Separation Science and Technology
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713708471

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To cite this Article Buys, T. S. and De Clerk, K.(1973) 'The Effect of Temperature on Production Rate in Chromatography', Separation Science and Technology, 8: 5, 551 — 565
To link to this Article: DOI: 10.1080/00372367308057045
URL: http://dx.doi.org/10.1080/00372367308057045

SEPARATION SCIENCE, 8(5), pp. 551–565, 1973

The Effect of Temperature on Production Rate in Chromatography

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Abstract

A simple theoretical model for the prediction of production rates in preparative chromatography shows that an optimum temperature exists in the case of constant mass flow rate. This result corresponds to experimental work reported by Rose et al. No optimum temperature exists in cases where a constant pressure drop is maintained at all temperatures.

In their experimental studies on the effect of temperature in preparative chromatography, Rose et al. (*1*) found an optimum temperature at which maximum yield is obtained. The present investigation is an attempt to interpret this result theoretically. The simplified theory of production rate developed by de Clerk (*2*) will be regarded as an adequate theoretical framework and will form the basis of the analysis.

THEORY

The relevant equation describing production rate is given by (see list of symbols)

$$E_p = \frac{(m_i - \Delta m_i)u_o}{w_{to}(1 + k)} \tag{1}$$

which defines the production rate as the mass recovered per unit time for a system where samples are repetitively introduced.

$$u_o = pu_i \; (p = P_i/P_o) \tag{2}$$

$$m_i - \Delta m_i = \frac{1}{2}m_i(1 + \mathrm{erf}\sqrt{2}R) \tag{3}$$

$$m_i = C_i V_i \tag{5}$$

$$V_i = (1 + k)\pi\sqrt{2\pi}r_c{}^2\varepsilon\left(\frac{\gamma}{p}\right)\left\{\left(\frac{(\alpha - 1)lk}{4R(1 + k)}\right)^2 - Hl\right\}^{1/2} \tag{5}$$

$$\gamma = \frac{2}{3}\left(\frac{p^3 - 1}{p^2 - 1}\right) \tag{6}$$

$$w_{to} = 12R\sigma_{to} \tag{7}$$

$$\sigma_{to} = \frac{\gamma(\alpha - 1)lk}{4R(1 + k)} \tag{8}$$

so that E_p follows as

$$E_p = \frac{\pi\sqrt{2\pi}\varepsilon r_c{}^2 C_i u_i}{24R}\left\{1 - \frac{16(1 + k)^2R^2H}{k^2(\alpha - 1)^2 l}\right\}^{1/2}(1 + \mathrm{erf}\sqrt{2}R) \tag{9}$$

The numerical results will be given in terms of a reduced E_p, i.e.,

$$E_p' = \frac{E_p}{\varepsilon r_c^2 C_i}$$

$$= \frac{\pi\sqrt{2\pi}u_i}{24R}\left\{1 - \frac{16(1 + k)^2R^2H}{k^2(\alpha -)^2 l}\right\}^{1/2}(1 + \mathrm{erf}\sqrt{2}R) \tag{10}$$

(In Rose's work the samples were introduced singly, resulting in his expression for production rate as the maximum separable sample volume divided by the retention time. This difference in approach should not lead to any qualitative discrepancies.)

The temperature dependence in Eq. (10) is implicitly contained in the variables u, k, α, and H. These dependences will be successively analyzed below.

Linear Inlet Flow Velocity (u_i)

Two distinct experimental constraints will be considered: (a) Constant pressure drop over column and (b) constant mass flow rate. In all cases the outlet pressure P_o is regarded as a constant.

Constant Pressure Drop (P_i, $p = P_i/P_o$ *Constant*). For laminar flow, the Blake-Kozeny equation (*3*) provides a good approximation to the pressure drop in packed columns. When this equation is suitably corrected for gas compressibility, it follows that

$$(p^2 - 1) = \frac{300\eta(1 - \varepsilon)^2 u_o l}{d_p{}^2 \varepsilon^3 P_o} \tag{11}$$

By invoking the ideal gas law in the form Pu = constant, it follows from Eq. (11) that

$$u(x) = \frac{u_o}{(p^2 - (p^2 - 1)x/l)^{1/2}} \tag{12}$$

so that (*4*)

$$u(x,T) = u(x,T_1)\frac{\eta(T_1)}{\eta(T)} \tag{13}$$

For He it has been shown empirically that (*4*)

$$\frac{\eta(T_1)}{\eta(T)} = \left(\frac{T_1}{T}\right)^{0.7} \tag{14}$$

Constant Mass Flow Rate (P_o *Constant*). The following set of mass balance equations apply to a system in which a constant mass flow rate is maintained at all temperatures:

$$\begin{aligned} u_o(T_1)\rho_o(T_1) &= u(x,T_1)\rho(x,T_1) = u_i(T_1)\rho_i(T_1) \\ &= u_o(T)\rho_o(T) = u(x,T)\rho(x,T) = u_i(T)\rho_i(T) \end{aligned} \tag{15}$$

If ideal behavior in the gas phase is assumed, $\rho = MP/RT$, so that

$$\frac{\rho_o(T)}{\rho_o(T_1)} = \frac{T_1}{T} \tag{16}$$

Equations (15) and (16) then yield

$$u_o(T) = u_o(T_1)T/T_1 \tag{17}$$

so that the outlet flow velocity is directly proportional to the temperature. Equation (17) may be rewritten in terms of the inlet flow velocity u_i by using the ideal gas law to yield

$$u_i(T) = u_i(T_1)\frac{p_1}{p}\frac{T}{T_1} = u_o(T_1)\frac{1}{p}\frac{T}{T_1} \tag{18}$$

where p_1 represents the value of P_i/P_o at the temperature T_1(i.e., P_{i1}/P_o). If Eq. (11) is considered at the temperatures T and T_1, respectively, it can be shown that

$$\frac{p^2 - 1}{p_1^{\,2} - 1} = \frac{u_o(T)}{u_o(T_1)}\frac{\eta(T)}{\eta(T_1)} \tag{19}$$

which is, according to Eq. (17), equivalent to

$$\frac{p^2 - 1}{p_1^{\,2} - 1} = \frac{T}{T_1}\frac{\eta(T)}{\eta(T_1)} \tag{20}$$

This equation can now be solved to give

$$p = \left\{1 + (p_1^{\,2} - 1)\frac{T}{T_1}\frac{\eta(T)}{\eta(T_1)}\right\}^{1/2} \tag{21}$$

which is the value of p required to maintain a constant mass flow rate at the inlet when the temperature is changed from T_1 to T. The flow velocity at the inlet is, according to Eqs. (18) and (21), related to the temperature by

$$u_i(T) = u_i(T_1)p_1\left(\frac{T}{T_1}\right)\left\{1 + (p_1^{\,2} - 1)\left(\frac{T}{T_1}\right)\frac{\eta(T)}{\eta(T_1)}\right\}^{-1/2} \tag{22}$$

For helium as carrier, this equation reduces to (see Eq. 14)

$$u_i(T) = u_i(T_1)p_1\left(\frac{T}{T_1}\right)\left\{(1 + (p_1^{\,2} - 1)\left(\frac{T}{T_1}\right)^{1.7}\right\}^{-1/2} \tag{23}$$

The Temperature Dependence of *k*

The mass distribution coefficient, k_j, for solute j, can, at small sample sizes, be approximated by (5)

$$k_j = k_{j0}e^{\lambda P} \tag{24}$$

where P is the local total pressure and k_{j0} and λ are given by

$$k_{j0} = \frac{n_s p}{n_m \gamma_{js}^{\infty} p_j^{\,0}}\exp\left[-\,(B_{jj} - v_j^{\,0})p_j^{\,0}/RT\right] \tag{25}$$

and

$$\lambda = (2B_{jm} - v_{js}^{\,\infty})/RT \tag{26}$$

B_{jm} is the second virial coefficient related to interactions between solute molecules and carrier gas molecules while B_{jj} corresponds to pure j. v_{js}^{∞} the partial molar volume of j in the stationary phase at infinite dilution, will in the present study be approximated by v_j^0, the molar volume of pure liquid j at the temperature T, if other data are not available. Although there is a difference between v_j^0 and v_{js}^{∞} (*5*), it is expected that the above approximation would not greatly influence the gross effect of temperature which is being investigated (see also Ref. *6*). The temperature dependence of the molar volume, v_j^0, of the liquid solute can be accounted for by means of an equation of the form (*7*)

$$v_j^0(t) = v_j^0(0°\text{C})\,(1 + a_1 t + a_2 t^2 + a_3 t^3) \tag{27}$$

where t is the temperature in °C. As a_1, a_2, and a_3 are usually much smaller than unity, it is expected that this temperature dependence would be negligible relative to the more marked temperature dependence of the second virial coefficients.

Various two-parameter (e.g., the Berthelot equation, see Ref. *8*) and three-parameter equations [e.g., the Stockmayer and Beattie equation, (*9*)] for the calculation of second virial coefficients as functions of temperature have been discussed in a paper by Guggenheim and McGlashan (*10*, see also Ref. *6*). These authors suggest a three-parameter equation:

$$B = V^c\left[0.487 - 1.206\frac{T^c}{T} - 0.551\left(\frac{T^c}{T}\right)^3\right] \tag{28}$$

which will be used for the calculation of B_{jj} and B_{jm}. It the case cf B_{jj}, V^c and T^c are the critical constants for pure $j(V_j^c, T_j^c)$, while for the calculation of B_{jm} for the mixture, V^c and T^c will be approximated by (*10*)

$$(V_{jm}^c)^{1/3} = \frac{1}{2}\{(V_j^c)^{1/3} + (V_m^c)^{1/3}\} \tag{29}$$

and

$$T_{jm}^c = (T_j^c T_m^c)^{1/2} \tag{30}$$

respectively. The latter formulas follow from the empirical combination rules for force constants (e.g., Ref. *10*).

Various approximations can be introduced to simplify the calculation of k as a function of temperature. First, the total pressure P is Eqs. (24) and (25) will be replaced by the mean column pressure (*11*, see also Eq. 16 of Ref. *12*)

$$P = \frac{\int_0^l P\,dx}{\int_0^l dx} = \frac{2}{3}P_0\left(\frac{p^3 - 1}{p^2 - 1}\right) \tag{31}$$

As the present paper is concerned with the investigation of the existence of an optimum temperature, this approximation in expected to be applicable in the sense that it would not obscure the effect of temperature. It is also expected that quantitative errors introduced by the above approximation would be negligibly small. Results reported by other workers make room for additional simplifying assumptions. From an analysis given by Littlewood (*13*, see also Ref. *14*), it is clear that the change of k with temperature is largely due to the effect of temperature on the vapor pressure $p_j{}^0$ of the pure solute j. The temperature dependence of $p_j{}^0$ can adequately be accounted for by the equation of Antoine (e.g., Ref. *15*)

$$\log p_j{}^0 = b_1 - \frac{b_2}{b_3 - T} \tag{32}$$

where the b_i are constants for a given substance (see Ref. *16* for tabulated values). Desty and Swanton (*17*) showed that for a large number of solutes in squalane, the γ^∞-values are practically independent of temperature. Approximations with respect to the temperature dependence of γ (or any thermodynamic quantity) can, however, not be made prior to an analysis of the thermodynamic properties of the system under consideration. In the numerical illustration which follows, squalane, benzene, and *n*-pentane are respectively used as stationary phase and solutes, so that it could be assumed that $\gamma_{js}{}^\infty$ equal to a constant over a range of temperatures (*17*).

As a final assumption, mobile phase nonideality can be neglected. It then follows that

$$k_j = \frac{n_s}{n_m}\frac{P}{\gamma_{js}{}^\infty p_j^0} \tag{33}$$

which can still be regarded as an adequate formulation for the present purpose. This has been verified by actual numerical comparison of the results obtained from Eqs. (24) and (33), respectively.

The Temperature Dependence of α

α is defined by

$$\alpha = k_2/k_1 > 1 \tag{34}$$

where k_1 and k_2 are the mass distribution coefficients for solutes 1 and 2, respectively. The temperature dependence of α will therefore be determined from the temperature dependences of k_1 and k_2 as outlined above. In most practical cases α is found to decrease with temperature (*18*, 19).

The Temperature Dependence of the Plate Height

Various attempts have been made to describe the temperature dependence of the plate height in chromatography (*14*, *20–24*). These vary from simple analytical expressions of the same form as the Van Deemter equation for the plate height (*22*) to more elaborate formulations (*14*, 23) introducing the temperature dependence via expressions for the temperature dependence of parameters like the diffusion coefficients, k, α, and u. In the present paper the latter procedure will be followed with a plate height expression given by

$$H = A + \frac{B'}{u_i} + (C_m + C_s)u_i \tag{35}$$

The inlet velocity is used as this allows for the neglect of pressure corrections down the column (*25*). A, B', C_m, and C_s are given by the following expressions (*26*) with the parameters defined in the list of symbols at the end of the paper:

$$A = 5d_p \tag{36}$$

$$B' = 2\gamma D_m \approx 1.2D_m \tag{37}$$

$$C_m = \frac{0.02d_p}{D_m} r_c^{\,y} \tag{38}$$

with $y \approx 2.1$ (see Ref. *26*) and

$$C_s = 0.25 \frac{k}{(1+k)^2} \frac{\theta^2 d_p^{\,2}}{D_s} \tag{39}$$

It now remains to find expressions describing the temperature dependences of D_m and D_s, the diffusion coefficients in the mobile and stationary phases, respectively. For D_m, the Chen and Othmer expression (*27*) applicable to binary gas mixtures will be used, i.e.,

$$D_m = \frac{0.43\left(\dfrac{T}{100}\right)^{1.81}\left[\dfrac{1}{M_j} + \dfrac{1}{M_m}\right]^{1/2}}{P\left(\dfrac{T_j^{\,c} T_m^{\,c}}{10{,}000}\right)^{0.1405}\left[\left(\dfrac{V_j^{\,c}}{100}\right)^{0.4} + \left(\dfrac{V_m^{\,c}}{100}\right)^{0.4}\right]^2} \,(\mathrm{cm^2/sec}) \tag{40}$$

with P in atmospheres.

For the stationary phase, the binary diffusion coefficient will be calculated from the expression (*28*)

$$D_s = \frac{7.4 \times 10^{-8}(X_s M_s)^{1/2} T}{\eta_s(T) V_j^{0.6}} \qquad (\text{cm}^2/\text{sec}) \tag{41}$$

in which the temperature dependence of the stationary phase viscosity will be accounted for by an expression of the form (*29*)

$$\eta_s(T) = C_1 \exp(C_2/T) \qquad (\text{poise}) \tag{42}$$

X_s is a parameter for the pure stationary phase; it is equal to unity for all nonassociated liquids, 2.6 for water, 1.9 for methanol, 1.5 for ethanol, etc. V_j is the molal volume of the pure solute at its normal boiling point.

DISCUSSION

The numerical results for production rate as a function of temperature are graphically represented in Fig. 1 for the two cases of constant mass flow rate and constant pressure drop. The curve for the former is seen to exhibit a definite maximum while a decrease over the whole temperature range is observed for the latter. The constant mass flow case corresponds to the way in which Rose et al. represented their results since their carrier gas flow rate is reported as a volume rate measured at atmospheric pressure and room temperature.

In order to clarify the origin of the optima, it is illuminating to rewrite E_p in the form

$$E_p' = f_1 f_2 \tag{43}$$

where

$$f_1 = \frac{p}{1+k} \frac{(1 + \operatorname{erf}\sqrt{2}R)}{2\varepsilon r_c^2} \frac{V_i}{w_{to}} \tag{44}$$

and

$$f_2 = u_i \tag{45}$$

$p/(1 + k)$ in f_1 was found to be practically the same for both cases. The difference mainly resided in the factors V_i/w_{to} and u_i. It is seen from Fig. 2 that the mathematical reason for the optimum stems from the opposing trends in f_1 and f_2. Inspection of Figs. 2 and 3 shows that the difference in the two cases stems primarily from the behavior of the inlet flow velocity which respectively increases and decreases with temperature for the con-

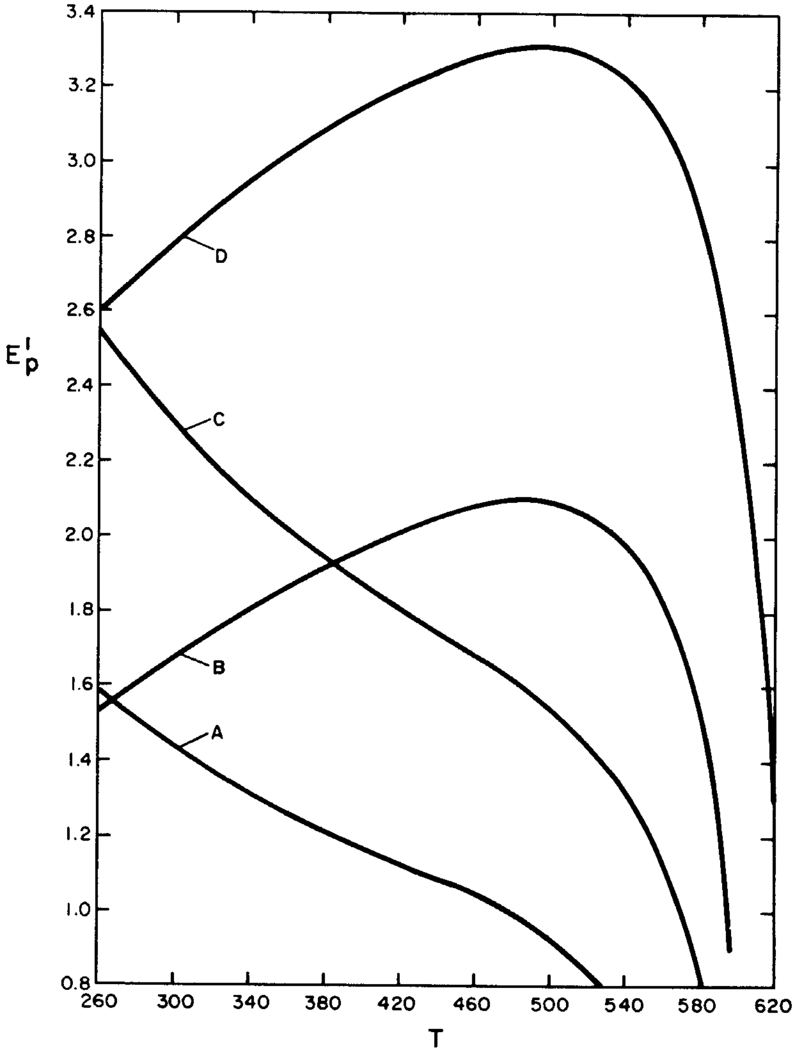

FIG. 1. Production rate as a function of temperature. A: constant pressure drop, $p = 1.5$, $u_0(T_1) = 5$ cm/sec ($T_1 = 298$ °K). B: constant mass flow rate, $u_0(T_1) = 5$ cm/sec. C: constant pressure drop, $p = 1.86$, $u_0(T_1) = 10$ cm/sec. D: constant mass flow rate, $u_0(T_1) = 10$ cm/sec.

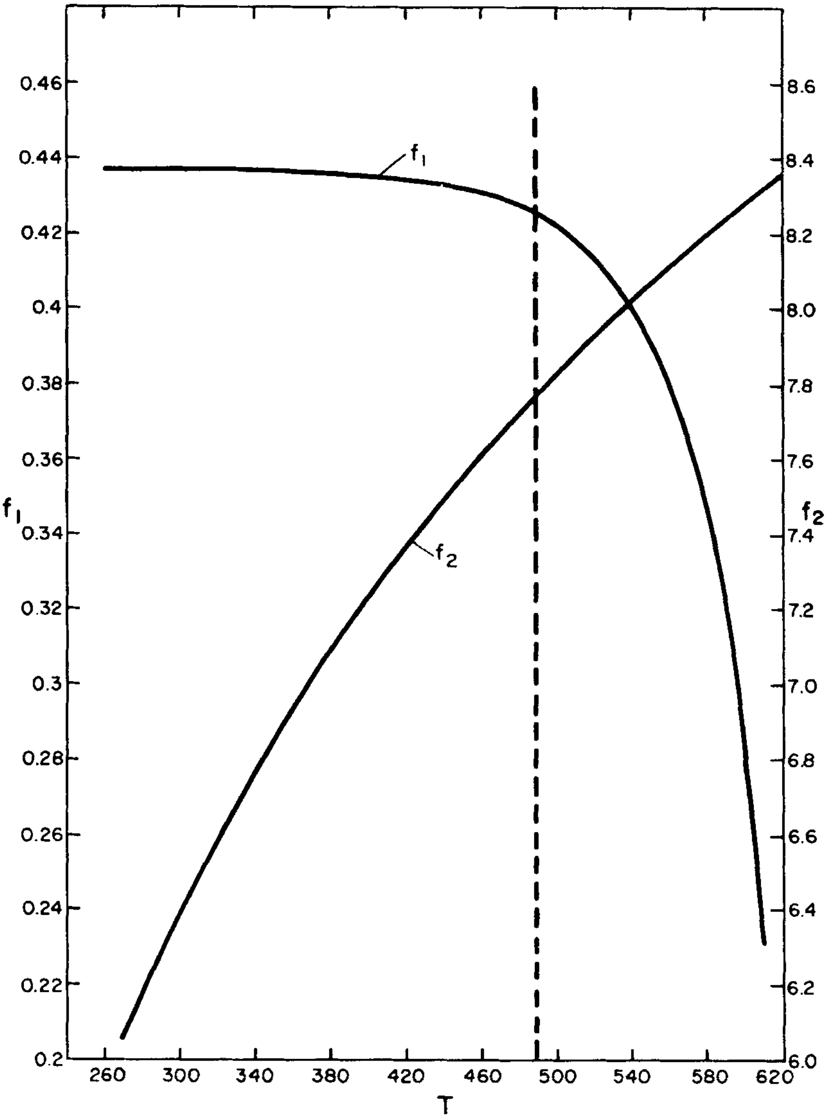

FIG. 2. Change of f_1 and f_2 with temperature; constant mass flow rate, $u_0(T_1) =$ 10 cm/sec ($T_1 = 298\,^\circ$K).

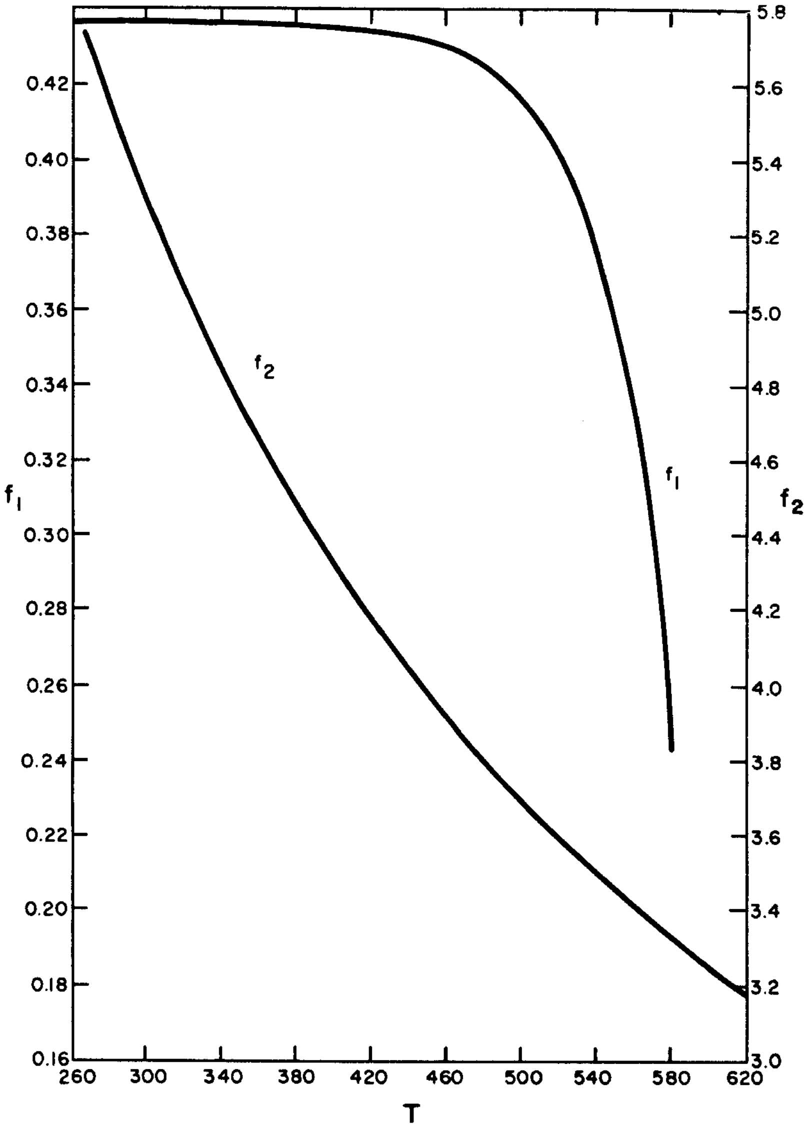

FIG. 3. Change of f_1 and f_2 with temperature; constant pressure drop, $p = 1.86$, $u_0(T_1) = 10$ cm/sec ($T_1 = 298\,°K$).

stant mass flow and constant pressure drop cases. A decrease in f_1 due to an increase in w_{t_0} and a decrease in V_i is common to both cases. For constant mass flow this decrease in f_1 is initially dominated by the increase in u_i and an optimum is consequently observed. It is obvious that no such optimum exists for the case of constant pressure drop. Since in practical chromatography the flow controlling valves are customarily of the constant mass flow type, the optimum temperatures in preparative work are significant.

SYMBOLS

a_i	($i = 1, 2, 3$) parameters in Eq. (27)
A	parameter in Van Deemter's equation for the plate height (Eqs. 35 and 36)
b_i	($i = 1, 2, 3$) parameters in Eq. (32)
B	second virial coefficient
B'	parameter in Van Deemter's equation for the plate height (Eqs. 35 and 37)
B_{jj}	second virial coefficient for pure j
B_{jm}	second virial coefficient related to interactions between solute molecules (j) and carrier gas molecules (m)
c_k	($k = 1, 2$) parameters in Eq. (42)
C_i	solute concentration at the inlet
C_m	mobile phase mass transfer term (Eqs. 35 and 38)
C_s	stationary phase mass transfer term (Eqs. 35 and 39)
d_p	mean packing particle diameter
D_m	mobile phase binary diffusion coefficient
D_s	stationary phase binary diffusion coefficient
E_p	chromatographic production rate (mass recovered per unit time) (Eq. 1)
E_p'	$= E_p/(\varepsilon r_c^2 C_i)$
f_i	($i = 1, 2$) convenient parameters (Eqs. 43, 44, and 45)
H	plate height
k	mass distribution coefficient
k_j	($j = 1, 2$) mass distribution coefficient for solute j
k_{j0}	convenient parameter (Eqs. 24 and 25)
l	column length
m_i	total mass of a specific solute in the inlet sample (subscript i refers to "inlet")
Δm_i	mass of solute discarded during fraction cutting
M	molecular weight

M_j	molecular weight of solute j
M_m	molecular weight of carrier gas
M_s	molecular weight of pure stationary phase
n_m	number of moles of pure mobile phase
n_s	number of moles of pure stationary phase
p	$= P_i/P_0$, pressure ratio at temperature T
p_1	$= P_{i1}/P_0$, pressure ratio at temperature T_1
p_j^0	vapor pressure of pure liquid solute j
P	local total pressure
P_i	pressure at the column inlet at temperature T
P_{i1}	pressure at the column inlet at temperature T_1
P_o	pressure at the column outlet
r_c	inside radius of column
R	resolution
t	temperature (°C)
T	temperature (K)
T^c	critical temperature
T_j^c	critical temperature of solute j
T_{jm}	critical temperature of solute–carrier gas mixture (Eq. 30)
T_m^c	critical temperature of pure carrier gas
$u(x)$	linear carrier flow velocity at axial position x
u_i	linear carrier flow velocity at the inlet
u_o	linear carrier flow velocity at the outlet
v_j^0	molar volume of pure solute j
v_{js}^{∞}	partial molar volume of solute j at infinite dilution in stationary phase
V^c	critical volume
V_j	molal volume of pure solute at its normal boiling point
V_j^c	critical volume of solute j
V_{jm}^c	critical volume of solute–carrier gas mixture
V_m^c	critical volume of pure carrier gas
w_{to}	total width of fraction cut out at outlet within column
x	axial coordinate
X_s	convenient parameter (Eq. 41)
y	convenient parameter (Eq. 38)

Greek Symbols

α	relative retention
ε	void fraction
η	viscosity

η_s	viscosity of stationary phase
γ	labyrinth factor
γ_{js}^{∞}	activity coefficient of solute in stationary phase at infinite dilution
λ	convenient parameter (Eqs. 24 and 26)
$\rho(x,T)$	density of mobile phase as a function of axial position x and temperature T
ρ_i	value of ρ at the inlet
ρ_o	value of ρ at the outlet
σ_{to}	total standard deviation at column outlet within the column
θ	ratio of thickness of stationary phase coating and d_p

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Received by editor January 24, 1973