter value; errors in retention time (%) are equal to the average absolute error divided by the average retention time × 100; errors in resolution are equal to the average absolute error in retention time differences (for two adjacent bands) divided by the average difference in retention times for all adjacent bands.

Table II. Summary of Comparisons of Experimental vs Computer-Simulated Retention Times for Phenol Mixture (as in Table III; Conditions as in Experimental Section except as Noted)

temp range, °C	programming rate, °C/min	retention time errors[a] min	retention time errors[a] ±%	resolution errors,[a] ±%
50–150	1	−4.3 ± 5.6	9.2	13.3
100–250	1	+1.10 ± 1.19	5.5	8.9
	4	+0.34 ± 0.15	3.0	4.0
	6	+0.22 ± 0.18	2.8	6.1
	8	+0.17 ± 0.08	2.1	6.9
	12	+0.03 ± 0.04	0.6	4.5
150–250	2	+0.04 ± 0.41	7.4	7.6
	12	−0.17 ± 0.12	4.2	8.0
isothermal				
100		1.36 ± 1.09	5.4	2.6
120		1.00 ± 0.79	4.5	5.5
140		0.95 ± 0.91	8.1	8.6
160		0.57 ± 0.77	8.4	14.0
180		0.25 ± 0.25	4.7	17.5
av errors, %			±5.1	±7.2

[a] See footnote *e* of Table I.

Table III. Summary of Comparisons of Experimental vs Computer-Simulated Bandwidths for the Phenol Mixture (as in Table IV for Retention Times; Conditions as in Experimental Section except as Noted)

temp range, °C	programming rate, °C/min	bandwidth errors[a] min	bandwidth errors[a] ±%
50–150	1	0.00 ± 0.75	12.9
50–250	4	0.07 ± 0.07	9.6
	12	0.03 ± 0.04	7.3
100–250	1	0.12 ± 0.16	9.3
	4	0.04 ± 0.09	6.0
	6	−0.01 ± 0.03	5.2
	8	−0.08 ± 0.11	12.8
	12	−0.01 ± 0.03	4.4
150–250	2	−0.01 ± 0.03	5.3
	12	−0.07 ± 0.02	14.3
isothermal			
100		0.07 ± 0.06	3.1
120		0.01 ± 0.26	4.0
140		0.08 ± 0.08	5.7
160		0.02 ± 0.06	4.8
180		−.03 ± 0.04	6.4
av error, %			±7.3

[a] See footnote *e* of Table I (bandwidth W replaces retention time t_p).

corresponding to the best-fit (dashed) curve through the data for smaller values of W. Table III summarizes our comparison of predicted vs experimental bandwidths for the separations of Table II, with predicted values corrected for $W_{ec} = 0.025$ min. The average error in predicted values of W has been reduced from 13% (no W_{ec} correction) to 7.3% (eq 14 values).

The present approach for predicting bandwidths uses a single experimental value of N (eq 10 with N constant for all conditions and solutes), based on the two temperature-programmed runs used as input. Thus different values of N can be tried until experimental and predicted bandwidths agree for the input runs. Alternatively, a value of N measured from separate isothermal runs can be used, as in the present case.

Accuracy of Computer Simulation: Resolution. The various approximations in the present treatment are such that adjacent bands are affected similarly. This implies that errors in predicted retention times should be highly correlated with retention time, and this was found to be the case (illustrated in Figure 3 for three different runs). This is fortunate, because it means that predictions of retention-time differences (and

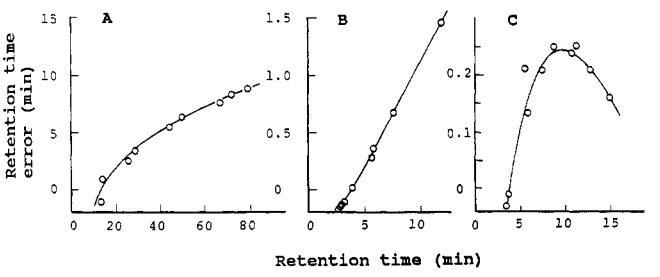


Figure 3. Correlation of errors in predicted retention times with retention time for phenol mixture: (A) 50–150 °C, 1 °C/min; (B) isothermal run at 180 °C; (C) 100–250 °C, 8 °C/min.

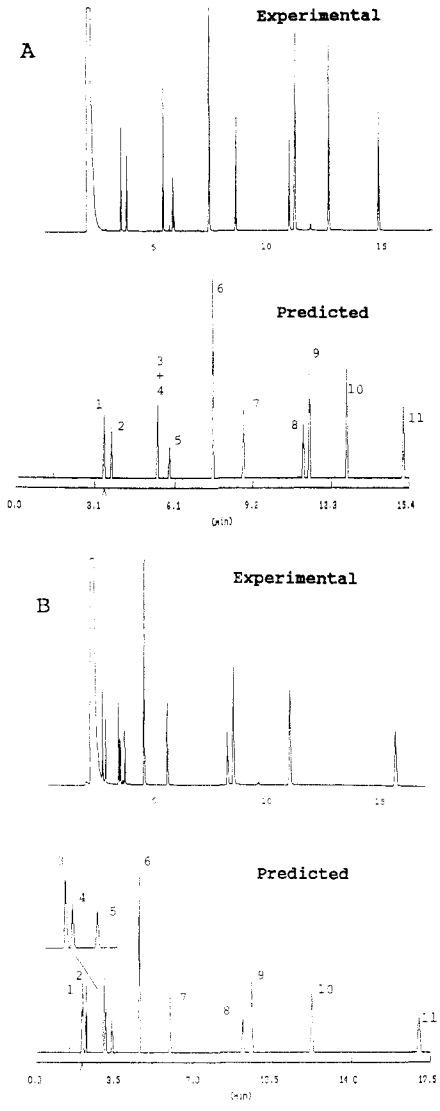


Figure 4. Comparisons of experimental and computer-simulated chromatograms: (A) 100–250 °C, 8 °C/min; (B) 150–250 °C, 2 °C/min (expanded chromatogram as insert).

resolution) will be much better than expected from the error in retention times alone, due to cancellation of errors for adjacent bands (having similar retention). A similar situation has been observed for the computer simulation of gradient elution based on the LSS approximation.

From the average errors in retention-time differences (±7.2%) and bandwidth (±7.3%), we can estimate that the average error in predicted values of resolution will be about ±10%, assuming that these errors are random—rather than being inversely correlated with each other (as required by eq 13 for additive errors). This accuracy of predicted resolution values should be adequate for the use of computer simulation in the optimization of a GC separation.

Further comparisons of resolution are shown in Figure 4, where computer-simulated and experimental chromatograms are compared for two runs from Tables I–III. The critical band-pairs are 1/2, 3/4, and 8/9; experimental and predicted values of R_s for these band pairs in Figure 4 agree within an average of ±0.3 units for a range in values of $0 < R_s < 5.6$; i.e., average error of ±11%.

Further Analysis of Errors from Computer Simulation. GC retention errors introduced by the LES approximation are similar to corresponding errors from the LSS approximation in predictions of gradient elution retention (*18*, *20*, *25*). In gradient elution and by analogy temperature programmed GC, there is an average value of k' and T ($\bar{k}$ and $\bar{T}$) for each solute during the separation. These values of $\bar{k}$ and $\bar{T}$ (which can be obtained as described above) are shown on the isothermal plots of log k' vs T in Figure 5 (dark circles for different programming rates; 50–250 °C program range). The values of A' (or log k_0) and S in eq 6 correspond to the straight line (LES approximation) through two such data points; e.g., the 4 and 12 °C/min runs for band 11. It is seen that this (dashed) line tracks the experimental plot of log k' vs T quite closely between the two points used to define A' and S, but the LES line deviates increasingly outside this range. Thus for another run at 1 °C/min (Figure 5), the LES line predicts a value of k' at this temperature (T = 126 °C) that is in error by about 1.5-fold. This in turn means a corresponding (but smaller) error in the prediction of retention time for band 11 in the 1 °C/min run.

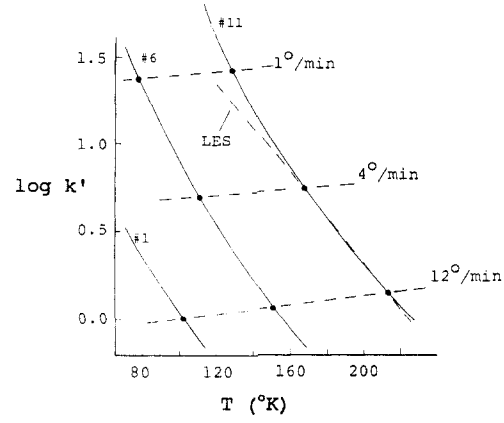


Figure 5. Illustration of the error introduced by the LES approximation in computer simulation. Solid curves are experimental plots of log k' vs T for phenol bands 1, 6, and 11. The solid points (●) indicate the temperature ($\bar{T}$) and retention ($\bar{k}$) of each band (for different runs; 1, 4, or 12 °C/min) when it has reached the column midpoint. The dashed line (LES) is the straight-line plot for eq 6 as derived from data for band 11 and the 4 and 12 °C/min runs as imput to DRYLAB GC.

Figure 5 suggests that predicted values of $\bar{k}$ (and retention time) will be slightly too high for the 6 °C/min run, and significantly too low for the 1 and 24 °C/min runs. The data of Tables I and II confirm the general conclusion from Figure 5 that the accuracy of retention predictions decreases as the separation conditions become more different from those used for the two input runs. The present software provides warnings of possible large errors in predicted separations, whenever separation conditions differ significantly from those for the two input runs.

On the basis of the above discussion and similar treatments of gradient elution (*18*, *20*, *24*), some recommendations can be made concerning the best conditions for the temperature-programmed runs used as input for computer simulation. First, the heating rates used for the two input runs that allow calculation of values of k_0 and S should optimally be in a ratio of between 3 and 4; e.g., 4 and 12 °C/min as in the simulations of Tables I and II. Second, the derived values of k_0 and S required in LES computer simulations are less reliable for early eluting bands. Therefore it is desirable that the first band in each of the two input runs has a retention time $t_R > 3t_0$. Finally, input runs that have very steep temperature programs (>12 °C/min) give less reliable predictions.

Optimization of the Temperature Program. In general we desire the adequate separation of the sample (usually corresponding to some minimum resolution for all adjacent band pairs) in minimum time. Dose (*3*) has described the selection of optimum values of the heating rate (°C/min) and starting temperature, using a Simplex algorithm that systematically searches for the best compromise between resolution and run time. The faster computer simulations pro-

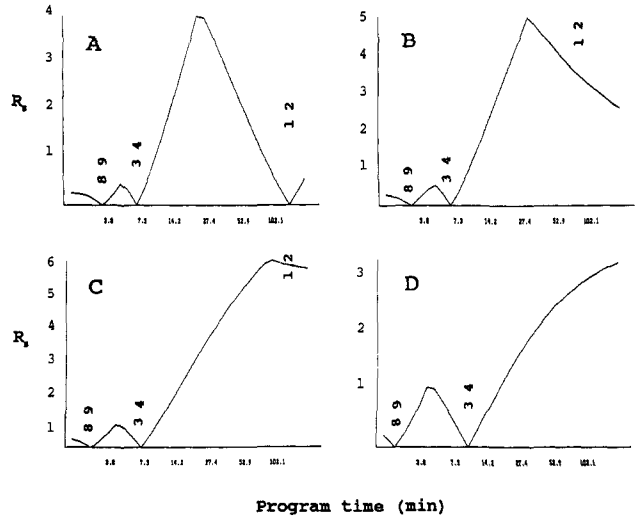


Figure 6. Predicted minimum resolution as a function of program time (or heating rate) and starting temperature. Final temperature 200 °C; other conditions as in Table I. Starting temperatures: (A) 25; (B) 50; (C) 75; (D) 100 °C.

Table IV. Computer Simulations as a Function of Heating Rate for 50–200 °C Temperature Program (Phenol Sample)

rate, °C/min	min R_s	crit band pair	retention last band, min
2.0	3.52	1, 2	57.7
2.5	3.86	1, 2	49.5
3.0	4.16	1, 2	43.5
3.5	4.43	1, 2	38.9
4.0	4.67	1, 2	35.4
4.5	4.88	1, 2	32.5
5.0	4.82	3, 4	30.0
5.5	4.46	3, 4	28.0
6.0	4.13	3, 4	26.3
6.5	3.82	3, 4	24.7

vided here (<0.1 s/chromatogram) permit a different strategy, which we will now illustrate for the case of the 11-component phenol mixture.

One option provided by the present software is the display of a relative resolution map (RRM, similar to a window diagram (*25*), in which the predicted resolution of the poorest-resolved ("critical") band pair is plotted against the run time t_P (or alternatively the heating rate). Figure 6A illustrates such a plot for the present phenol sample, based on a 25–200 °C temperature program. The critical band pairs are indicated in the RRMs of Figure 6: 1/2, 3/4, and 8/9. For reasonable resolution ($R_s > 1$), only band pairs 1/2 and 3/4 need be considered. Note also that the relative retention of each of these band pairs is reversed at some characteristic heating rate or value of t_P; i.e., for $R_s = 0$ in Figure 6A.

The initial temperature T_0 can be varied for each RRM, as illustrated in Figure 6 where RRMs are shown for the phenol sample and different values of T_0: 25, 50, 75, and 100 °C for parts A–D, respectively. Additional RRMs were examined for temperatures either <25 °C or >100 °C, but these conditions appeared less promising.

The choice of preferred conditions (initial temperature, heating rate) on the basis of Figure 6 depends on our goal. If maximum resolution in some reasonable time (e.g., <50 min) is desired, Figure 6 suggests that the initial temperature should be about 50 °C (B), and the heating rate should be about 5 °C/min, in which case the minimum resolution (for bands 1/2 and 3/4) will be $R_s \approx 5.0$ in a run time ≈30 min. This recommendation can be fine tuned by examining heating rates close to 5 °C/min (see Table IV); a heating rate of 4.6 °C/min

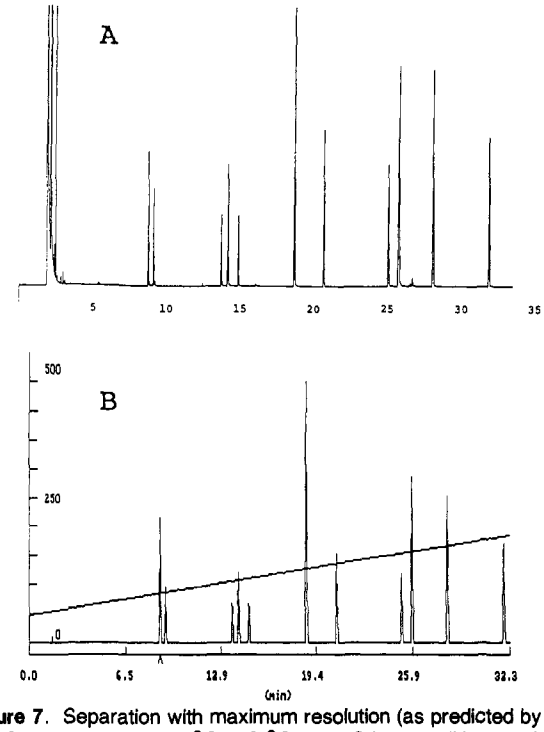


Figure 7. Separation with maximum resolution (as predicted by Figure 6). Conditions: 50–200 °C, 4.6 °C/min. Other conditions as in Table I. (A) Experimental chromatogram; (B) predicted chromatogram.

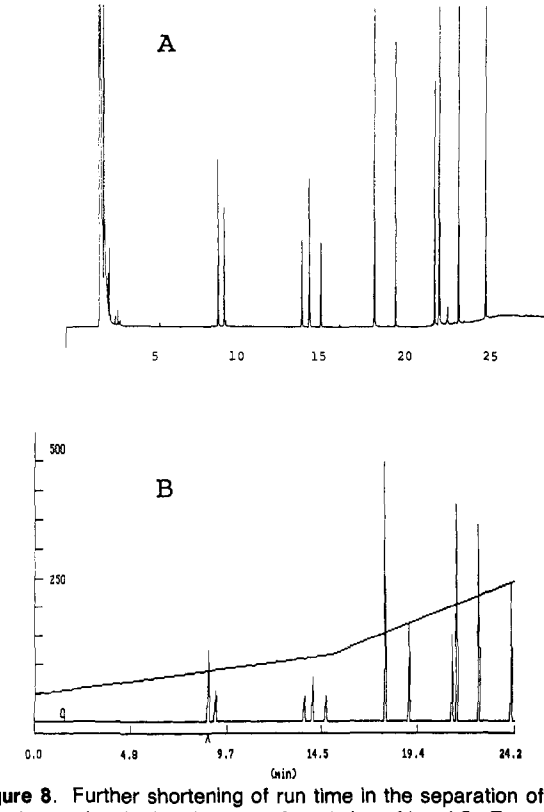


Figure 8. Further shortening of run time in the separation of Figure 7 by increasing the heating rate after elution of band 5. Temperature program of 50/120/250 °C in 0/15/25 min; other conditions as in Figure 7. (A) Experimental chromatogram; (B) predicted chromatogram.

is near optimum. Figure 7B shows the predicted separation, while Figure 7A shows the actual experimental run. There is close agreement between the two chromatograms, and the predicted resolution for the poorest resolved band pair (R_s = 4.8 for bands 1/2 in Figure 7B) is in good agreement with the experimental value (R_s = 5.2 in Figure 7A). Retention

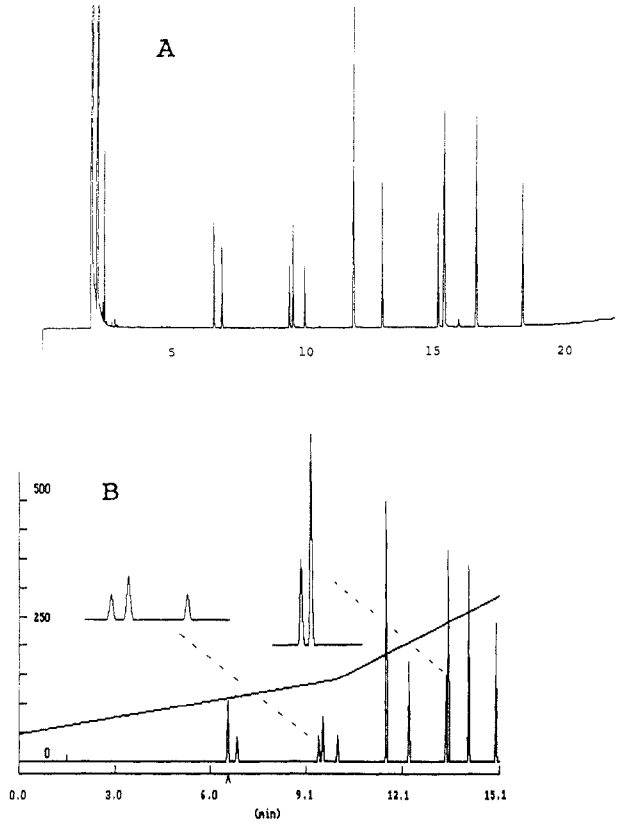


Figure 9. Separation with resolution $R_s > 2.5$ in minimum time. Temperature program of 50/142/300 °C in 0/10/15 min; other conditions as in Figure 7. (A) Experimental chromatogram; (B) predicted chromatogram (expanded chromatograms as inserts).

times agree between the two runs within ±0.2% (average).

The separation of Figure 7 can be further improved by using a segmented temperature program to shorten the run time without any loss in resolution (increase in heating rate after the elution of band 5). Trial-and-error computer simulations resulted in the proposed separation of Figure 8B, which was confirmed in the experimental run of Figure 8A. A resolution of $R_s = 5.2$ is maintained (as in Figure 7), while the run time is shortened from 31 to 25 min. The average error in predicted retention times was ±1.4%.

Alternatively, it might be desired to obtain some minimum resolution for all bands (e.g., $R_s > 2.5$), in the shortest possible run time. The RRMs of Figure 6 were used to guide trial-and-error simulations for each starting temperature, with the conclusion that a linear program and any starting temperature between 25 and 75 °C gives a similar run time (19–21 min) for a resolution of $R_s = 2.5$. Arbitrarily selecting 50 °C for the starting temperature, followed by the design of a segmented temperature program as in Figure 8, it was predicted that the run time could be further reduced to just 15 min. Figure 9 compares the predicted and experimental chromatograms. Retention time predictions (±11%) for this run are not as good, because the heating rate in the second segment is 32 °C/min, i.e., well outside the input rates of 4 and 12 °C/min (cf. discussion of Figure 5). The prediction of resolution is, however, quite acceptable.

It should be noted that the final temperature must be increased from 200 °C in the run of Figure 7 to 250 °C in Figure 8 and 300 °C in Figure 9, because an increase in heating rate (4.6 to 13 to 32 °C/min in the final segment) results in elution of the sample at a higher average temperature.

Other possible requirements for a final separation can be visualized. In every case it should be possible to quickly select promising (or "optimum") separation conditions by the use of computer simulation as illustrated here.

CONCLUSIONS

The basic theory of temperature-programmed GC separation can be simplified for easier understanding and faster calculation by the use of a linear-elution-strength (LES) approximation. We have used this approach to design a personal-computer program that can rapidly predict GC separations as a function of the temperature program: initial and final temperatures, heating rate, and program shape (e.g., segmented or linear). Isothermal separation can also be predicted as a function of temperature. The experimental data required for these computer simulations are obtainable from just two temperature-programmed runs with the sample of interest. For 13 such separations (widely varying conditions) of a mixture of 11 phenols, the average error of predicted retention times was ±5.1%, bandwidths ±7.1%, and resolution ≈ ±10%.

Because GC band spacing can vary with temperature in isothermal separations, temperature-programmed separations can be quite sensitive to optimum choices of starting temperature, heating rate, and temperature-program shape. The present computer-simulation program allows sample resolution to be mapped as a function of these variables with minimum effort, which can greatly facilitate method development for GC. This is illustrated for the above phenol sample.

GLOSSARY

A, B	constants in eq 2
A'	constant in eq 6
b	temperature-program steepness parameter (eq 7)
F	mobile phase flow rate (mL/min)
GC	gas chromatography
k_i	solute capacity factor
$\bar{k}$	value of k' when a solute has reached the column midpoint
k_e	value of k' at elution
k_0	initial value of k' in temperature-programmed GC or gradient elution (eq 4)
k_w	value of k' in liquid chromatography for water as mobile phase
LC	liquid chromatography
N	column plate number
r	fractional movement of a solute through the column (eq 9)
R_s	resolution between two adjacent bands (eq 13)
S	constant in eq 5 or 6
t	time after sample injection and the beginning of the temperature program
t_g	solute retention time in gradient elution (LC)
t_0	column dead time (min)
t_P	program time for a linear temperature program
t_R	solute retention time in temperature-programmed GC
T	column temperature; usually in °C, except eqs 1 and 2
$\bar{T}$	average column temperature during the separation of a given band, equal to T when the band has reached the halfway point in the column
T_e	temperature at the time of elution of a given solute
T_f	final temperature in temperature-programmed GC
T_0	initial temperature in temperature-programmed GC
V_m	column dead volume (mL)
W	baseline bandwidth (min)
W_{expt}	experimental values of W; extra-column band broadening is ignored
W_{calc}	predicted value of W (eq 14)
W_{ec}	extra-column contribution to bandwidth (eq 14)
W_1, W_2	values of W for two adjacent bands 1 and 2
$W_{1/2}$	bandwidth at half-height
β	phase ratio of the column
$\Delta H_{v,i}$	enthalpy of vaporization of the solute i from the stationary-phase liquid
$\Delta S_{v,i}$	entropy of vaporization of the solute i from the stationary phase liquid

ΔT change in temperature during a programmed temperature GC run

ϕ volume fraction of strong solvent B in a mobile phase A/B used in liquid chromatography

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Retention Volume and Intensity of Analyte and System Peaks in Ion-Exchange Chromatography with Bulk-Property Detectors

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Computer simulations and experimental investigations were carried out on the behavior of analyte and two system peaks in ion-exchange chromatography by indirect photometric detection. The computer programs were constructed with PASCAL based on the plate theory and the acid partition model. The calculation results coincide with the experimental observations obtained with benzoate and benzenesulfonate eluents. The acid partition model by Jackson and Haddad was verified. The intensity of the analyte peaks also varies, as does that of the system peaks, with the experimental conditions. When the second system peak appears near an analyte peak, mutual influences are large, resulting in distorted peaks. Generally, a neutral salt eluent is preferable for reproducible analysis, as the second system peak hardly appears when it is used.

In analytical ion-exchange chromatography with bulk-property detectors (*1*) such as an electric conductivity detector or an ultraviolet (UV) absorption detector in the indirect mode (*2*), a few peaks in addition to the analyte peaks are observed. They have been called "system peaks", "pseudopeaks", and so on.

Okada and Kuwamoto (*3*) studied the behavior of two system peaks (referred to as "dip peaks") in ion-exchange chromatography of anions by conductivity and UV absorption detection using tartrate eluents. They discovered that, as the sample was injected, ion exclusion of sample cations took place, and subsequently the eluent anion that had been replaced by the sample ion moved to form the first dip. The second dip was determined to correspond to the deficient zone of the eluent ion. They did not consider the behavior of the conjugate acid (HB) of the eluent anion (B^-) in the column or the shift of the acid–base equilibrium in the column as the sample was injected. Nor did they observe the analyte peak.

Jackson and Haddad (*4*) studied the behavior of the system peaks in ion-exchange chromatography of anions by indirect absorption detection using phthalate eluents. As the sample was injected, both the eluent anion and the conjugate acid were released from the stationary phase, and B^- passed directly through the column to form the injection peak. HB passed through the column in a reversed-phase partition mode to form the second pseudopeak (they called it a system peak). In practice, an HB-deficient zone often moves to form the system peak.

The model of Jackson and Haddad is thought to be adequate to explain, qualitatively, the experimental facts relating to the two system peaks. However, it does not give a quantitative discussion of the peaks' intensities. There remain some specific problems that cause the intensity of the peak to be quantified to vary with experimental conditions, and the system peaks to be observed even with a strong acid eluent (*5*).

In connection with this, the present author has performed calculations based on the plate theory in accordance with the model of Jackson and Haddad in order to clarify the relationship between the behavior of analyte and system peaks according to various experimental parameters. A bibasic anion such as a phthalate ion has been used as the eluent in many cases. However, in the present study, aqueous solutions of monobasic acid (HB), its salt (NaB), and a mixture of the two were adopted as the eluents for simplicity of calculation, and the elution of monovalent sample ions was dealt with. Because

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