Short communication

Linear programming of inlet pressure or flow-rate in isothermal gas chromatography with near-vacuum outlet pressure

Tal M. Nahir*, Jeffrey A. Gerbec

Department of Chemistry, California State University, Chico, CA 95929-0210, USA

Abstract

The equation of motion for a peak in a gas chromatography experiment is shown to be exact whenever the column outlet pressure is approximately zero. Based on steady-state assumptions, this equation is solved for an isothermal analysis with a single-ramp inlet-pressure or flow-rate program. Theoretical calculations of retention times are confirmed experimentally for two *n*-alkanes using a capillary column connected to a mass-selective detector. A slight but consistent discrepancy between theoretical and measured results is interpreted as a failure of the steady-state assumption when the magnitude of the rate of change of inlet pressure is large.   © 2001 Elsevier Science B.V. All rights reserved.

Keywords: Pressure programming; Retention prediction; Flow-rate; Alkanes

1. Introduction

The development of electronic pressure controllers has led to a widespread use of direct programming of gas flow in gas chromatography (GC) [1]. Often, the pressure at the inlet of the column is varied linearly with respect to time to produce a pressure ramp during the analysis.

Examples involving the application of pressure programming in GC include separation and determination of 4-nonylphenol isomers [2], detection of residual solvents in drugs by fast GC [3], simultaneous determination of benzyl alcohols and corresponding alkenes by GC–MS [4], and the analysis for tramadol [5] and methylmalonic acid [6] in serum and plasma. The programming of pressure at a junction between two columns with different station-

ary phases was also exploited in the development of pressure-tunable column ensembles [7,8].

A detailed and general numerical procedure for the prediction of retention times of compounds during a pressure-programmed analysis has been outlined and demonstrated [9]. To illustrate the effect of the pressure perturbation alone, that analysis focused on isothermal runs. Other reports also considered pressure programming in gas chromatography, often in conjunction with temperature programming [10,11]. It was shown that no analytic solution to the general differential equation for a peak motion could be found in a pressure-varying mode [12,13].

This work centers on a unique GC experimental arrangement where the pressure at the column outlet is near vacuum; this is usually the case when a quadrupole mass-selective detector is used [14], or when a pump is connected to the end of a column and draws the gases through the system [15]. The equations describing the motion of a solute in the

*Corresponding author. Fax: +1-530-898-5234.
E-mail address: tnahir@csuchico.edu (T.M. Nahir).

column are considerably simpler than they are in a more general configuration where the outlet pressure is not negligible. As long as steady-state assumptions are valid, the theoretical solutions for retention times are confirmed experimentally.

However, a discrepancy is noted when rapid changes occur at the column inlet.

2. Experimental

All experiments were conducted on a Hewlett-Packard HP 6890 GC connected to a HP 5973 mass-selective detector. The column was a nominal 30 m×0.250 mm I.D., 0.25 μm coating thickness HP-5MS (crosslinked 5% phenylmethylsiloxane). Near-vacuum outlet pressure was confirmed by a Hewlett-Packard 59864B ionization gauge controller, and the readings were always on the order of 10^{-5} Torr (1 Torr=133.322 Pa). The mobile phase was ultra-high purity grade helium (Sierra Airgas, Sacramento, CA, USA). Oven (and column) temperatures are reported according to the programmed values which were assigned to the GC through the software program; no significant differences were noted between the displayed "set" and "actual" values. Mass spectra were recorded at rates of either 5 Hz (*m/z* ratio range between 19 and 300) or 47 Hz (*m/z* ratio range between 27.5 and 29.5, which allows for the observation of $^{14}N_2^+$ at 28 and $^{12}C^1H_3^{12}C^1H_2^+$ from hydrocarbons at 29).

Approximately 2 μl nonane vapor (headspace) or 0.2 μl diesel liquid (source for nonadecane) were manually injected into the column at several temperatures. For nonane, the isothermal runs were conducted at 35, 45 and 70°C to yield retention factors (*k*) near 10, 6 and 2, respectively. Similar *k* values for nonadecane were obtained at 167, 180 and 209°C, respectively.

The hold-up and retention times were always measured at the apex of the peaks of interest. Split ratios were maintained at 50:1 throughout the investigation, since a significant dependence of the measured hold-up and retention times on the split ratio was noticed. For instance, at 40°C and inlet pressure of 25 kPa (vs. ambient atmospheric pressure), the holdup time was 1.555 min and the retention time for isooctane was 3.242 min at 50:1

split ratio; in contrast, the corresponding values were 1.630 min and 3.378 min at 1:1 split ratio. While the "error" in the measured times is up to 5%, the calculated retention factors differ by only 1%.

Pressures are reported vs. ambient atmospheric conditions, approximately 100 kPa throughout this investigation (as measured and displayed by the HP 6890 chromatograph). Care was taken to assure that every series of measurements was conducted during a single period, such that the ambient pressure remained practically constant throughout. Otherwise, since the assigned magnitude of the applied inlet pressures is relative to the ambient pressure, a significant deviation from the theoretical predictions was observed. No measurements were conducted when the inlet pressures dropped below approximately 5 kPa above atmospheric pressure, since the GC system did not apply the set pressures reliably in this range.

Mathematical solutions were obtained, in part, using Mathematica (Wolfram Research, Inc., Champaign, IL, USA).

3. Results and discussion

In this work, we follow fundamental principles from GC theory, which suggest that the retention of a compound can be described using thermodynamic and fluid-dynamic functions [16]. The possibility that the magnitude of the retention factor, *k*, may depend on column pressure [17] is neglected here, and the partitioning of a compound between the stationary and mobile phases is related to its temperature-dependent thermodynamic properties alone. Consequently, for a series of isothermal runs with identical temperatures, the thermodynamic contributions are the same, and the modification of the retention time of a compound can only be accomplished through fluid-dynamic effects, such as by changing the magnitude of the pressure at the column inlet.

3.1. The equation of peak motion

The general influence of varying the inlet and outlet pressures on chromatographic parameters has already been widely documented [18]. As expected, increasing the inlet pressure, while maintaining a
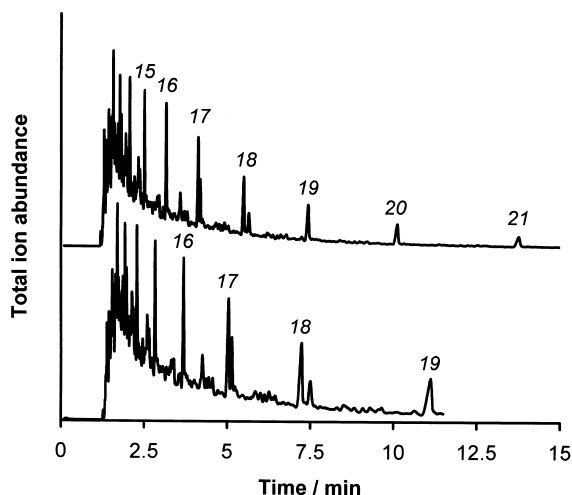
Fig. 1. Chromatograms of diesel at 180°C with initial inlet pressure of 100 kPa. The top trace shows the response when the inlet pressure was programmed to increase at a rate of +8 kPa/min, and the bottom trace was obtained with a −8 kPa/min program (the pressure had dropped below 5 kPa when the run was stopped just past the nonadecane peak). The numbers above the peaks designate the number of carbon atoms in the corresponding *n*-alkane.

constant outlet pressure, accelerates the elution of compounds. Fig. 1 shows the effects of increasing and decreasing the inlet pressure under isothermal conditions. Clearly, the *n*-alkanes in a diesel sample elute faster as the inlet pressure is gradually increased during the analysis.

To explain the nature of the change in retention characteristics as a function of changing the flow parameters in our GC system, we follow a well-established approach. The general equation of motion for a solute band (or a peak) inside a column during a gas chromatography experiment is given by:

$$\frac{dz}{dt} = \frac{L}{Q(z, t)\, t_{\mathrm{m}}(1 + k)} \tag{1}$$

where z is the distance from the inlet, t is the time from injection, L is the length of the column, $Q(z, t)$ is the local velocity factor, t_{m} is the holdup time, and k is the retention factor which is assumed to depend on temperature alone [19]. When the outlet pressure is near vacuum ($p_{\mathrm{out}} \to 0$), the ratio between the outlet pressure and the inlet pressure approaches zero, and the expression for local velocity factor is simplified to:

$$Q(z) = \frac{3}{2}\sqrt{1 - \frac{z}{L}} \tag{2}$$

In addition, the magnitude of the holdup time is given by:

$$t_{\mathrm{m}} = \frac{32L^2}{3r_{\mathrm{c}}^2}\,\frac{\eta}{p_{\mathrm{in}}} \tag{3}$$

where r_{c} is the column radius, η is the temperature-dependent viscosity of the gas inside the column, and p_{in} is the pressure at the column inlet [20]. The conclusions from a previous analysis suggest that these expressions for $Q(z)$ and t_{m} apply to any situation in which the ratio of the inlet pressure to the outlet pressure is greater than 10 [21], including high-pressure GC experiments [22].

Incorporating Eqs. (2) and (3), which are unique to the condition of near-vacuum outlet pressure, into Eq. (1), yields the desired differential equation of motion for a solute band. It can be shown that this equation is exact by following common procedures [23]. This fact can be directly attributed to the time independence of Q, which resulted from the complete elimination of time-dependent inlet-pressure terms in the more general equation, where the magnitude of p_{out} is not negligible. Solving the differential equation for an isothermal experiment and a linear pressure ramp with the initial condition of $z = 0$ at $t = 0$ yields:

$$\psi(z,t) = \frac{32}{3}\frac{L^2}{r_{\mathrm{c}}^2}\left(1 - \frac{z}{L}\right)^{\frac{3}{2}}$$
$$+ \frac{1}{\eta(k + 1)}\left(p_{\mathrm{in},\,0}t + \frac{g_{\mathrm{p}}}{2}t^2\right) = \frac{32}{3}\frac{L^2}{r_{\mathrm{c}}^2} \tag{4}$$

where $p_{\mathrm{in},\,0}$ is the inlet pressure at $t = 0$, and g_{p} is the rate of increase of p_{in} with respect to time.

3.2. Varying pressure mode

The retention time of a compound is measured at $z = L$. Combining Eqs. (1)–(3) and integrating from $z = 0$ to L and $t = 0$ to t_{r} for an isothermal experiment where the inlet pressure changes with time, yields:

$$\int_0^{t_{\mathrm{r}}} p_{\mathrm{in}}\, dt = \frac{32L^2\eta}{3r_{\mathrm{c}}^2}(k + 1) \tag{5}$$

Under conditions of unchanging pressure, the retention time is simply:

$$t_{r,0} = t_m(k+1) = \frac{32L^2\eta}{3r_c^2 p_{in}}(k+1) \tag{6}$$

The same expression can be obtained by letting $z = L$ and $g_p = 0$ in Eq. (4) and solving for t.

When the inlet pressure is programmed to linearly change at a rate of g_p, the isothermal retention time for a compound is found by either solving for t at $z = L$ in Eq. (4), or by integrating Eq. (5) and rearranging:

$$t_r = \left[-p_{in,0} + \sqrt{p_{in,0}^2 + \frac{64L^2}{3r_c^2} g_p(k+1)\eta} \right] \Big/ g_p \tag{7}$$

In terms of $t_{r,0}$, which can be obtained experimentally by setting the inlet pressure throughout the run to $p_{in,0}$, the last equation becomes:

$$t_r = \left(-p_{in,0} + \sqrt{p_{in,0}^2 + 2g_p t_{r,0} p_{in,0}} \right) \Big/ g_p \tag{8}$$

A series of experiments has confirmed the validity of Eq. (8). For instance, the results in Fig. 2 show the predicted and actual retention time for two hydrocarbons under several isothermal conditions, which yield different and representative values for the retention factors.

3.3. Varying flow mode

In a similar fashion to the analysis of a linearly changing inlet pressure, the isothermal retention time under conditions of a linearly changing flow-rate can be found. The volumetric flow-rate of the carrier gas, F, ordinarily given in terms of conditions outside the column (i.e. room temperature and pressure), is related to quantities inside the column [24]. Assuming a conservation of mass and the validity of the ideal gas law, the relationship between the flow-rates inside and outside the column can be given in terms of conditions at the column inlet ($z = 0$):

$$F = f_m(z=0) \frac{p_{in}}{p_{room}} \frac{T_{room}}{T_{column}} \tag{9}$$

An expression for $f_m(z=0)$, which is equal to $\pi r^2 dz/$
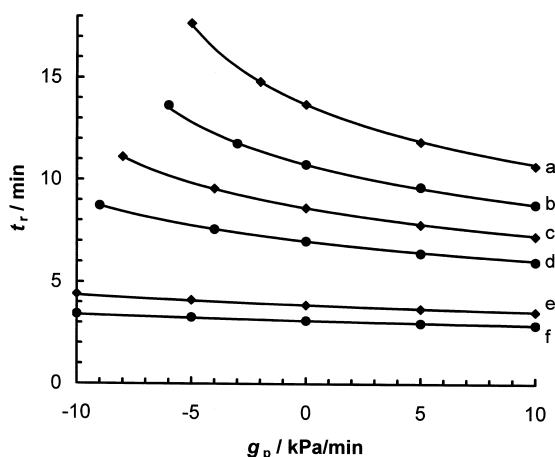

Fig. 2. Isothermal retention times for nonane and nonadecane as a function of a linearly changing inlet-pressure program. The initial inlet pressure, $p_{in,0}$, was 100 kPa and a single pressure ramp with magnitude of g_p was applied in all cases. Circles are for nonane, diamonds are for nonadencane, solid lines show the corresponding retention times from Eq. (8), and markers designate actual measurements. The letters indicate six experimental configurations: a = nonadecane, $k = 10$; b = nonane, $k = 10$; c = nonadecane, $k = 6$; d = nonane, $k = 6$; e = nonadecane, $k = 2$; f = nonane, $k = 2$. Desired retention factors were obtained by changing the column temperature (see Experimental section).

dt evaluated at $z = 0$, can be substituted from Eq. (1) with $k = 0$, and the inlet pressure which is required to effect a flow-rate F is:

$$p_{in} = \sqrt{\frac{16L\eta}{\pi r_c^4} \frac{T_{column}}{T_{room}} p_{room}F} \tag{10}$$

This expression can now be substituted for the inlet pressure in the integrand of Eq. (5). Upon integration under the conditions of a constant flow-rate with a magnitude of F_0, the corresponding retention time, $t_{r,0}$, is similar in form to the expression in Eq. (6). If the flow-rate changes linearly with time at a rate of g_F from an initial value of F_0, the retention time for a compound can be expressed in terms of $t_{r,0}$:

$$t_r = \left\{ -2F_0 + \left[2\left(2F_0^{3/2} + 3g_F t_{r,0}\sqrt{F_0}\right)^2 \right]^{1/3} \right\} \Big/ 2g_F \tag{11}$$

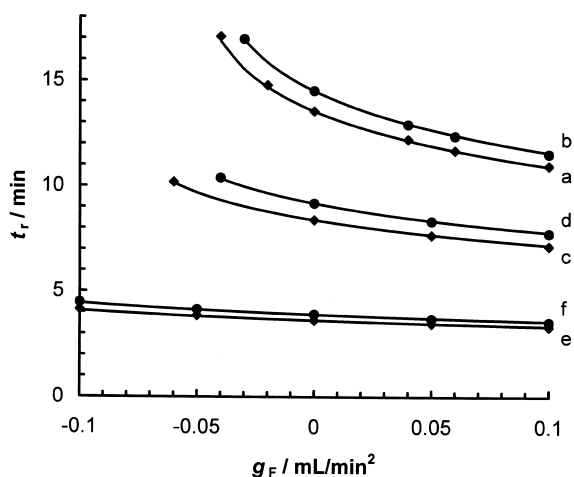Fig. 3 shows the good agreement between predicted

Fig. 3. Isothermal retention times for nonane and nonadecane as a function of a linearly changing flow-rate program. The initial flow-rate, F_0, was 1.0 ml/min and a single flow-rate ramp with a magnitude of g_F was applied in all cases. Markers are indicated for Fig. 2, and a solid lines show the corresponding retention times from Eq. (11).

and actual results for a series of isothermal runs with linearly programmed flow-rates.

3.4. Non-steady-state flow

A close examination of the results in Figs. 2 and 3 reveals a small but consistent deviation from the theoretically predicted retention times. For instance, the retention times are increasingly longer than expected when the inlet pressure or flow-rate decrease with time; the opposite trend is seen when g_p or g_F are positive. The general response suggests that a more significant discrepancy may be observed when pressure ramps are an order of magnitude larger than those discussed so far in this work [25].

A possible explanation for this variance between theoretical and experimental results may be related to a failure of traditional theory of gas flow in a capillary column, which assumes an instantaneous establishment of steady-state pressure profiles [26]. This assumption may not always be valid, especially when the magnitude of g_p is large and the inlet-pressure changes rapidly. To illustrate this point, consider a hypothetical experiment, in which the inlet pressure is programmed to abruptly increase

after the injection to a new (constant) p_{in}. A time-dependent process is therefore initiated as the concentration profile evolves from an initial steady state to a final steady state. Since the magnitude of the flow of gas is directly proportional to the pressure gradient [27], and since the inlet pressure is increased rapidly, the analyte may temporarily experience a steeper pressure gradient (near the inlet) than it would under the final steady-state configuration; the analyte will therefore be expected to move faster (relative to the steady-state situation) in this region during the time-dependent transition period.

An actual experiment supports this claim for the existence of a time lag in the establishment of steady-state pressure profiles. Several isothermal analyses (at 70°C) were performed on a sample containing nonane vapor. In the first run, the inlet pressure was maintained at 200 kPa and the measured retention time was 2.07 min. In the second run, the inlet pressure was increased from 100 to 200 kPa at $g_p = 250$ kPa/min. Although the inlet pressure in the second run never exceeded the inlet pressure in the first run, the retention time for nonane was significantly shorter at 2.01 min. Another set of runs showed the opposite trend when the inlet pressure was decreased at a large rate. In one run, the inlet pressure was maintained at 100 kPa and the measured retention time was 3.10 min. In another run, the inlet pressure was decreased from 200 to 100 kPa at $g_p = -250$ kPa/min. Although the inlet pressure in the second run was never lower than the inlet pressure in the earlier run, the retention time for nonane was significantly longer at 3.22 min.

4. Conclusions

The close agreement between theoretical and experimental retention times for representative *n*-alkanes suggests the applicability of steady-state analysis when the inlet pressure or the flow-rate are changed at moderate levels. However, a significant discrepancy between predicted and actual results is seen under more extreme temporal changes in pressure or flow parameters. Such behavior may be explained by observing the evolution of the system as a function of time. An investigation of a transient-state model is currently underway.

References

[1] B.W. Hermann, L.M. Freed, M.Q. Thompson, R.J. Phillips, K.J. Klein, W.D. Snyder, J. High Resolut. Chromatogr. 13 (1990) 361.

[2] K.K. Chee, M.K. Wong, H.K. Lee, J. Microcol. Sep. 8 (1996) 29.

[3] T.K. Chen, J.G. Phillips, W. Durr, J. Chromatogr. A 811 (1998) 145.

[4] A.E. Reed-Hagen, J.S. Janiszewski, R.O. Cole, R.S. Obach, J. Chromatogr. B 744 (2000) 333.

[5] S. Ho, J. Wang, W. Liaw, C. Ho, J. Li, J. Chromatogr. B 736 (1999) 89.

[6] M.M. Kushnir, G. Komaromy-Hiller, J. Chromatogr. B 741 (2000) 231.

[7] R. Sacks, C. Coutant, A. Grall, Anal. Chem 72 (2000) 524A.

[8] C. Coutant, R. Sacks, Anal. Chem. 72 (2000) 5450.

[9] S. Bezzani, D. Pierani, P. Moretti, G. Costello, J. Chromatogr. A 848 (1999) 229.

[10] F.R. Gonzalez, A.M. Nardillo, J. Chromatogr. A 757 (1997) 109.

[11] J. Chen, L. Zhang, Y. Tian, L. Wang, J. Chromatogr. A 795 (1998) 305.

[12] F.R. Gonzalez, A.M. Nardillo, J. Chromatogr. A 766 (1997) 147.

[13] Z. Wu, J. Chromatogr. A 840 (1999) 137.

[14] P.E. Miller, M.B. Denton, J. Chem. Educ. 63 (1986) 617.

[15] H. Smith, E.T. Zellers, R. Sacks, Anal. Chem. 71 (1999) 1610.

[16] F.R. Gonzalez, A.M. Nardillo, J. Chromatogr. A 842 (1999) 29.

[17] V.B. Berezkin, A.A. Korolex, I.V. Malyukova, J.High Resolut. Chromatogr. 20 (1997) 333.

[18] A.I.M. Keulemans, Gas Chromatography, Reinhold, New York, 1957, p. 139.

[19] F.R. Gonzalez, A.M. Nardillo, J. Chromatogr. A 757 (1997) 97.

[20] T.M. Nahir, K.M. Morales, Anal. Chem. 72 (2000) 4667.

[21] H. Purcell, Gas Chromatography, Wiley, New York, 1962, p. 68.

[22] M.M. Robson, K.D. Bartle, P. Myers, J. Microcol. Sep. 10 (1998) 116.

[23] W.E. Boyce, R.C. DiPrima, Elementary Differential Equations and Boundary Value Problems, 3rd Edition, Wiley, New York, 1977, p. 36.

[24] W. Jennings, E. Mittlefehldt, P. Stremple, Analytical Gas Chromatography, Academic Press, San Diego, 1997, p. 115.

[25] R.D. Gauw, P.J. Stoffolano, D.L. Kuhlenbeck, V.S. Patel, S.M. Garver, T.R. Baker, K.R. Wehmeyer, J. Chromatogr. B 744 (2000) 283.

[26] C. Leonard, R. Sacks, Anal. Chem. 71 (1999) 5501.

[27] W.E. Harris, H.W. Habgood, Programmed Temperature Gas Chromatography, Wiley, New York, 1966, p. 23.