THEORY OF PARTITION CHROMATOGRAPHY

HANS VINK

Institute of Physical Chemistry, University of Uppsala, Uppsala (Sweden)

(Received December 9th, 1963)

The theory of chromatographic processes has been dealt with in numerous recent articles and some excellent reviews of the subject are available[1–5]. The treatments vary from a phenomenological approach in the equilibrium theories, which are based on the "effective plate" concept, to rate theories, where the approach is kinetic. The object of the latter is to elucidate the actual mechanism of the chromatographic process and to determine the concentration profile of the elution curve as a function of fundamental parameters such as flow rate, feed concentration, partition coefficient, solute diffusion coefficient, etc. The treatment along these lines requires the specification of a model and the introduction of some simplifying assumptions such as linear sorption isotherms, plug flow of the moving phase, neglect of longitudinal diffusion, etc. Some recent contributions in this field are listed in refs. 6–9.

In the present article a kinetic approach based on a simple physical model of a chromatographic column is presented. The model is fairly general and may be applied to most of the different chromatographic procedures in use. A detailed treatment will, however, be given here only for the case in which the different solutes do not interact with each other. It applies best therefore to different types of partition chromatography, such as gel filtration and some forms of gas–liquid chromatography.

We will start by specifying the model. It is based on a model treatment of diffusion processes advanced in a recent article by the author[10]. It was shown that diffusion problems can be handled by means of a model consisting of a subdivision of space into compartments, separated by membranes. In this model all the resistance to diffusion is concentrated in the membranes, which thus constitute the resistance elements of the model, whereas the compartments constitute the capacity elements. The diffusion coefficient for a solute in a medium can be reproduced by choosing the proper value for the permeation coefficient of the membranes. This principle can be applied to a chromatographic column by representing the moving and stationary phases of the column by compartments, separated by a membrane and visualizing them as constituted of two long grooves separated by the membrane. A cross section is shown in Fig. 1. Owing to the basic assumptions of the model, the concentrations in a cross section are uniform within each compartment. The expression for concentration equilibration for a single solute within a narrow strip of the grooves may then be readily derived. Taking also into account the possibility of an unequal partition of the solute between the two phases, the following expression is obtained:

$$\frac{1}{\gamma} c_2 - c_1 = \left(\frac{1}{\gamma} c_2^\circ - c_1^\circ\right) e^{-mt} \qquad (1)$$

with

$$m = a\left(\frac{1}{V_1} + \frac{1}{\gamma V_2}\right) \tag{2}$$

where

V_1, V_2 = volumes per unit membrane area of respective compartments
c_1, c_2 = concentrations of solute in respective compartments
a = permeation constant for solute
γ = solute partition coefficient.

In addition the following mass conservation relation holds for the solute:

$$c_1 V_1 + c_2 V_2 = c_1^\circ V_1 + c_2^\circ V_2 \tag{3}$$

From eqns. (1) and (3) it follows that

$$c_1 = c_1^\circ + \left(\frac{c_2^\circ}{\gamma} - c_1^\circ\right)\frac{\gamma V_2}{V_1 + \gamma V_2}\left(1 - e^{-mt}\right) \tag{4}$$

$$\frac{1}{\gamma} c_2 = c_1^\circ + \left(\frac{c_2^\circ}{\gamma} - c_1^\circ\right)\frac{\gamma V_2}{V_1 + \gamma V_2}\left(1 + \frac{V_1}{\gamma V_2} e^{-mt}\right) \tag{5}$$

These relations are now applied to the model of the chromatographic column. The column is divided into cells of equal width l and the operation of the column is assumed to take place in discontinuous steps of duration τ. The procedure of the operation is as follows. During the time interval τ the solutions on the two sides of the membrane in every cell are equilibrated according to eqn. (1). At the end of the step the solutions in the moving phase of each cell are instantaneously shifted to the next

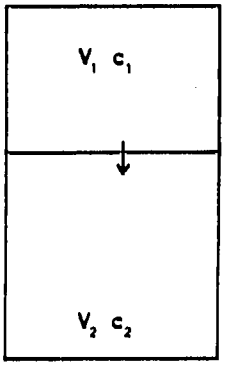

Fig. 1. Cross section of the column model.

cell and the equilibration procedure is repeated. If the velocity of the moving phase in the longitudinal direction of the column is v then obviously $l = v\tau$. A schematic representation of the column operation is shown in Fig. 2. The cells are numbered from left to right and the solution is assumed to enter the column from the left side. The concentrations in the ith cell at time t are denoted by f_{it} and γg_{it} for the moving and stationary phase respectively. Neglecting for the moment longitudinal diffusion and using eqns. (4) and (5) the material balance equations may be written down:

$$f_{i+1,\,t+\tau} = f_{it} + (g_{it} - f_{it})\frac{\gamma V_2}{V_1 + \gamma V_2}\left(1 - e^{-m\tau}\right) \tag{6}$$

$$g_{i,\,t+\tau} = f_{it} + (g_{it} - f_{it})\frac{\gamma V_2}{V_1 + \gamma V_2}\left(1 + \frac{V_1}{\gamma V_2} e^{-m\tau}\right) \tag{7}$$

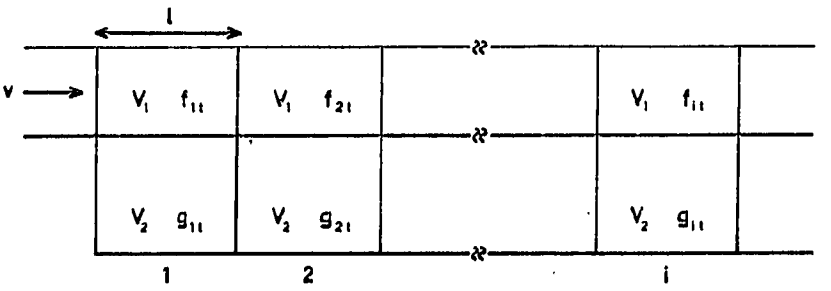

Fig. 2. Schematic representation of the column operation.

From these relations the differential equations for the column operation may readily be derived. The spatial variable x is introduced, and since the cell width is $v\tau$, where v is the velocity of the moving phase, eqns. (6) and (7) may be written

$$f(x + v\tau, t + \tau) = f(x,t) + [g(x,t) - f(x,t)] \frac{\gamma V_2}{V_1 + \gamma V_2} (1 - e^{-m\tau}) \quad (8)$$

$$g(x,t + \tau) = f(x,t) + [g(x,t) - f(x,t)] \frac{\gamma V_2}{V_1 + \gamma V_2} \left(1 + \frac{V_1}{\gamma V_2} e^{-m\tau}\right) \quad (9)$$

Expanding the left members and the exponential terms in the right members into power series and rearranging, we get

$$\frac{\partial f}{\partial x} v\tau + \frac{\partial f}{\partial t} \tau = (g - f) \frac{\gamma V_2}{V_1 + \gamma V_2} m\tau + \text{higher terms in } \tau \quad (10)$$

$$\frac{\partial g}{\partial t} \tau = -(g - f) \frac{V_1}{V_1 + \gamma V_2} m\tau + \text{higher terms in } \tau \quad (11)$$

Substituting for m from eqn. (2) and dividing by τ, we get for the limit $\tau = 0$

$$\frac{\partial f}{\partial t} + v \frac{\partial f}{\partial x} = \frac{a}{V_1} (g - f) \quad (12)$$

$$\frac{\partial g}{\partial t} = -\frac{a}{\gamma V_2} (g - f) \quad (13)$$

Here the parameter a determines the rate of the lateral diffusion in the column. It may be shown[10] that, if diffusion in the stationary phase is the rate determining step,

$$a = 2 \frac{D_2}{V_2} \quad (14)$$

where D_2 is the solute diffusion coefficient in the stationary phase. At this stage longitudinal diffusion may also be taken into account by superposing on eqns. (12) and (13) the concentration changes obtained from the diffusion equation (15)

$$\frac{\partial c}{\partial t} = D \frac{\partial^2 c}{\partial x^2} \quad (15)$$

Thus, the final equations take the form

$$\frac{\partial f}{\partial t} + v\frac{\partial f}{\partial x} = \frac{D_2}{V_1 V_2}(g - f) + D_1\frac{\partial^2 f}{\partial x^2} \tag{16}$$

$$\frac{\partial g}{\partial t} = -\frac{D_2}{\gamma V_2^2}(g - f) + D_2\frac{\partial^2 g}{\partial x^2} \tag{17}$$

The same equations may of course also be derived from a continuous-flow model. Equations (16) and (17) contain the following fundamental parameters:

v = velocity of the moving phase
γ = solute partition coefficient
D_1, D_2 = diffusion coefficients in the moving and stationary phases respectively
V_1, V_2 = volumes per (interphase) area of the moving and stationary phases respectively.

All these parameters are in principle determinable. The solution of the differential equations thus gives the solute distribution in the column as a function of time and position. In the case of a mixture of non-interacting solutes, different values have only to be assigned to the parameters γ, D_1 and D_2 to obtain the distributions of the different solutes, and hence the separation efficiency of the column. However, as analytical solution of the differential equations seems impossible, a procedure is presented for numerical solution of the problem using the original eqns. (6) and (7). The effect of longitudinal diffusion may be considered by adding to the right members of these equations the concentration changes due to longitudinal diffusion. Using the diffusion-model treatment in the longitudinal direction (see Fig. 2) and assuming constant diffusion coefficients, the following concentration increments according to eqn. (9) in ref. 10 are obtained

$$\Delta f_{it} = \tfrac{1}{2}\alpha_1(f_{i-1,t} - 2f_{it} + f_{i+1,t}) \tag{18}$$

$$\Delta g_{it} = \tfrac{1}{2}\alpha_2(g_{i-1,t} - 2g_{it} + g_{i+1,t}) \tag{19}$$

where α_1 and α_2 are determined by the diffusion coefficients in the respective phase. Noting that the volumes per area of the compartments in the model for longitudinal diffusion are $v\tau$, eqn. (15) in ref. 10, gives

$$D_i = \tfrac{1}{2}v^2\tau\alpha_i \tag{20}$$

$$i = 1,2$$

As $\alpha_i \leqslant 1$, this equation obviously imposes a lower limit on τ for longitudinal diffusion. The final equations are now obtained from eqns. (6) and (7) and eqns. (18) and (19). With the substitutions

$$\eta = \frac{\gamma V_2}{V_1 + \gamma V_2}(1 - e^{-m\tau}) \tag{21}$$

$$\xi = \frac{\gamma V_2}{V_1 + \gamma V_2}\left(1 + \frac{V_1}{\gamma V_2}e^{-m\tau}\right) \tag{22}$$

and with a new time unit having the length τ, we get

$$f_{t+1,\,t+1} = (1 - \eta)\, f_{tt} + \eta g_{tt} + \tfrac{1}{2}\alpha_1(f_{t-1,t} - 2\, f_{tt} + f_{t+1,t}) \tag{23}$$

$$g_{t,t+1} = (1 - \xi) f_{tt} + \xi\, g_{tt} + \tfrac{1}{2}\alpha_2(g_{t-1,t} - 2\, g_{tt} + g_{t+1,t}) \tag{24}$$

From these equations the distribution of solute in the chromatographic column may be obtained. Here, a simplified treatment is considered in which longitudinal diffusion is neglected. Thus instead of eqns. (23) and (24) the following are used:

$$f_{t+1,\,t+1} = (1 - \eta)\, f_{tt} + \eta\, g_{tt} \tag{25}$$

$$g_{t,\,t+1} = (1 - \xi)\, f_{tt} + \xi\, g_{tt} \tag{26}$$

From eqn. (26) we get by recursion

$$g_{t,\,t+1} = (1 - \xi)\, f_{tt} + \xi\{(1 - \xi)\, f_{t,\,t-1} + \xi[(1 - \xi)\, f_{t,\,t-2} + \cdots\} =$$

$$= (1 - \xi)\, f_{tt} + (1 - \xi)\xi f_{t,\,t-1} + (1 - \xi)\xi^2\, f_{t,\,t-2} + \cdots (1 - \xi)\xi^t f_{10} \tag{27}$$

Insertion of this into eqn. (25) gives

$$f_{tt} = (1 - \eta)\, f_{t-1,\,t-1} + \eta(1 - \xi)\, f_{t-1,\,t-2} + \eta(1 - \xi)\xi\, f_{t-1,\,t-3} +$$

$$+ \eta(1 - \xi)\, \xi^{t-2}\, f_{t-1,0} \tag{28}$$

A matrix (f_{ij}) of order n is now defined, having its elements determined by eqn. (28) with $j = t + 1$ and $i, j = 1, 2 \cdots n$. With reference to Fig. 2 the following interpretation of the element f_{ij} is obtained. It specifies the concentration in the moving phase in the ith cell at the time $(j - 1)\tau$. The time will always be given as the time at the beginning of an equilibration period. Thus, a row of the matrix represents the concentration in a particular cell at different times from $t = 0$ to $t = (n - 1)\tau$ and a column of the matrix represents the concentration distribution in the chromatographic column at a particular instance of time. The initial conditions are specified by the values of f_{1j} for $j = 1, 2, \cdots n$ and f_{i1} for $i = 1, 2, \cdots n$. The value of f_{1j} may be interpreted as the concentration in the solution that enters the column at the time

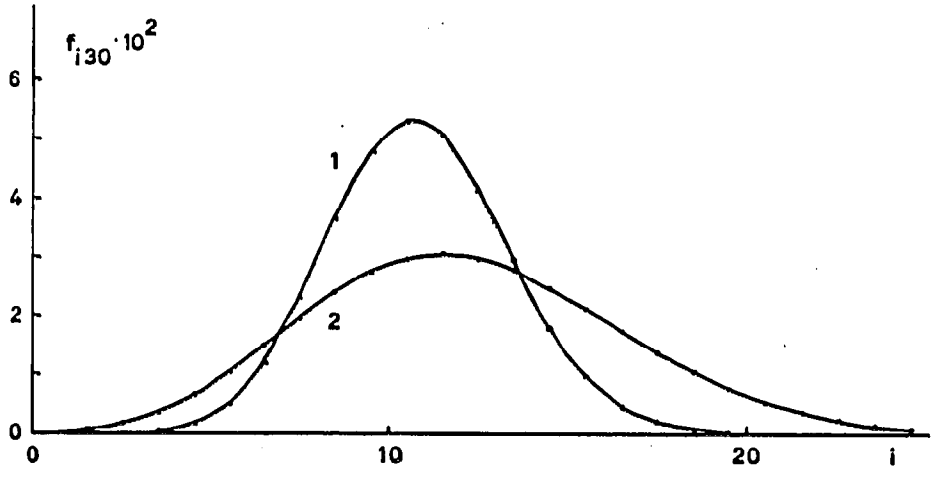

Fig. 3. Solute distribution in the moving phase of the column. For curve 1, $\tau \gg \tau^1/_2$ (*i.e.* equilibrium is established); for curve 2, $\tau = \tau^1/_2$ ($\tau^1/_2$ = half-time for attainment of equilibrium in lateral diffusion).

$(j - 1)\tau$ and that of f_{i1} as the concentration in the ith cell at $t = 0$. Specifying the coefficients in eqn. (28) and the initial values f_{1j} and f_{i1} and assigning to all f_{it} with zero or negative indices the value zero, all the elements f_{ij} in the matrix may be calculated from eqn. (28).

The calculations may conveniently be carried out with digital computers. Then matrixes of very high orders may be obtained, in which the conditions of continuous operation of the column are approached. In the present work a few calculations were carried out with hand-operated calculators giving matrixes of the 30th order. The results are shown in the form of the last columns, representing the solute distribution in the moving phase at the end of the time period considered ($t = 30\tau$). They are presented diagrammatically in Fig. 3. In the calculations the following initial conditions and values on the parameters determining the coefficients in eqn. (28) were used:

$f_{11} = 1, f_{1j} = f_{i1} = 0$ for $i, j = 2, 3, \cdots n$.
$\gamma = 1$
$V_1/V_2 = 0.5$
$\eta = {}^2/_3$ and ${}^1/_3$ for curve 1 and 2 respectively
$\zeta = {}^2/_3$ and ${}^5/_6$ for curve 1 and 2 respectively.

It should be noted that owing to the basic assumptions in the diffusion model (uniform concentrations in the compartments separated by the membrane) the geometry of the column filling does not enter into the treatment explicitly, but is taken into account by the ratio V_1/V_2. It is easy to show that where the stationary phase consists of a filling of tight-packed spherical beads the ratio

$$\frac{V_1}{V_2} = \frac{3\sqrt{2}}{\pi} - 1 \approx 0.350.$$

Thus, in the present calculations a rather loosely packed column is considered.

The results shown in Fig. 3 demonstrate the influence of lateral diffusion (local non-equilibrium) on the chromatographic process. It has a negative effect on the separation efficiency, it causes the broadening of a peak but affects only slightly its translational velocity. Thus, in general it is not possible to separate substances in a column on the basis of differences in diffusion coefficients. Only if one of the substances has a very small diffusion coefficient may it be separated from other substances with considerably higher diffusion coefficients. Thus it may be concluded that in partition chromatography separation is mainly due to differences in partition coefficients. The present calculations can of course only give a superficial picture of the possibilities of the method and further work, including more detailed computations with the aid of digital computers is in progress.

Finally some of the approximations made in the present treatment are considered. In the first place longitudinal diffusion has been neglected. The latter is most pronounced in the moving phase and causes the broadening of a chromatographic peak, but leaves its translational velocity unaffected. Therefore from the present calculations the optimal performance of an ideal column is obtained.

The diffusion model used in this treatment may be considered to give a first order approximation of the diffusion process (*e.g.* diffusion into a spherical particle (radius = r) is represented by an exponential function with the half-time $\tau_{1/2} =$

0.039 r^2/D, in close agreement with VERMEULEN's[11] approximate formula $\tau_{1/2} = 0.030\ r^2/D$). Higher order approximations could be obtained by a repeated application of the diffusion model, *e.g.* a spherical particle could be considered to consist of several concentric zones, each representing an element of the diffusion model. However, this would considerably complicate the numerical calculations and it is felt that the first order approximation is sufficient to bring out the essential features of the lateral diffusion effect.

The discreet operation of the column also introduced an approximation. However, by decreasing the length of the time period τ, conditions for the continuous operation of a column are approached. The magnitude of the deviation from the conditions for continuous operation may be estimated from calculations with different τ values.

SUMMARY

A rate theory for partition chromatography, based on a simple physical model, is presented. It has the object of determining the concentration profile of an elution curve from fundamental parameters, characteristic of the solute and the column operation. A method for a numerical solution of the problem with the aid of digital computers is also given.

REFERENCES

1 T. VERMEULEN, *Advances in Chem. Eng.*, 2 (1958) 147.
2 C. J. HARDY AND F. H. POLLARD, *J. Chromatog.*, 2 (1959) 1.
3 F. HELFFERICH, *Ion Exchange*, McGraw-Hill, New York, 1962.
4 R. A. KELLER, G. H. STEWART AND J. C. GIDDINGS, *Ann. Rev. Phys. Chem.*, 11 (1960) 347.
5 H. W. HABGOOD, *Ann. Rev. Phys. Chem.*, 13 (1962) 259.
6 P. B. HAMILTON, D. C. BOGUE AND R. A. ANDERSSON, *Anal. Chem.*, 32 (1960) 1782.
7 J. C. GIDDINGS, *J. Chromatog.*, 2 (1959) 44.
8 J. C. GIDDINGS, *J. Chromatog.*, 5 (1960) 46.
9 J. E. FUNK AND G. HOUGHTON, *J. Chromatog.*, 6 (1961) 193.
10 H. VINK, *Acta Chem. Scand.*, 18 (1964) 409.
11 T. VERMEULEN, *Ind. Eng. Chem.*, 45 (1953) 1664.