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Equilibrium elution chromatography

The column-origin boundary condition

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ABSTRACT

Linear, equilibrium chromatography on a finite column has been re-examined using the rate model. Unlike most previous descriptions, the boundary condition at the column origin is treated as reflective. The development of the band profile on the column behaves in a physically and mathematically reasonable fashion. In this regard, long-standing disagreements on this fundamental issue are finally eliminated. For almost all practical situations, the use of Gaussian profiles for theoretical descriptions of on-column equilibrium chromatography appears valid.

INTRODUCTION

Developments in theories, applications and instrumentation of elution chromatography continue unabated. The interdependence of these three attributes was well illustrated by Snyder and Kirkland [1]. Among the many theoretical approaches are efforts to extract physico-chemical parameters from experimental elution curves [2–7]. A requirement in these efforts is that the relationship between the peak profile and the various parameters be both accurate and well understood. Along these lines, we have been re-examining [8,9] some of the most elementary aspects of column chromatography in order to explore the effects of approximations that have been routinely imposed, over the years, in modeling the chromatographic process. Our long-term goals are either to justify the use of these approximations or to alter theory accordingly.

We begin by restricting our considerations to only the hypothetical case of linear, two-phase equilibrium chromatography. This is usually the starting point for more complete theories that incorporate non-linearities and non-equilibrium considerations. For our current objectives, therefore, we assume fast mass transfer, that the density of the mobile phase remains constant over the length of the column, that the sorption isotherm is linear and that the velocity of the mobile phase is well represented by its constant average. Under these simplifying conditions, the chromatographic

process, what Snyder [10] termed column development, is modeled according to the partial differential equation of diffusion with forward drift [11,12]:

$$\frac{\partial c_{\mathrm{m}}}{\partial t} = -u \cdot \frac{\partial c_{\mathrm{m}}}{\partial z} + D \cdot \frac{\partial^2 c_{\mathrm{m}}}{\partial z^2} + \frac{1}{\varepsilon} \cdot \frac{\partial c_{\mathrm{s}}}{\partial t}$$

$$\frac{\partial c_{\mathrm{s}}}{\partial t} = -k_1 c_{\mathrm{s}} + k_2 c_{\mathrm{m}}$$

where D is an effective dispersion constant of the solute in the mobile phase, u is the velocity of the mobile phase in the axial (z) direction, ε is the fraction void volume and k_1 and k_2 are the rate constants for transfer between phases. For a linear isotherm and fast interphase kinetics, these equations reduce to the rate expression for linear, equilibrium chromatography:

$$\frac{\partial c}{\partial t} = -u_{\mathrm{e}} \cdot \frac{\partial c}{\partial z} + D_{\mathrm{e}} \cdot \frac{\partial^2 c}{\partial z^2} \tag{1}$$

where $u_{\mathrm{e}} = u/(1 + k')$, $D_{\mathrm{e}} = D/(1 + k')$ and k' is the capacity factor or equilibrium mass distribution ratio. This paper focuses entirely on the solution to the latter hypothetical system and on its relevance to chromatographic theory and, to a lesser extent, practice.

Traditionally, there has been more than one scheme for solving eqn. 1. By and large, the reasons for the choices have been a combination of mathematical convenience and justifiability under certain operating conditions. A very general discussion, not restricted to chromatographic systems, has been developed by Kreft and Zuber [13]. Some schemes involve solving for the on-column profile $c(z,t)$ and others for the elution profile $P(t)$. Further, the boundary conditions employed in these situations have been one of two types: the infinite column in which $-\infty < z < +\infty$ and the semi-infinite column in which $0 \leqslant z < +\infty$. The true column is neither of these, but rather is finite, a fact that can subtly influence the form of the solution to eqn. 1. The present discussion begins with a brief description of the conventional models: infinite, semi-infinite and finite.

The infinite column

Grubner [14], Grushka [15], Kučera [16] and Jönsson [17], among others, have treated the column as if it were infinite. The initial conditions are such that at time zero, the sample is only at the z-origin. The column extends without limit in the positive and negative directions. Eqn. 1 can then be solved and gives exactly the Gaussian curve for the on-column profile at any fixed time $t > 0$, regardless of the magnitude of either the diffusion constant or the mobile phase velocity. The solution can be expressed as the fractional concentration per unit length at time t and axial position z as

$$c(z,t) = \frac{1}{\sqrt{4\pi D_{\mathrm{e}} t}} \cdot \exp\left[-\frac{(z - u_{\mathrm{e}} t)^2}{4 D_{\mathrm{e}} t} \right] \tag{2}$$
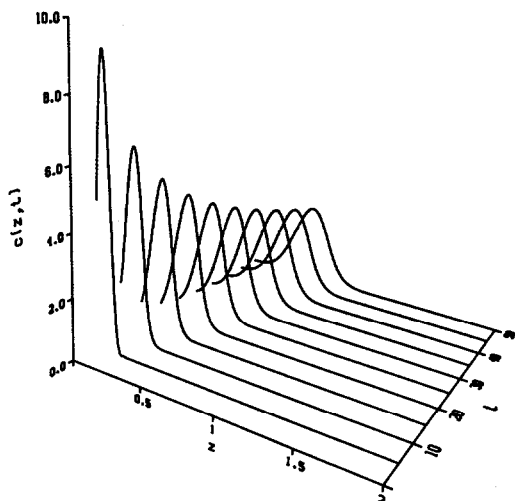
Fig. 1. On-column concentration probability profile for the infinite column. The sample is initially at $z = 0$ at time zero in which $-\infty < z < \infty$, $u_e = 0.01$ (in the positive z-direction), $D_e = 0.0002$. The figure has not been extended into the negative column coordinate region. Time is in units of D_e/u_e^2.

An example set of curves is shown in Fig. 1. Kučera [16] assigned the elution profile to be the function $c(L,t)$, where L is the fixed column length. Kreft and Zuber [13] referred to the use of $c(L,t)$ as "detection in resident fluid".

In contrast, Jönsson [17] argued that the elution profile is more appropriately obtained by what Kreft and Zuber termed "detection in flux", having units of fractional concentration per unit time:

$$P(t) = \int_L^\infty \frac{\partial c(z,t)}{\partial t} \cdot dz$$

As a consequence, Kučera and Jönsson obtained different predictions for elution chromatograms which we shall distinguish by subscripts K and J, respectively. Jönsson presented an analytical expression for the detection in flux elution curve:

$$P_J(t) = \left(\frac{u_e}{2} + \frac{L}{2t}\right) \cdot \frac{1}{\sqrt{4\pi D_e t}} \cdot \exp\left[-\frac{(L - u_e t)^2}{4D_e t}\right] \quad (\text{time}^{-1})$$

For comparison, Kučera's detection in resident fluid elution curve may be written as

$$P_K(t) = c(L,z) = \frac{1}{\sqrt{4\pi D_e t}} \cdot \exp\left[-\frac{(L - u_e t)^2}{4D_e t}\right] \quad (\text{length}^{-1})$$

Jönsson noted the apparent inappropriateness of the dimensionality of $P_K(t)$ for an elution profile. Kreft and Zuber's more thorough consideration shows that normaliza-

tion taking into account the dimensional difference between flux and concentration accounts for the seeming conflict.

The semi-infinite column

Kubin [18] and Yamaoka and Nakagawa [19] used a semi-infinite column in their derivations. The boundary conditions in this case correspond to a column which is infinite only in the positive z-direction. At time zero, the concentration of solute is zero everywhere but at the origin. At the origin, the concentration is unity at time zero and zero thereafter; that is, $c(0,t) = \delta(t)$, the Kronecker delta. This boundary condition produces a profile solution expressed as the fractional concentration per unit time at time t and axial position z. Jönsson gave the following expression for the on-column profile in this case:

$$c(z,t) = \frac{z}{\sqrt{4\pi D_e t^3}} \cdot \exp\left[-\frac{(z - u_e t)^2}{4D_e t} \right] \tag{3}$$

although as quoted, $c(z,t)$ has not been correctly normalized for $0 \leqslant z < \infty$. Fig. 2 shows normalized (semi-infinite) $c(z,t)$ for a set of conditions comparable to those in Fig. 1. At constant time $t > 0$, the on-column profile in eqn. 3 is non-Gaussian. This is in contrast to the profile on the fully infinite column, eqn. 2. Jönsson pointed out that the $\delta(t)$ boundary condition for the semi-infinite column gives the unrealistic result that the profile develops an instantaneous node at the origin when the separation begins as Fig. 2 shows. This happens even in the limit of zero mobile phase velocity, an extreme condition which should reproduce the on-column profile at the diffusion-only limit: broadening downstream from the origin.
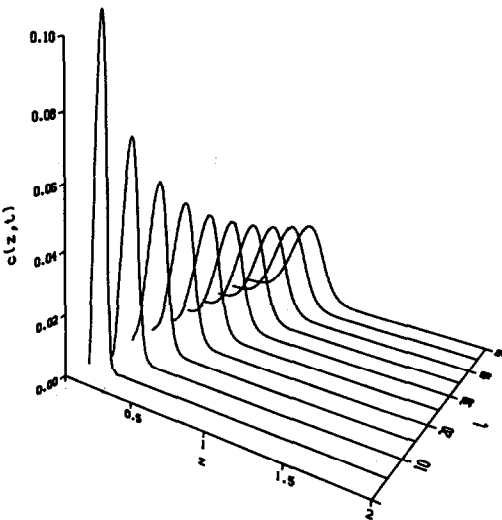

Fig. 2. On-column concentration probability profile for the semi-infinite column. Conditions as in Fig. 1, except $0 \leq z < \infty$.

The finite column

The aforementioned contradictory solutions purposely avoid any end effect by invoking a column that is infinite in the $+z$ direction. One should bear in mind that the end effect has also been neglected in theories that do incorporate mass transfer and other non-equilibrium effects. No chromatographic theory based on the rate equation has invoked boundary conditions associated with a truly finite column. However, in another study, we did address the finite column using the plate model of chromatography in a way that is valid at high capacity factors [9]. In addition, for a column semi-infinite in the negative direction, the influence of just the end effect on statistical moments in equilibrium chromatography was the subject of an earlier report [8].

THEORY

The boundary condition we invoke at the column origin differs from that used by Kubin and others that was described above, whether for equilibrium or non-equilibrium systems. In recognition that a solute molcule at $z = 0$ cannot retreat backward from that point to $z < 0$ since the column doesnot exist there, we have what is referred to as a reflecting barrier at the origin [20]. In the mathematics of heat-transfer studies, this is equivalent to an insulation boundary condition [21,22]. In fact, Sommerfeld used, as an heuristic illustration of reflection, diffusion in a cylindrical column. At the bottom of the column at time zero is a small amount of concentrated $CuSO_4$ solution and above that is a layer of pure water extending to infinite height and into which the colored solution diffuses [22]. The phenomenon is easily demonstrated and also easily pictured mentally. This reflecting barrier boundary condition in chromatographic terms may be written as [20,23]

$$\left(D_e\frac{\partial c}{\partial z} - u_e c\right)_{z=0} = 0$$

Cox and Miller [20], following Smoluchowski [24] and Sommerfeld [22], solved the diffusion equation with drift, that is, eqn. 1 with a reflecting barrier at the origin. The solution corresponds to the concentration profile of the solute as a function of position and time while the solute is on a semi-infinite column. This, in turn, approximates the behavior of a band that has been appropriately dealt with at the origin and that has not yet approached the elution point L where the end effect applies. In the early stages of chromatography then, the on-column profile is well represented by Cox and Miller's expression (after correction for some typographical errors):

$$c(z,t) = \frac{1}{\sqrt{\pi D_e t}}\left\{\exp\left[-\frac{(z - u_e t)^2}{4D_e t}\right]\right\} - \frac{u_e}{D_e}\left[1 - \Phi\left(\frac{z + u_e t}{\sqrt{2D_e t}}\right)\right]\exp\left(\frac{zu_e}{D_e}\right)$$
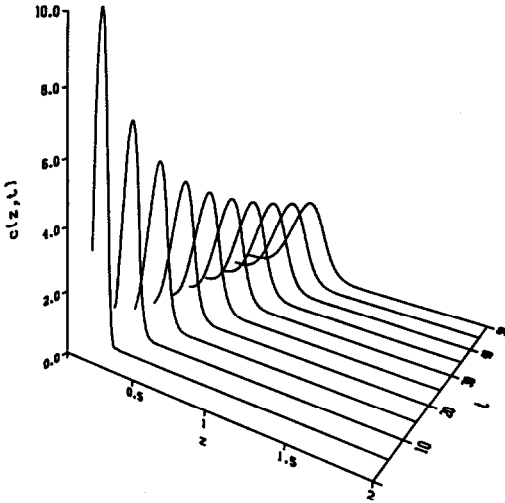
$$\text{for } t \ll \frac{L}{u_e} \quad (4)$$

Fig. 3. On-column concentration probability profile for the semi-infinite column with a reflection boundary condition at the origin. Other conditions as in Figs. 1 and 2.

where $\Phi(x)$ is the standard normal integral:

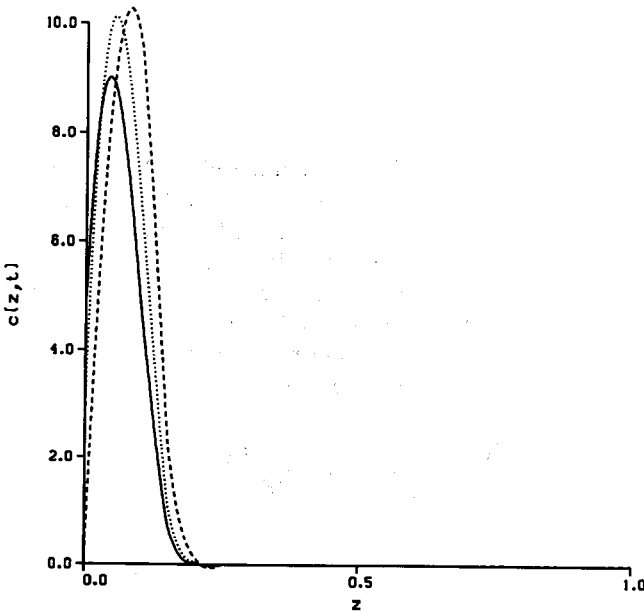$$\Phi(x) = \frac{1}{\sqrt{2\pi}} \int_{-\infty}^{x} \exp\left(-\frac{y^2}{2}\right) dy$$

Fig. 4. Comparison of the on-column profiles at $t = 5.0 \; D_e/u_e^2$, a representative short time for the infinite (solid line), semi-infinite (dashed line) and semi-infinite with reflection (dotted line) systems in Figs. 1–3.
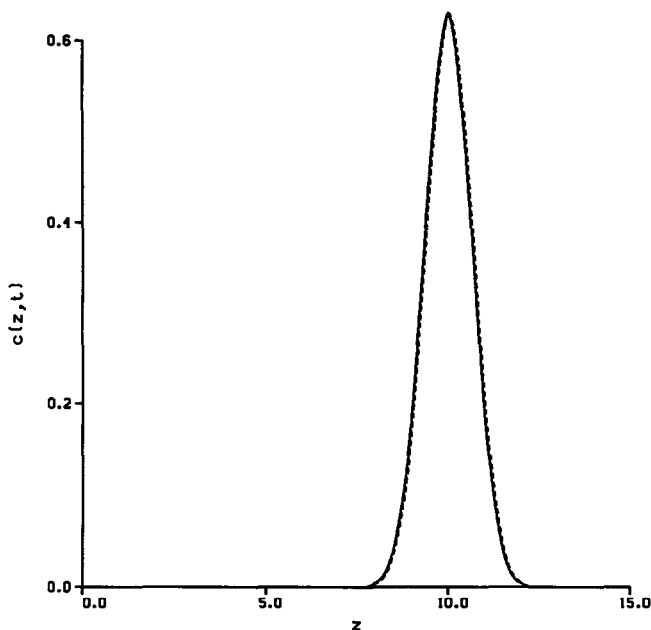
Fig. 5. Comparison of the on-column profiles at $t = 1000.0 \, D_e/u_e^2$, a representative long time for the three sets of boundary conditions as in Fig. 4. The dotted line cannot be easily distinguished from the solid line (infinite column result).

Eqn. 4 is identical with Kreft and Zuber's equation for a semi-infinite bed with injection in flux and detection in resident fluid. Fig. 3 illustrates the effect of introducing reflection at the origin. Fig. 4 compares the various calculated on-column profiles at short times. Note that the profile with reflection at the origin "leads" the peak from the infinite model profile. For long times, all three profiles converge, as shown in Fig. 5, becoming indistinguishable from a common Gaussian profile. This can be verified mathematically. For long chromatography times, we can use an approximation for the second term on the right in eqn. 4. From Abramowitz and Stegun [25], the asymptotic expansion for $x > 0$

$$1 - \Phi(x) = \frac{Z(x)}{x}\left(1 - \frac{1}{x^2} + \cdots\right)$$

enables us to show that

$$\frac{u_e}{D_e}\left[1 - \Phi\left(\frac{z + u_e t}{\sqrt{2D_e t}}\right)\right]\exp\left(\frac{zu_e}{D_e}\right) \rightarrow$$

$$\frac{1}{\sqrt{4\pi D_e t}}\left\{\exp\left[-\frac{(z - u_e t)^2}{4D_e t}\right]\right\}\left[1 + \frac{(z - u_e t)}{u_e t} + \cdots\right] \tag{5}$$

Exploring eqn. 4 graphically as in Fig. 5 demonstrates that for long times, $z - u_e t$ is nearly normally distributed about zero with a standard deviation that is $ca.\ \sqrt{2D_e t}$. In that case, the first-order term in the series expansion is negligible when $\sqrt{2D_e t}/u_e t \ll 1$. Consequently, eqn. 4 reduces to eqn. 2, the Gaussian distribution, at times $t \gg 2D_e/u_e^2$.

At least as far as equilibrium chromatography is concerned, we see that behavior at the column origin ultimately has a negligible effect on band development provided that we are not dealing with very short columns or unusually fast effective diffusion relative to peak migration rate.

DISCUSSION

With regard to one of the two column boundaries, the origin, Jönsson had dismissed the semi-infinite model of Kubin as physically unrealistic. The justification was that it gave a node in the on-column profile at the origin at all times other than $t = 0$, as can be seen in Fig. 2. However, the infinite models are equally unrealistic because they allow diffusion of solute into a non-existent part of the column, $z < 0$. It is apparent, though, that in the high velocity limit, these conflicts lose their impact. The awkwardness of both of these physical situations is completely vitiated when it is recognized that the boundary condition at the column origin corresponds to a reflection, that is, the probability flux through the origin is zero. At the very least, it is gratifying that as a direct consequence of using a reflection at the origin of the column, the on-column profile neither extends to negative column coordinates nor bears a node at the origin.

In a recent note [8], we drew attention to the end effect associated with elution at the column terminus. This involves another boundary condition necessary for solving the differential eqn. 1 under physically appropriate restraints. That is, the realistic cessation of diffusion and drift that occurs at the column terminus results in an elution profile that does not generally correspond to previous versions, although it does under certain limiting conditions. In that work, we had derived statistical moments of the equilibrium chromatogram on a column in which $-\infty < z \le L$. The end effect was mathematically determined by incorporating an absorbtion sink at $z = L$. In this way, solute reaching the elution coordinate is removed and cannot reappear on the column via dispersive effects. The drawback with those results might have been that the column was viewed as semi-infinite, extending towards $-\infty$. However, we have demonstrated in this work that, except in highly unusual circumstances, the effect of this oversight on the developing profile and consequently on the elution profile should be non-essential. The technique for addressing the end effect in the above reference should be valid.

The developments presented here seem very satisfactory when applied to linear equilibrium chromatography. It is our hope next to explore what changes, if any, arise when using these boundary conditions where kinetic effects have also been included.

ACKNOWLEDGMENT

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