

Note

Velocity programming of chromatographic separations: a mathematical model

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(Received October 19th, 1983)

The use of mobile phase, stationary phase and other programming and gradient techniques has expanded in chromatographic practice. Among these techniques are temperature-programmed gas chromatography¹, gradient elution² and flow (pressure) programming³. These methods can dramatically decrease the separation time, frequently without a decrease in the resolution of the output peaks. It is likely that these techniques, and combinations of them, will be applied to both large- and small-scale systems in the future.

This study was concerned with flow programming, in which the inlet pressure of the fluid to a column is increased, so that the flow-rate increases with time. The advantage of velocity programming over temperature programming is that it can reduce the processing time, and hence band spreading and skewness, for wide-ranging mixtures, while keeping the column at low temperature. Ettre *et al.*³ discussed flow programming for packed columns. Poy⁴ reported renewed interest in flow programming for capillary gas chromatography. If the mobile phase velocity in liquid-solid adsorption chromatography is increased with time, a better separation and a shorter analysis time can be achieved, according to Liteanu and Gocan². Scott and Lawrence⁵ showed experimentally that high-boiling fractions of essential oil were separated on silica-gel in one third of the time by linearly increasing the flow-rate from 0.4 to 1.4 ml/mm over 90 min. Nygren's⁶ exponential flow programming in gas-liquid capillary chromatographic columns yielded chromatograms similar to those in linear temperature-programmed gas chromatography. Snyder⁷ showed that separations in liquid-solid adsorption chromatography gave the same resolution per unit time with either flow programming or temperature programming. Although the practical value of flow programming has been demonstrated, its mathematical explication seems not to have received much attention.

A mathematical procedure, based on use of temporal moments, has been devised for describing gradient and programming methods in chromatographic separations^{8,9}. McCoy⁸, in examining temperature-programmed gas chromatography, showed that the procedure generalized earlier results for retention time by including band spreading and skewness. Duarte and McCoy⁹ estimated the quantitative advantages of stationary spatial temperature gradients and suggested an operating procedure for realizing those benefits. The present objective was to apply this mathematical method to velocity-programmed chromatographic separations. The math-

emathical analysis applies generally to gas or liquid mobile phases in packed-column or open-tube chromatography.

THEORETICAL

The models for chromatography in a long column yield differential expressions for the normalized moments^{8,9}:

$$d\mu'_1 = f dz \quad (1)$$

$$d\mu_2 = g dz \quad (2)$$

$$d\mu_3 = h dz \quad (3)$$

The terms f , g and h are known functions of z for gradient chromatography. For programmed chromatography f , g , and h are functions of t . In this case $d\mu'_1 = dt$ represents the incremental time for the migrating solute, and we may write eqns. 1, 2 and 3 as

$$dz = dt/f(t) \quad (4)$$

$$d\mu_2 = dt g(t)/f(t) \quad (5)$$

$$d\mu_3 = dt h(t)/f(t) \quad (6)$$

Eqns. 4-6 may be integrated when f , g and h are explicit for a given chromatographic model and process. Once moment expressions have been calculated, HETP and resolution readily follow according to their respective definitions:

$$\text{HETP} = \mu_2^2/(\mu'_1)^2 \quad (7)$$

$$R_s = \frac{\mu_{1A} - \mu_{1B}}{\sqrt{\mu_{2A}} + \sqrt{\mu_{2B}}} \quad (8)$$

In essence, the method of analysis we have developed is a way of solving (or obtaining information from) partial differential equations with non-constant coefficients. The reason the method works is that the changes in time (programming) or in space (imposed gradients) are small compared with the concentration changes in the column. In other words, the concentration profiles (pulses) have concentration changes that are at least an order of magnitude larger than the property changes of programming or gradient methods.

A simple model for chromatography¹⁰ contains the essential velocity-dependent features of convection and longitudinal dispersion:

$$\varepsilon(1 + k)\partial c/\partial t + v\partial c/\partial z - D_a\partial^2 c/\partial z^2 = 0 \quad (9)$$

in terms of the species concentration $c(z,t)$. With initial and boundary conditions

$$c(z, 0) = 0 \quad (10)$$

$$c(0,t) = c_0(t) \quad (11)$$

$$c(\infty, t) = \text{finite} \quad (12)$$

one can calculate the coefficients in moment eqns. 1, 2 and 3:

$$f = \varepsilon(1 + k)/v \quad (13)$$

$$g = 2D_a \varepsilon^2(1 + k)^2/v^3 \quad (14)$$

$$h = 12 D_a^2 \varepsilon^3 (1 + k)^3/v^5 \quad (15)$$

The velocity dependence of longitudinal dispersion in packed columns may be represented as¹¹

$$D_a = \gamma_1 + \gamma_2 v \quad (16)$$

where

$$\gamma_1 = 0.7 D_{AB} \quad (17)$$

and

$$\gamma_2 = 1.75 d_p/\varepsilon \quad (18)$$

This expression accurately represents the axial dispersion data collected by Dullien¹² for a broad range of velocities:

$$10^{-3} \leq v d_p/\varepsilon D_{AB} \leq 10^7 \quad (19)$$

For open tubes of radius R the velocity dependence of D_a is given by the well known equation^{11,12}

$$D_a = D_{AR} + \eta v^2 \quad (20)$$

where

$$\eta = R^2/48D_{AB} \quad (21)$$

Linear velocity programming

For linear velocity programming we have uniformly in the column

$$v(t) = v_i + \beta t \quad (22)$$

Substituting into eqns. 13 and then 4 and integrating up to the retention time μ'_1 gives, for a column of length z ,

$$z = \frac{1}{\varepsilon(1+k)} \left(v_i \mu'_1 + \frac{1}{2} \beta \mu'^2_1 \right) \quad (23)$$

or, solving for μ'_1 ,

$$\mu'_1 = \frac{1}{\beta} [-v_i + \sqrt{v_i^2 + 2\beta\varepsilon(1+k)z}] \quad (24)$$

for both packed columns and capillary columns.

For second and third central moments, eqns. 5 and 6 may be integrated (with $dv = \beta dt$) to give for packed columns

$$\Delta\mu_2 = \frac{2\varepsilon(1+k)}{\beta} [\gamma_1(1/v_i - 1/v_r) + \gamma_2 \ln(v_r/v_i)] \quad (25)$$

and

$$\Delta\mu_3 = \frac{12\varepsilon^2(1+k)^2}{\beta} \left[\frac{\gamma_1^2}{3} (v_i^{-3} - v_r^{-3}) + \gamma_1\gamma_2(v_i^{-2} - v_r^{-2}) + \gamma_2^2 (v_r^{-1} - v_i^{-1}) \right] \quad (26)$$

where the velocity at the retention time is

$$v_r = v_i + \beta\mu'_1 \quad (27)$$

For open-tube columns we obtain

$$\Delta\mu_2 = \frac{2\varepsilon(1+k)}{\beta} [D_{AB} (v_i^{-1} - v_r^{-1}) + \eta(v_r - v_i)] \quad (28)$$

and

$$\Delta\mu_3 = \frac{12\varepsilon^2(1+k)^2}{\beta} \left[\frac{D_{AB}^2}{3} (v_i^{-3} - v_r^{-3}) + 2D_{AB}\eta(v_i^{-1} - v_r^{-1}) + \eta^2(v_r - v_i) \right] \quad (29)$$

Exponential velocity programming

For an exponentially increasing velocity,

$$v = v_i e^{\alpha t} \quad (30)$$

so that

$$v_r = v_i \exp(\alpha\mu'_1) \quad (31)$$

Integration of the differential first-moment equation (with $dt = dv/\alpha v$) yields

$$L = (v_r - v_i)/\alpha \varepsilon (1 + k) \quad (32)$$

or

$$\mu'_1 = \frac{1}{\alpha} \ln[1 + L\alpha\varepsilon(1 + k)/v_i] \quad (33)$$

For packed columns we have

$$\Delta\mu_2 = \frac{2\varepsilon(1 + k)}{\alpha} \left[-\frac{1}{2}\gamma_1(v_r^{-2} - v_i^{-2}) - \gamma_2(v_r^{-1} - v_i^{-1}) \right] \quad (34)$$

and

$$\Delta\mu_3 = \frac{12\varepsilon^2(1 + k)^2}{\alpha} \left[-\frac{\gamma_1}{4}(v_r^{-4} - v_i^{-4}) - \frac{2\gamma_1\gamma_2}{3}(v_r^{-3} - v_i^{-3}) - \frac{1}{2}\gamma_2^2(v_r^{-2} - v_i^{-2}) \right] \quad (35)$$

For open-tube columns we have

$$\Delta\mu_2 = 2\varepsilon(1 + k) \left[\frac{D_{AB}}{2\alpha}(v_i^{-2} - v_r^{-2}) + \eta\mu'_1 \right] \quad (36)$$

$$\Delta\mu_3 = \frac{12\varepsilon(1 + k)}{\alpha} \left[\frac{D_{AB}^2}{4}(v_i^{-4} - v_r^{-4}) + \eta D_{AB}(v_i^{-2} - v_r^{-2}) + \alpha\eta^2\mu'_1 \right] \quad (37)$$

Stepwise velocity programming

For stepwise programming the velocity increments between discrete time intervals are

$$v = v_n \text{ for } t_{n-1} < t < t_n \quad (38)$$

with

$$v_i = v_1 \text{ for } t_{n-1} = t_0 = 0 \quad (39)$$

and

$$v_r = v_N \text{ for } t_n = t_N = \mu'_1 \quad (40)$$

Piecewise integration over the discrete intervals of eqn. 4 yields

$$L = \frac{1}{\varepsilon(1+k)} \sum_{n=1}^N v_n (t_n - t_{n-1}) \quad (41)$$

or

$$\mu'_1 = \left[\varepsilon(1+k)L + v_r t_{N-1} - \sum_{n=1}^{N-1} v_n(t_n - t_{n-1}) \right] / v_r \quad (42)$$

From eqns. 5 and 6, we find for packed columns:

$$\Delta\mu_2 = 2\varepsilon(1+k) \sum_{n=1}^N (\gamma_1/v_n^2 + \gamma_2/v_n) (t_n - t_{n-1}) \quad (43)$$

and

$$\Delta\mu_3 = 12\varepsilon^2(1+k)^2 \sum_{n=1}^N (\gamma_1/v_n^2 + \gamma_2/v_n)^2 (t_n - t_{n-1}) \quad (44)$$

and for capillary columns:

$$\Delta\mu_2 = 2\varepsilon(1+k) \left[D_{AB} \sum_{n=1}^N (t_n - t_{n-1})/v_n^2 + \eta\mu'_1 \right] \quad (45)$$

and

$$\Delta\mu_3 = 12\varepsilon(1+k) \sum_{n=1}^N (t_n - t_{n-1}) (D_{AB} + \eta v_n^2)/v_n^4 \quad (46)$$

DISCUSSION

To illustrate the effect of velocity programming, calculations for the moments are displayed in Fig. 1 for the case of linear programming. The parameters chosen were $\varepsilon = 0.4$, $L = 100$ cm, $v_i = 0.1$ cm/sec, $k = 20$, $D_{AB} = 0.143$ cm²/sec, $\gamma_1 = 0.10$ cm²/sec, $\gamma_2 = 0.50$ cm and $\eta = 3.28 \cdot 10^{-5}$ sec. The value of γ_2 corresponds to particles of diameter 0.114 mm and the value of η corresponds to a capillary tube radius of 0.015 cm. The strong decrease in retention time (first moment), broadening (second moment), and skewness (third moment) with β , the rate of velocity increase, is not unlike that found for temperature programming⁸. The principal reason for this behavior is that the reduced retention time causes dispersive processes to have less effect.

The separation efficiency of the column declines with rate of flow program-

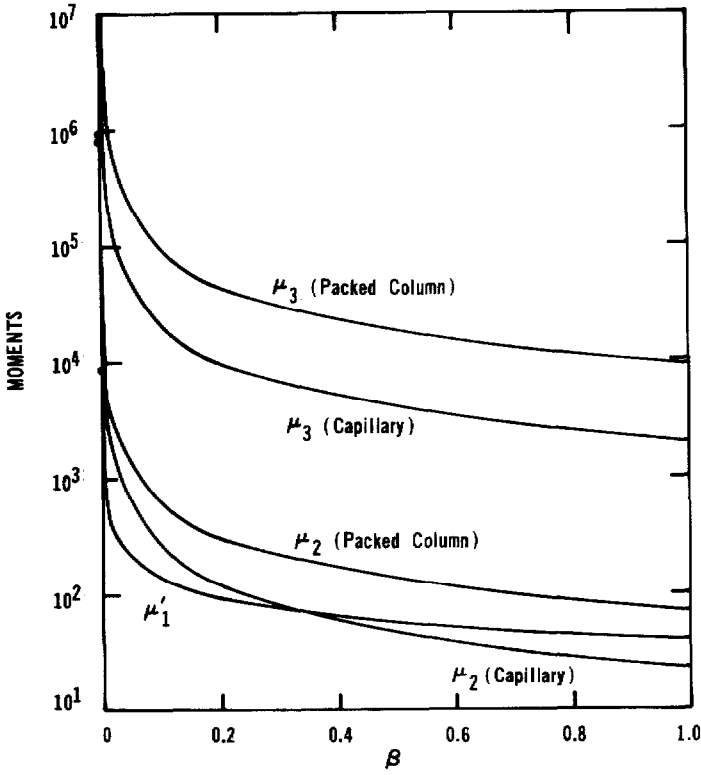


Fig. 1. Effect of increasing rate of flow programming on first, second, and third moments for gas partition chromatography in packed and capillary columns.

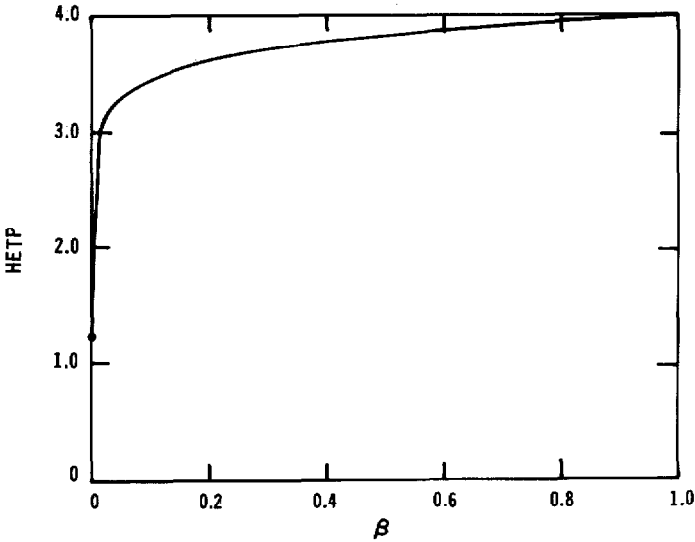


Fig. 2. Increase in HETP due to increase in the rate of flow programming.

ming, as shown in Fig. 2 (for a packed column) where HETP increases with β . The consequent decrease in resolution of two components is also found in temperature-programmed chromatography⁸ and temperature-gradient gas chromatography⁹. In spite of the decline in efficiency, the separation process is improved because the retention time is lessened.

The velocity dependence of the longitudinal dispersion coefficient is central to quantifying the effect of velocity programming on band spreading and skewness. Although the fluid-to-particle or fluid-to-wall mass transfer coefficient also will depend weakly on velocity for a more detailed mathematical model than the one employed here, the dispersion is strongly dependent on velocity and its effect cannot be safely ignored. Because the velocity dependence of the dispersion coefficient is much simpler than the temperature dependence of the partition ratio, the integrations are much simpler for flow programming than for temperature programming.

CONCLUSION

The moment theory provides a framework for estimating the quantitative effect of gradient and programming procedures in chromatographic separations. For many separation processes governed by rate process, a complete solution, either numerical or analytical, to the differential equations provides more information than is actually needed or can conveniently be used. The first and second temporal moments, on the other hand, provide precisely the information required for the calculation of HETP or more specifically for two different components the resolution as defined by eqn. 8.

The model chosen here to describe chromatography in an open tube or a packed column ignores details of fluid-to-solid mass transfer, intraparticle diffusion and liquid-film diffusion for partition chromatography. However, the model does include the important effect of longitudinal dispersion and its velocity dependence for both packed columns and open-tube capillary columns. Because the retention time, given by the first moment, decreases with increasing rate of flow programming, the second and third moments also decrease, lessening the band spreading and skewness of output peaks.

SYMBOLS

c	space- and time-dependent solute concentration in the mobile phase;
D_a	axial dispersion coefficient (cm ² /sec);
D_{AB}	molecular diffusion coefficient (cm ² /sec);
d_p	particle diameter (cm);
HETP	height equivalent to a theoretical plate (cm);
k	partition ratio;
R	open-tube radius (cm);
R_s	resolution;
t	time (sec);
v	average (superficial) mobile phase velocity (cm/sec);
v_i	velocity at time $t = 0$ (cm/sec);
v_r	velocity at retention time (cm/sec);

- z column length (cm);
 β rate of velocity increase for linear programming (cm/sec²);
 ε fractional void space;
 μ'_1 normalized first moment (sec);
 μ_n normalized n th central moments (sec ^{n});
 $\Delta\mu = \mu(z) - \mu(0)$, change of a moment between column inlet and outlet.

ACKNOWLEDGEMENT

The author thanks B. Kim and N. L. Pham for helpful discussions.

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