

CHROM. 23 870

# Finite difference modelling of continuous-flow electrophoresis

Terese M. Grateful and Edwin N. Lightfoot, Jr.\*

Department of Chemical Engineering, University of Wisconsin-Madison, 1415 Johnson Drive, Madison, WI 53706 (USA)

(First received July 23rd, 1991; revised manuscript received November 12th, 1991)

---

## ABSTRACT

A numerical scheme is used to describe the operation of isothermal continuous-flow electrophoresis. The model used accounts for the effects of diffusion, electroosmosis, and nonuniformities in convection, without the limitations on experimental parameter ranges imposed by previous solutions. Results from the numerical scheme are verified by comparison with these limiting case solutions. The flexibility of the numerical scheme provides a basic framework for the description of continuous-flow electrophoresis.

---

## INTRODUCTION

Along with the growth of biotechnology comes an ever increasing need for separation methods for analytical, preparative and production scale separations. Although electrophoresis has widespread application as an analytical separative tool, its potential as a production scale separation method has not been realized. Limitations imposed by complex convective heat and mass transfer processes and the lack of reliable descriptions for these processes have hindered development in even the most promising equipment in current use.

Continuous-flow electrophoresis (CFE) [1] is an attractive method for the scale-up of electrophoresis, but even it has yet to be described in enough detail and in a manner encompassing a sufficiently broad range of operating conditions to serve as a basis for process design. This deficiency exists, not because of a lack of effort in this area, but instead because previous work has primarily focused on limiting ranges of operating conditions. Although the solutions from these prior efforts do provide useful insight into the operation of CFE under limiting conditions, as indicated in the review in the next section, there is a need for a more general approach.

It now appears necessary to use a numerical description for the CFE process which not only agrees with the limiting case solutions, but also provides a solution where these asymptotic solutions are inadequate. We begin this process here, using a modified form of the method of Biscans *et al.* [2] to explore the analyses for isothermal operation. Thermal effects, as well as concentration effects, are of secondary importance in many applications, and we defer consideration of these to a later effort.

## THEORY

For this development, we will focus on the CFE apparatus represented schematically in Fig. 1. The apparatus consists of a rectangular flow chamber with chamber dimensions such that  $L \gg w \gg 2d$ . Carrier electrolyte flows in the axial ( $x$ -) direction, and an electric field is imposed across the width of the chamber, perpendicular to the electrolyte flow. The faces of the chamber at  $y = \pm d$  are usually cooled. The sample is introduced into the chamber at the upstream end, and the trajectory of each sample component is determined by the vector sum of the species-dependent motion (electrophoresis) and the nonselective fluid motion (axial buffer flow and electroosmotic flow). Spatial variations exist in

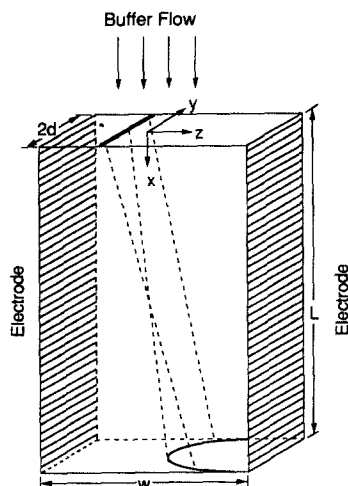


Fig. 1. Continuous-flow electrophoresis apparatus. Narrow lines indicate solute trajectories for the limiting case of zero solute diffusivity.

both components of the nonselective fluid motion, and it is this position-dependent velocity which contributes greatly to the dispersion in this system and also complicates its description.

We limit our discussion at this time to the case of isothermal operation. We also limit this discussion to the case where the concentrations of the species to be separated are sufficiently low that electrokinetic effects [3] and electrohydrodynamic spreading [4] are of secondary importance.

Assuming constant properties, we can use the following form of the continuity equation:

$$v_x \frac{\partial c_i}{\partial x} + v_{z,i} \frac{\partial c_i}{\partial z} = D_{im} \left( \frac{\partial^2 c_i}{\partial x^2} + \frac{\partial^2 c_i}{\partial y^2} + \frac{\partial^2 c_i}{\partial z^2} \right) \quad (1)$$

where  $D_{im}$  is the effective binary diffusivity of component  $i$  in the buffer medium,  $v_x$  is the  $x$ -component of the buffer velocity and  $v_{z,i}$  is the sum of the electrophoretic velocity of species  $i$  ( $v_{ef,i}$ ) and the  $z$ -component of the buffer flow caused by electroosmosis ( $v_z$ ). The terms  $v_x$  and  $v_{z,i}$  can be expressed as

$$v_x = v_0 [1 - (y/d)^2] \quad (2)$$

and

$$v_{z,i} = v_{ef,i} + v_z = v_{ef,i} + v_{eo} \left\{ 1 - \frac{3}{2} [1 - (y/d)^2] \right\} \quad (3)$$

where  $v_0$  is the maximum axial velocity and  $v_{eo}$  is the

electroosmotic velocity. Positive values of  $v_{ef,i}$  and  $v_{eo}$  indicate movement in the positive  $z$ -direction.

The boundary conditions for eqn. 1 are

- (a)  $c_i = 0$   $z = \pm \infty$
- (b)  $\partial c_i / \partial y = 0$   $y = 0, \pm d$
- (c)  $c_i = c_{i,0} \delta(z)$   $x = 0$
- (d)  $c_i \rightarrow 0$   $x \rightarrow \infty$

where  $c_{i,0}$  is the mass input per unit area and  $\delta(z)$  is a unit impulse function defined by  $\delta(z) = 0, z \neq 0$  and  $\int_{-\infty}^{\infty} \delta(z) dz = 1$ .

We can rewrite eqns. 1–3 in terms of dimensionless parameters as

$$v_x^* \frac{\partial c_i^*}{\partial x^*} + v_{z,i}^* \frac{\partial c_i^*}{\partial z^*} = Pe_0^{-1} \left( \frac{\partial^2 c_i^*}{\partial x^{*2}} + \frac{\partial^2 c_i^*}{\partial y^{*2}} + \frac{\partial^2 c_i^*}{\partial z^{*2}} \right) \quad (4)$$

$$v_x^* = [1 - (y^*)^2] \quad (5)$$

$$v_{z,i}^* = \frac{v_{ef,i}}{v_0} + \frac{v_{eo}}{v_0} \left\{ 1 - \frac{3}{2} [1 - (y^*)^2] \right\} \quad (6)$$

where:  $x^* = x/d$ ;  $y^* = y/d$ ;  $z^* = z/d$ ;  $c_i^* = c_i d / c_{i,0}$  and  $Pe_0 = v_0 d / D_{im}$ . The boundary conditions become:

- (a)  $c_i^* = 0$   $z^* = \pm \infty$
- (b)  $\partial c_i^* / \partial y^* = 0$   $y^* = 0, \pm 1$
- (c)  $c_i^* = \delta(z^*)$   $x^* = 0$
- (d)  $c_i^* \rightarrow 0$   $x^* \rightarrow \infty$ .

Two quantities of potential interest can be defined: the average concentration,  $c_{i,avg}^*$ , where

$$c_{i,avg}^* = \frac{\int_{-1}^1 c_i^*(L/d, y^*, z^*) dy^*}{\int_{-\infty}^{\infty} \int_{-1}^1 c_i^*(L/d, y^*, z^*) dy^* dz^*} \quad (7)$$

and the bulk, or flow-averaged, concentration,  $c_{i,b}^*$ , where

$$c_{i,b}^* = \frac{\int_{-1}^1 c_i^*(L/d, y^*, z^*) v_x^* dy^*}{\int_{-\infty}^{\infty} \int_{-1}^1 c_i^*(L/d, y^*, z^*) v_x^* dy^* dz^*} \quad (8)$$

From these expressions for  $c_{i,avg}^*$  or  $c_{i,b}^*$  and eqns.

4–6, we can see that the interactions of the experimental parameters can be summarized in terms of the following dimensionless groups:  $L/d$ ;  $Pe_0$ ;  $v_{ef,i}/v_0$ ;  $v_{eo}/v_0$ .

Analytic solutions to eqns. 4–6 can be obtained using various simplifying assumptions, but these solutions are only valid for specific limiting cases. We review these solutions below.

#### Previous work

*Strickler and Sacks [5]*. Strickler and Sacks examined the limiting case where the effects of diffusion can be neglected, and the solute profiles are strictly a result of the hydrodynamics. The angle of the deflection of a solute molecule in the chamber is determined by the ratio  $v_{z,i}/v_x$ , where

$$\frac{v_{z,i}}{v_x} = \frac{v_{ef,i} + v_{eo} \left\{ 1 - \frac{3}{2} [1 - (y/d)^2] \right\}}{v_0 [1 - (y/d)^2]} = \left( \frac{v_{ef,i}}{v_0} \right) \left[ \frac{1 + k_i}{1 - (y/d)^2} - \frac{3}{2} k_i \right] \quad (9)$$

and  $k_i = v_{eo}/v_{ef,i}$ . The result of the  $y$ -dependence shown in eqn. 9 is called the “crescent effect”, for the crescent-shaped solute profile seen in CFE experiments. We can see from eqn. 9 that, in order to minimize the dispersion for a desired product, the electroosmotic velocity  $v_{eo}$  should be equal and opposite to the electrophoretic velocity  $v_{ef,i}$  of the desired product. Satisfying this condition eliminates the  $y$ -dependence of the migration angle for that solute and consequently eliminates the crescent-shaped profile.

*Ivory [6]*. Ivory incorporated the effects of diffusion in both the  $x$ - and  $z$ -directions, but neglected diffusion in the  $y$ -direction. This assumption was justified as a reasonable assumption as long as the mean diffusional displacement in the  $y$ -direction ( $\lambda_y$ ) is much smaller than the half-thickness ( $d$ ). This criterion was written as

$$\frac{\lambda_y}{d} \approx \frac{(2D_{im}t)^{1/2}}{d} \approx \left[ \frac{L/d}{Pe(y)} \right]^{1/2} \ll 1 \quad (10)$$

where  $Pe(y) = Pe_0 v_x^*(y^*)$  and  $t \approx L/v_x$  is the solute residence time.

The solution to eqn. 4 when the diffusion in the  $y$ -direction is neglected is

$$c_i^* = \left( \frac{\gamma x^*}{\sqrt{2\pi}} \right) \frac{K_1[\gamma(x^{*2} + z^{*2})^{1/2}]}{(x^{*2} + z^{*2})^{1/2}} \exp \left[ \frac{Pe_0}{2} (x^* v_x^* + z^* v_{z,i}^*) \right] \quad (11)$$

where

$$\gamma^2 = Pe_0^2 (v_x^{*2} + v_{z,i}^{*2}) / 4$$

$K_1(\cdot)$  is the modified Bessel function of the second kind of order one. Eqn. 11 can be numerically integrated to get  $c_{i,avg}^*$  or  $c_{i,b}^*$ .

*Reis et al. [7]*. Reis et al. did consider diffusion in the  $y$ -direction, but they used the approximation based on the Gill and Sankarasubramanian [8] extension of Taylor’s method [9] for describing convective dispersion. This solution is valid for large values of  $(L/d)/Pe_0$ , such that the system residence time is sufficiently long that an asymptotic state is approached in which diffusion in the  $y$ -direction exactly balances the disturbance caused by the nonuniform axial velocity.

The solution, which is valid only for the special case when electroosmotic flows are not present ( $v_{eo} = 0$ ), is

$$c_{i,b}^* = \frac{1}{6\pi} \int_0^\infty \frac{\exp \left[ - \left( \frac{\zeta^2}{4\tau} + \frac{L_1^2}{4\xi} \right) \right]}{\sqrt{\xi\tau}} d\tau \quad (12)$$

where

$$\zeta = (z - v_{ef,i}t)/d$$

$$\tau = tD_{im}/d^2$$

$$L_1 = \frac{(L - \langle v_x \rangle t)}{dPe_0}$$

$$\langle v_x \rangle = \frac{1}{2d} \int_{-d}^d v_x dy$$

$$\xi = \int_0^\tau k_2(\theta) d\theta$$

$$k_2 = \left( \frac{1}{Pe_0} \right)^2 + \frac{8}{945} - \frac{8}{\pi^6} \sum_{n=1}^\infty \frac{\exp[-(n\pi)^2\theta]}{n^6}$$

In order to get the expression in eqn. 12, the

assumption was made that the ratio  $\alpha \approx 1$ , where  $\alpha$  was defined as

$$\alpha = \frac{\langle c_i v_x \rangle}{\langle c_i \rangle \langle v_x \rangle} \tag{13}$$

where  $\langle \cdot \rangle = \int_{-1}^1 \cdot dy^*$ . This ratio allows the conversion between the average concentration and the bulk concentration.

*Biscans et al.* [2]. *Biscans et al.* proposed neglecting only axial diffusion as truly unimportant relative to axial convection. Eqn. 4 can then be written as

$$v_x^* \frac{\partial c_i^*}{\partial x^*} + v_{z,i}^* \frac{\partial c_i^*}{\partial z^*} = Pe_0^{-1} \left( \frac{\partial^2 c_i^*}{\partial y^{*2}} + \frac{\partial^2 c_i^*}{\partial z^{*2}} \right) \tag{14}$$

Finite difference methods were used to solve the equation on a plane of constant  $x^*$  for grid points in  $y^*$  and  $z^*$  using an iterative procedure. The  $x^*$ -coordinate was then incremented, and the solution was determined on that  $y^*-z^*$  plane. The boundary conditions used were

- (a)  $c_i^* = 0 \quad z^* = z_0^*, z_i^*$
- (b)  $c_i^* = 0 \quad y^* = \pm 1$

The boundary condition at  $x^* = 0$  was not explicitly expressed in the article but was described as a squared input occupying 20–30% of the cell. Boundary condition (b) limits the validity of the solution to the case where the sample is introduced to only a small portion of the cell (in the  $y^*$ -direction) and the sample residence time is sufficiently short. This criterion can be expressed as

$$\left( \frac{\Delta_y}{d} \right)^2 \gg 3 \left( \frac{L/d}{Pe_0} \right) \tag{15}$$

where  $\Delta_y$  is the shortest distance between the sample input and the walls at  $y^* = \pm 1$ .

*Present work*

The solutions listed above are all limited in applicability to specific parameter ranges. The solution described by Ivory [6] is only applicable when  $(L/d)/Pe_0$  is small, while that of Reis *et al.* [7] is valid for large  $(L/d)/Pe_0$ . The method used by *Biscans et*

*al.* [2] is limited to both reasonably small  $(L/d)/Pe_0$  and small input sample dimensions as given in eqn. 15.

Our goal is a solution capable of covering the entire parameter space of practical interest. We use for this purpose an approach similar to that of *Biscans et al.* [2], neglecting only axial diffusion as truly unimportant relative to axial convection. Our scheme differs from that of *Biscans* primarily in two ways. We have used a more general boundary condition in the  $y^*$ -direction, so our scheme is not restricted by the limitation expressed in eqn. 15. Also, we do not use an iterative numerical solution, but rather a modified version of an alternating direction implicit scheme, proposed by Peaceman and Rachford [10], to find the numerical solution to eqn. 14.

For this approach, we can rewrite eqn. 14 in the form [11]

$$\frac{\partial c_i^*}{\partial x^*} = A_1 c_i^* + A_2 c_i^* \tag{16}$$

where  $A_1$  and  $A_2$  are linear operators, defined as

$$A_1 c_i^* = (Pe_0 v_x^*)^{-1} \frac{\partial^2 c_i^*}{\partial z^{*2}} - \frac{v_{z,i}^*}{v_x^*} \frac{\partial c_i^*}{\partial z^*} \tag{17}$$

$$A_2 c_i^* = (Pe_0 v_x^*)^{-1} \frac{\partial^2 c_i^*}{\partial y^{*2}} \tag{18}$$

The following two-step scheme is then used to get an approximation to eqn. 16:

$$\left( 1 - \frac{\Delta x^*}{2} A_{1h} \right) \tilde{C}^{j+1/2}(m, n) = \left( 1 + \frac{\Delta x^*}{2} A_{2h} \right) C^j(m, n) \tag{19}$$

$$\left( 1 - \frac{\Delta x^*}{2} A_{2h} \right) C^{j+1}(m, n) = \left( 1 + \frac{\Delta x^*}{2} A_{1h} \right) \tilde{C}^{j+1/2}(m, n) \tag{20}$$

where  $C^j(m, n)$  and  $C^{j+1}(m, n)$  are approximations of  $c_i^*(x_j^*, y_m^*, z_n^*)$  and  $c_i^*(x_{j+1}^*, y_m^*, z_n^*)$ , respectively, and  $\tilde{C}^{j+1/2}(m, n)$  is an intermediate variable. The terms  $A_{1h}$  and  $A_{2h}$  are the second-order finite difference approximations for  $A_1$  and  $A_2$ , respectively, given by

$$A_{1n}C^j(m, n) = (Pe_0 v_x^*)^{-1} \left[ \frac{C^j(m, n+1) - 2C^j(m, n) + C^j(m, n-1)}{(\Delta z^*)^2} \right] - \frac{v_{z,i}^*}{v_x^*} \left[ \frac{C^j(m, n+1) - C^j(m, n-1)}{2\Delta z^*} \right] \quad (21)$$

$$A_{2n}C^j(m, n) = (Pe_0 v_x^*)^{-1} \left( \frac{C^j(m+1, n) - 2C^j(m, n) + C^j(m-1, n)}{(\Delta y^*)^2} \right) \quad (22)$$

The following finite difference boundary conditions are used:

- (a)  $C^j(m, 0) = C^j(m, N) = 0$
- (b)  $-3C^j(0, n) + 4C^j(1, n) - C^j(2, n) = 0$
- (c)  $-3C^j(M, n) + 4C^j(M-1, n) - C^j(M-2, n) = 0$

with the "initial" condition

- (d)  $C^j(m, n) = 1, \quad x^* = 0, \quad -1 \leq y^* \leq 1, \quad z^* = 0$

which approximates the delta function mass type input used in the solutions of Ivory and Reis. The  $y^*$  range for the finite difference scheme is given by  $y_0^* \leq y_m^* \leq y_M^*$  where  $y_0^* = -1$  and  $y_M^* = 1$ . The range for  $z^*$  is  $z_0^* \leq z_n^* \leq z_N^*$  where the boundaries at  $z_0^*$  and  $z_N^*$  are set such that these boundaries do not significantly impact the solution. This choice allows us to use the "infinite boundary" condition (a). Boundary conditions (b) and (c) are second-order, one-sided approximations for boundary conditions (b) in eqn. 4.

The requirement for the solution of this numerical scheme to show the correct convective-dispersive character is a limit on the step size in  $z^*$  [11]:

$$\Delta z^* \leq \frac{2}{Pe_0} \left( \frac{v_0}{v_{z,i}} \right) \quad (23)$$

This condition does, however, place a lower limit on the time it takes to determine the solution by imposing a rather large minimum size for the matrix of concentrations.

## RESULTS

As shown earlier, the experimental parameters necessary to determine either  $c_{i,avg}^*$  or  $c_{i,b}^*$  can be summarized in terms of the following dimensionless groups:  $L/d$ ;  $Pe_0$ ;  $v_{ef,i}/v_0$ ;  $v_{eo}/v_0$ . Table I contains a summary of several recently reported experiments using the CFE apparatus. We have used the data provided in these references to obtain approximate

useful ranges for the important dimensionless groups, and these ranges are reported in Table II. It is in terms of these four dimensionless parameters that we base our discussion.

For the numerical scheme to be generally applicable, it is necessary that the numerical solution approach the asymptotic solutions developed by Ivory [6] and by Reis *et al.* [7] under the limiting conditions of low and high values of  $(L/d)/Pe_0$ , respectively, as well as show realistic behavior between these two limits.

In an effort to verify this behavior, a series of computer simulations was performed. Figs. 2–5 compare the bulk concentrations as a function of chamber position calculated using the solutions of Ivory, Reis and the finite difference scheme presented in the previous section. The experimental parameters used in the simulations were:  $Pe_0 = 2 \cdot 10^4$ ;  $v_{ef,i}/v_0 = 2.5 \cdot 10^{-3}$ ;  $v_{eo}/v_0 = 0$ . For these simulations only the dimensionless length of the chamber ( $L/d$ ) was varied, with  $L/d = 2 \cdot 10^2$ ,  $5 \cdot 10^3$ ,  $1 \cdot 10^4$  and  $2 \cdot 10^4$ . For these values of  $L/d$ , the value of  $(L/d)/Pe_0$  ranges from 0.01–1.0.

In Fig. 2,  $(L/d)/Pe_0 = 0.01$ , and we can see that the finite difference solution matches the solution of Ivory almost exactly. At this low value of  $(L/d)/Pe_0$ , the concentration profile seen is primarily a function of hydrodynamics, giving a purely "convective peak" which agrees with the development of Ivory.

In Fig. 3,  $(L/d)/Pe_0 = 0.25$ , and the convective solution no longer suffices. The hint of a double peak is now apparent, with the dispersive type solution predicted by Reis appearing as a shoulder on the convective peak. In Fig. 4, with  $(L/d)/Pe_0 = 0.5$ , the situation is reversed, with the convective peak now a shoulder on the dispersive peak. In Fig. 5,  $(L/d)/Pe_0 = 1.0$ , and the peak closely approximates the dispersive solution of Reis; the convective peak is no longer present. The difference between the concentrations predicted by the finite difference solution and the solution of Reis is due primarily to the error introduced into the Reis *et al.* solution by the assumption stated in eqn. 13 (*i.e.*  $\alpha \approx 1.0$ ).

TABLE I  
EXPERIMENTAL DATA

Apparatus	Dimensions (cm)			Solutes	Residence time (min)	Ref.
	$L$	$w$	$2d$			
ACE 710 <sup>a</sup>	20	NA <sup>b</sup>	0.08	Erythrocytes	NA	[12]
	18	4	0.03	Cells	0.5	[13]
CFE system <sup>c</sup>	120	6	0.15	Cytochrome <i>c</i> , myoglobin, $\beta$ -lactoglobulin, ovalbumin	4	[14]
	120	8.2	0.18	Granules containing growth hormone	10.4	[15]
VaP 21 <sup>d</sup>	25	10	0.05	Liposomes	1.5	[16]
			0.07	Chromosomes	2.1	[17]
VaP 22 <sup>d</sup>	50	10	0.05	Alcohol dehydrogenase in yeast extract	5–20	[18]
				Alcohol dehydrogenase in yeast extract	2.5–10	[19]
				Lysosyme in <i>E. coli</i> extract	7.8–14.7	[20]
				Hemoglobin	11.4	[21]
				$\alpha$ -amylase from <i>E. coli</i> extract	5	[22]
				Myoglobin, catalase, thyroglobulin	5	[23]
				Formaldehyde dehydrogenase, formate dehydrogenase, methanol oxidase	5	[24]
VaP 220 <sup>d</sup>	100	16	0.05	Endosomes, lysosomes	3.3	[25]
				Formaldehyde dehydrogenase, formate dehydrogenase, methanol oxidase	3.3	[24]
Lab models	100	15	0.05	Alcohol dehydrogenase in yeast extract	5	[18]
	30	4	0.3	Hemoglobin, cytochrome <i>c</i> , bovine serum albumin	4	[26]

<sup>a</sup> Hirschmann (Munich, FRG).

<sup>b</sup> Not available.

<sup>c</sup> McDonnell Douglas (St. Louis, MO, USA).

<sup>d</sup> Bender & Hobein (Munich, FRG).

TABLE II  
EXPERIMENTAL PARAMETER RANGES

Parameter	Approximate range
$L/d$	200–4000
$Pe_0$ <sup>a</sup>	$10^3$ – $10^5$
$\left  \frac{v_{ef}}{v_0} \right ^b, \left  \frac{v_{eo}}{v_0} \right ^c$	$10^{-3}$ – $10^{-1}$

<sup>a</sup> Using estimates of solution properties.

<sup>b</sup> Estimated from concentration profiles given in references.

<sup>c</sup> Generally the same order of magnitude as  $(v_{ef}/v_0)$ .

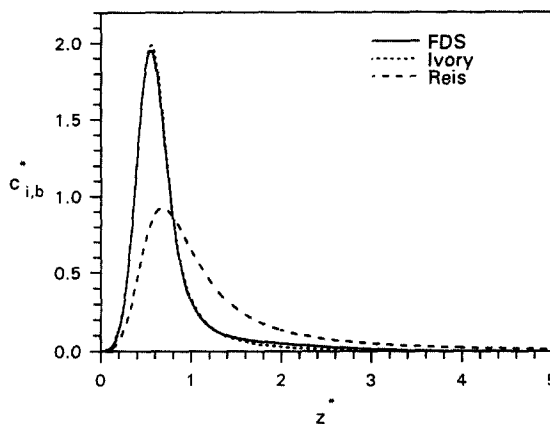


Fig. 2. Comparison of the bulk averaged concentration  $c_{i,b}^*$  using the solution of Ivory, Reis *et al.* and the finite difference solution of the present work (FDS).  $L/d = 2.0 \cdot 10^2$ ,  $Pe_0 = 2 \cdot 10^4$ ,  $v_{ef}/v_0 = 2.5 \cdot 10^{-3}$ ,  $v_{eo}/v_0 = 0.0$ .

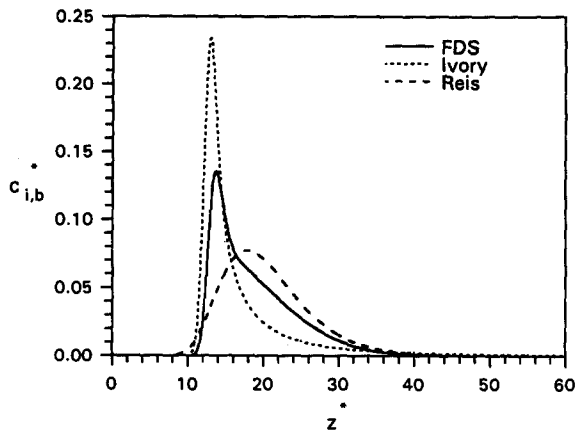


Fig. 3. Comparison of the bulk averaged concentration  $c_{i,b}^*$  using the solution of Ivory, Reis *et al.* and the finite difference solution of the present work (FDS).  $L/d = 5 \cdot 10^3$ ,  $Pe_0 = 2 \cdot 10^4$ ,  $v_{ef}/v_0 = 2.5 \cdot 10^{-3}$ ,  $v_{eo}/v_0 = 0.0$ .

Fig. 6 shows the progression of the concentration profile, calculated using the finite difference solution, from the convective result to the dispersive result. The experimental parameters are the same as in Figs. 2–5, with  $L/d$  ranging from  $2 \cdot 10^3$ – $2 \cdot 10^4$ . At low values of  $(L/d)/Pe_0$ , we see the steep, long-tailed peak of the convective solution. At large values of  $(L/d)/Pe_0$ , the effect of diffusion in the  $y$ -direction becomes important because the solute residence time is sufficiently long that the solute molecules are able to sample the entire  $y$ -range, leading to a

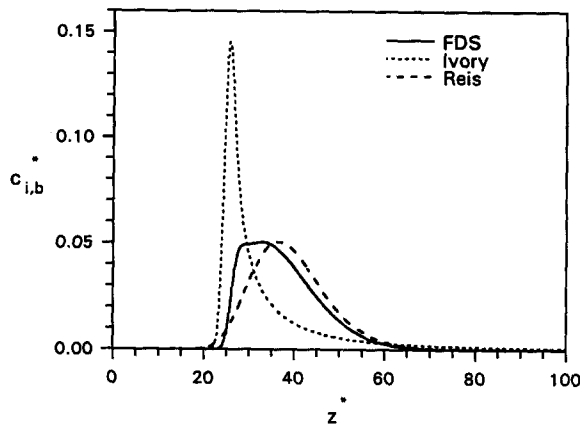


Fig. 5. Comparison of the bulk averaged concentration  $c_{i,b}^*$  using the solution of Ivory, Reis *et al.* and the finite difference solution of the present work (FDS).  $L/d = 2 \cdot 10^4$ ,  $Pe_0 = 2 \cdot 10^4$ ,  $v_{ef}/v_0 = 2.5 \cdot 10^{-3}$ ,  $v_{eo}/v_0 = 0.0$ .

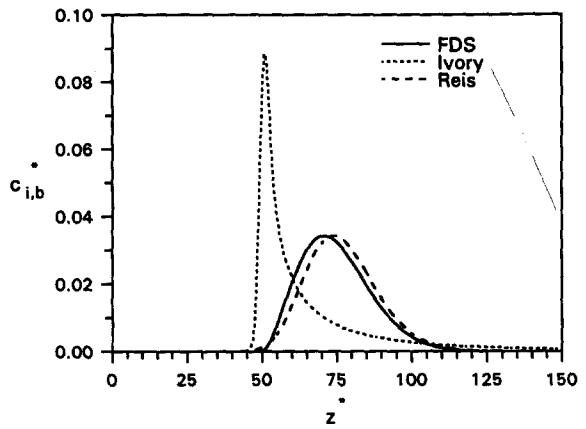


Fig. 4. Comparison of the bulk averaged concentration  $c_{i,b}^*$  using the solution of Ivory, Reis *et al.* and the finite difference solution of the present work (FDS).  $L/d = 1 \cdot 10^4$ ,  $Pe_0 = 2 \cdot 10^4$ ,  $v_{ef}/v_0 = 2.5 \cdot 10^{-3}$ ,  $v_{eo}/v_0 = 0.0$ .

Gaussian shaped peak. At the intermediate values of  $(L/d)/Pe_0$ , it appears that both peaks are present. The “double peak” seem is similar to that sometimes seen in chromatography [27] and in other mathematically similar systems [28].

It is important to note that the preceding profiles were calculated using the condition of no electroosmosis ( $v_{eo} = 0$ ). However, under normal experimental conditions, electroosmosis does occur, and it is thus important to be able to include its effects in

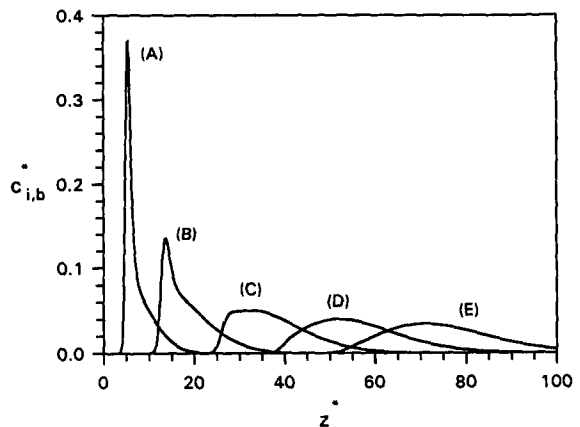


Fig. 6. Effect of the dimensionless length of the chamber  $L/d$  on the bulk averaged concentration  $c_{i,b}^*$  using the finite difference solution of the present work.  $Pe_0 = 2 \cdot 10^4$ ,  $v_{ef}/v_0 = 2.5 \cdot 10^{-3}$ ,  $v_{eo}/v_0 = 0.0$ . Curves are for  $L/d = 2 \cdot 10^3$  (A),  $5 \cdot 10^3$  (B),  $1 \cdot 10^4$  (C),  $1.5 \cdot 10^4$  (D),  $2 \cdot 10^4$  (E).

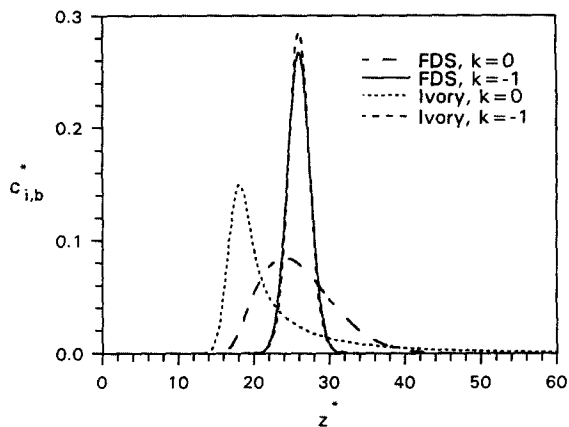


Fig. 7. Comparison of the effect of electroosmotic flow on the bulk averaged concentration  $c_{i,b}^*$  using the solution of Ivory and the finite difference solution of the present work (FDS) for  $v_{eo}/v_0 = 0.0$  and  $v_{eo}/v_0 = -8.67 \cdot 10^{-3}$ .  $L/d = 2 \cdot 10^3$ ,  $Pe_0 = 2.63 \cdot 10^3$ ,  $v_{ef}/v_0 = 8.67 \cdot 10^{-3}$ .

any description of the system. As was noted, the solution proposed by Reis *et al.* does not include the effect of electroosmosis. In Fig. 7 we show the results of a comparison between the solution of Ivory and the finite difference scheme for the conditions:  $Pe_0 = 2.63 \cdot 10^3$ ,  $v_{ef,i}/v_0 = 8.67 \cdot 10^{-3}$  and  $L/d = 2 \cdot 10^3$ . We compare the solutions obtained for both  $v_{eo}/v_0 = 0$  and  $v_{eo}/v_0 = -8.67 \cdot 10^{-3}$ , corresponding to  $k_i = v_{eo}/v_{ef,i} = 0, -1$ . As was predicted by the expression derived by Strickler and Sacks, dispersion is minimized as the value of the electrophoretic velocity approaches a value equal and opposite to the electroosmotic velocity ( $v_{eo} \rightarrow -v_{ef,i}$ ).

It is interesting to note in Fig. 7 that, while the solution provided by eqn. 11 does not give the correct concentration profile for  $v_{eo}/v_{ef,i} = 0$ , it is indeed valid for  $v_{eo}/v_{ef,i} = -1$ , independent of the value of  $(L/d)/Pe_0$ . Diffusion in the  $y$ -direction ceases to be important in the calculation of the final solute profile when the trajectory is independent of the  $y$ -position.

## DISCUSSION

We have verified that the results from the finite difference solution match those of the asymptotic solutions for the limiting cases. This fact, and the observation that the solution behaves as expected

over the transition from the convection-dominated to the dispersion-dominated regime, verify that the use of the finite difference approximation does not introduce any significant error into the solution, and affirm our confidence in the applicability of the finite difference scheme to the entire range of the parameter space.

Although the solutions of Reis *et al.* and Ivory are analytical and thus much less time-consuming to evaluate, their use must be limited to conditions under which their assumptions hold. The use of the inappropriate model will give an error not only in the peak location, but in the peak shape as well.

The finite difference solution proposed by the present work can be easily modified to incorporate nonuniform, nonrectangular sample inputs and nonisothermal conditions, as well as alternate velocity profiles. Our scheme provides the basic framework for the description of the operation of CFE over currently useful conditions.

The intent of the present work is to show the utility of a numerical description for the system given; therefore, no optimization of the numerical method or computer code was performed. It is useful to note, however, that for a sample run such as that seen in the finite difference results shown in Fig. 7, the code took 9.5 cpu hours to execute on a VAXstation 3100 (Digital Equipment Corporation, Maynard, MA, USA). This simulation was composed of 1000 steps in  $x$  and a matrix of  $y, z$  values that was  $40 \times 1750$ . It is the stiffness of the differential equation (see eqn. 23) which requires a large number of matrix elements to accurately described the system.

## SYMBOLS

$A_1, A_2$	linear operators
$A_{1h}, A_{2h}$	second order approximations to $A_1, A_2$
$c_i$	concentration of species $i$
$\langle c_i \rangle$	concentration averaged with respect to $y$
$c_i^*$	dimensionless concentration
$c_{i,avg}$	average concentration
$c_{i,b}^*$	bulk, or flow-averaged, concentration
$c_{i,0}$	mass input per unit area
$d$	half-thickness of the chamber
$D_{im}$	effective binary diffusivity of species $i$
$k_i$	$v_{eo}/v_{ef,i}$
$L$	length of the electrode region



$Pe_0$	$v_0 d / D_{im}$
$t$	time
$v_0$	maximum axial velocity in the chamber
$v_{ef,i}$	electrophoretic velocity of species $i$
$v_{eo}$	electroosmotic velocity
$v_x$	axial or $x$ -component of the buffer velocity
$\langle v_x \rangle$	axial velocity averaged with respect to $y$
$v_x^*, v_{z,i}^*$	dimensionless velocities
$v_{z,i}$	sum of $v_{ef,i}$ and $v_z$
$w$	width of the chamber
$x, y, z$	rectangular coordinates
$x^*, y^*, z^*$	dimensionless coordinates
$\Delta x^*, \Delta y^*, \Delta z^*$	step sizes for $x^*, y^*, z^*$
$\alpha$	$\langle c_i v_x \rangle / (\langle c_i \rangle \langle v_x \rangle)$
$\delta(z)$	unit impulse function
$\lambda_y$	mean diffusional displacement in the $y$ -direction

## REFERENCES

- 1 K. Hannig, in J. R. Norris and D. W. Ribbons (Editors), *Methods in Microbiology 5B*, Academic Press, London, 1971, Ch. VIII, p. 513.
- 2 B. Biscans, P. Alinat, J. Bertrand and V. Sanchez, *Electrophoresis (Weinheim, Fed. Repub. Ger.)*, 9 (1988) 84.
- 3 M. Bier, O. A. Palusinski, R. A. Mosher and D. A. Saville, *Science (Washington, DC)*, 219 (1983) 1281.
- 4 P. H. Rhodes, R. S. Snyder and G. O. Roberts, *J. Colloid Interface Sci.*, 129 (1989) 78.
- 5 A. Strickler and T. Sacks, *Ann. N.Y. Acad. Sci.*, 209 (1973) 497.
- 6 C. F. Ivory, *J. Chromatogr.*, 195 (1980) 165.
- 7 J. Reis, E. N. Lightfoot and H. Lee, *AIChE J.*, 20 (1974) 362.
- 8 W. N. Gill and R. Sankarasubramanian, *Proc. R. Soc. London, A.*, 316 (1970) 341.
- 9 G. I. Taylor, *Proc. R. Soc. London, A*, 219 (1953) 186.
- 10 D. W. Peaceman and H. H. Rachford, Jr., *J. Soc. Ind. Appl. Math.*, 3 (1955) 28.
- 11 J. C. Strikwerda, *Finite Difference Schemes and Partial Differential Equations*, Wadsworth and Brooks/Cole Advanced Books and Software, Pacific Grove, California, 1989.
- 12 K. Hannig, M. Kowalski, G. Klöck, U. Zimmermann and V. Mang, *Electrophoresis (Weinheim, Fed. Repub. Ger.)*, 11 (1990) 600.
- 13 J. Bauer, *J. Chromatogr.*, 418 (1987) 359.
- 14 K. A. Knisley and L. S. Rodkey, *Electrophoresis (Weinheim, Fed. Repub. Ger.)*, 11 (1990) 927.
- 15 D. Hayes, C. Exton, T. Salada, K. Shellenberger, J. Waddle and W. C. Hymer, *Electrophoresis (Weinheim, Fed. Repub. Ger.)*, 11 (1990) 976.
- 16 R. Kessler and H. Manz, *Electrophoresis (Weinheim, Fed. Repub. Ger.)*, 11 (1990) 979.
- 17 F. F. Bier, U. Bettag, T. Rheingans, H. Adrian, J. Barths, M. Hausmann, H. Bühring, P. Rohwer, J. Dölle and C. Cremer, *Electrophoresis (Weinheim, Fed. Repub. Ger.)*, 10 (1989) 690.
- 18 S. Hoffstetter-Kuhn and H. Wagner, *Electrophoresis (Weinheim, Fed. Repub. Ger.)*, 11 (1990) 451.
- 19 S. Hoffstetter-Kuhn, R. Kuhn and H. Wagner, *Electrophoresis (Weinheim, Fed. Repub. Ger.)*, 11 (1990) 304.
- 20 R. Kuhn and H. Wagner, *J. Chromatogr.*, 481 (1989) 343.
- 21 R. A. Mosher, D. Dewey, W. Thormann, D. A. Saville and M. Bier, *Anal. Chem.*, 61 (1989) 362.
- 22 R. Kuhn and H. Wagner, *Electrophoresis (Weinheim, Fed. Repub. Ger.)*, 10 (1989) 165.
- 23 S. Nath, H. Schütte, H. Hustedt and W. Deckwer, *Electrophoresis (Weinheim, Fed. Repub. Ger.)*, 11 (1990) 612.
- 24 S. Nath, H. Schütte, G. Weber, H. Hustedt and W. Deckwer, *Electrophoresis (Weinheim, Fed. Repub. Ger.)*, 11 (1990) 937.
- 25 M. Marsh, in A. M. Tartakoff (Editor), *Methods in Cell Biology, Vol. 31, Vesicular Transport, Part A*, Academic Press, New York, 1989, Ch. 17, p. 319.
- 26 M. J. Clifton, N. Jouve, H. de Balmann and V. Sanchez, *Electrophoresis (Weinheim, Fed. Repub. Ger.)*, 11 (1990) 913.
- 27 S. G. Weber and P. W. Carr, in P. R. Brown and R. A. Hartwick (Editors), *High Performance Liquid Chromatography*, Wiley, New York, 1989, p. 1.
- 28 A. M. Lenhoff and E. N. Lightfoot, *Chem. Eng. Sci.*, 41 (1986) 2795.