Research Article

Joule heating effects on separation efficiency in capillary zone electrophoresis with an initial voltage ramp

An analytical model is developed to quantify the Joule heating effects on the separation efficiency in CZE with an initial voltage ramp. This model considers the temporal variations of nonuniform temperature and flow fields in the course of voltage ramping. The temperature dependence of electrical conductivity, dynamic viscosity, and mass density of the fluid is also taken into account. We demonstrate that the application of an initial voltage ramp delays the development of pressure-driven flows induced passively by the axial temperature gradients. The thermal dispersion is thus significantly reduced, resulting in a higher theoretical plate number in CZE. Such improvement in the separation efficiency is apparent in noncoated capillaries at high electric fields with an appropriate voltage ramp-up time. These predictions are consistent with previous observations in both aqueous and nonaqueous CZE that took place in uncoated capillaries. In coated capillaries where the EOF is suppressed, however, our model predicts a lower plate number in the presence of an initial voltage ramp.

Keywords: Capillary zone electrophoresis / Dispersion / Joule heating / Separation efficiency / Voltage ramp

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1 Introduction

CZE is a routine analytical tool for the separation of charged biomolecules such as peptides and proteins [1, 2]. As reviewed by Gaš et al. [3–5], there are a variety of sources that may contribute to the sample dispersion and thus reduce the efficiency of electrophoretic separation. One such source is the Joule heating caused by an electric current passing through the electrolyte solution [6–11]. It is widely accepted that Joule heating effects yield radial temperature gradients [12–17] resulting in a parabolic profile of electrophoretic velocity of solute molecules [18–26]. Hence, the sample zone is additionally broadened due to the Taylor–Aris dispersion [27, 28]. This typically insignificant contribution, however, cannot explain the decrease in separation efficiency at high electric fields [24, 25]. Xuan and Li [29] recently explained this deviation with the disturbance to EOF field induced by an axially nonuniform temperature distribution. Such axial temperature gradients could arise from the nonuniform dissipation of Joule heat along a capillary with either variable heat transfer conditions [30, 31] or reservoir-based thermal end effects [32–34].

More recently, Palonen et al. [35] observed higher separation efficiency in nonaqueous electrophoretic separation that took place in a chemically coated capillary with an initial voltage ramp, i.e., the voltage was gradually increased to the final magnitude instead of an abrupt application. By examining the peak width at various electric fields, capillary internal diameters and electrolyte ionic strengths, these authors concluded that the band broadening associated with the abrupt voltage application has a thermal origin. Such an improvement in the separation efficiency due to the initial voltage ramp was also reported previously in both nonaqueous [36] and aqueous CZE [37–39] in uncoated capillaries. In addition, this voltage ramping was shown to avoid the loss of samples that could take place when the rate of thermal expansion of liquid, due to Joule heating, is more rapid than the electromigration rate of the slowest moving solute [40]. It is probably the lower thermal volume expansion, as suggested by Palonen et al. [35], that improves the electrophoretic separation in the presence of an initial voltage ramp.
In this paper we extend the analytical model developed by the authors in [29] to take into account the temporal variations of temperature and flow fields in thermostated CZE during the course of voltage ramping. The thermal expansion of the BGE solution is also considered. We demonstrate that the initial voltage ramping delays the development of axially nonuniform temperature and flow fields so that the solute molecules migrating in the injection region are less dispersed. The resultant improvement in separation efficiency in CZE is investigated in terms of the theoretical plate number for solutes of different character.

2 Theory

Consider a thermostated CZE, the injection and detection regions of the capillary (see the schematic in Fig. 1a) are both exposed to stationary air (i.e., unthermostated) while the majority of the capillary in the middle is thermostated by forced air (or liquid) cooling. As a result, the fluid temperatures in the injection and the detection regions are higher than that in the middle (see Fig. 1b). Since fluid electrical conductivity is increased with temperature, the electric field in the middle low-temperature region should be higher than the rest in order to meet the requirement of current continuity (see Fig. 1c). Then, the requirement of mass continuity forces the appearance of axial pressure gradients causing different disturbances to the EOF field in the three regions (see the inset flow profiles in Fig. 1a). In this section, we first derive the time-dependent fluid temperature field and flow field in each region of the capillary during the course of voltage ramping. The resultant transient flow field consisting of the fluid electro-osmosis and the solute electrophoresis is then applied to determine the variance of the solute zone and hence the plate number in CZE.

2.1 Transient temperature field and flow field in each region of the capillary

As the capillary length in each region ($L_i$, $i = 1–3$ for the injection region, forced air-cooling region and detection region, respectively; see Fig. 1) is much larger than the internal diameter, the transition regions in both temperature and flow fields near the capillary ends (i.e., reservoir-based thermal end effects [32–34]) and at the junctions of unthermostated and thermostated regions are ignored [31, 41]. The enhancement or depletion of the concentration of BGE in such transition regions, which was first investigated by Gaš [30], is therefore neglected in this study. Within each region itself, the fluid temperature and velocity remain constant and achieve pseudo-steady state if the characteristic time scales for both thermal and viscous diffusions across the capillary cross-section are assumed much shorter than that of solute migration time [42]. The justification of this assumption is provided in the Addendum. Therefore, the fluid temperature $T_i(r, t)$ in region $i$ is given by

$$\frac{1}{r} \frac{\partial}{\partial r} \left[ r k_i \frac{\partial T_i(r, t)}{\partial r} \right] + \kappa_0 [1 + \alpha (T_i - T_0)] E_i^2(t) = 0$$

(1)

where $r$ is the radial coordinate, $\kappa_0$ is the fluid electrical conductivity at the room temperature $T_0$ with $\alpha$ being the temperature coefficient, $k_i$ is the fluid thermal conductivity that may also vary with temperature, and $E_i(t)$ is the time-dependent electric field strength. The initial and boundary conditions include the initial temperature $T_i(0, z) = T_0$, the symmetry condition $\partial T_i/\partial r(0, z) = 0$, and the convective heat transfer around the capillary outer surface $\partial T_i/\partial r(R_i, z) = -U_i[T(R_i, z) - T_0]/k_i$, where $R_i$ is the capillary internal radius and $U_i = 1/R_i \ln(R_i/R_0)/k_w + \ln(R_i/R_0)/k_p + 1/h R_i$ is the overall heat transfer coefficient between the fluid and the ambient. In the last expression, $h_i$ denotes the surface heat transfer coefficient, and the subscripts $w$ and $p$ signify the properties of the capillary wall and the polyimide coating, respectively. For simplicity, the bracketed time
dependence in the electric, temperature, and flow fields to be derived below are omitted unless otherwise indicated. While the cross-sectional temperature profile is available from Eq. (1) \[14, 18\], we replace the fluid temperature with its cross-sectional average \(T_i\) \[34\] in order that the equations hereafter are more compact without loss of generality. Averaging all terms in Eq. (1) over the capillary cross-section and incorporating the convective heat dissipation thus yield

\[
\bar{T}_i = T_0 + \frac{k_0 R_i E_i^2}{2U_i - \alpha k_0 R_i E_i^2} \tag{2}
\]

Neglecting the streaming current \[43, 44\], the continuity of electric current through the capillary leads to

\[
k_0 [1 + \alpha(T_i - T_0)] E_i = k_0 [1 + \alpha(T_2 - T_0)] E_2 \tag{3}
\]

and \(E_1 = E_2\) if the heat transfer conditions (or, \(U_i\) in Eq. 2) are assumed to be identical in the injection \(i = 1\) and detection \(i = 3\) regions. Substituting Eq. (2) into Eq. (3) gives

\[
\frac{E_1}{1 - \lambda_1 E_1^2} = \frac{E_2}{1 - \lambda_2 E_2^2} \tag{4}
\]

where \(\lambda_i = \alpha k_0 R_i / 2U_i\) has the dimension of the squared reciprocal of electric field. In addition, the summation of the voltage drop in each region of the capillary should satisfy

\[
E_1 + E_2 \delta = E_{avg} (1 + \delta) \tag{5}
\]

where \(E_{avg}\) denotes the average electric field applied across the whole capillary column that varies with time during the initial voltage ramping, and \(\delta = L_2 / (L_1 + L_3)\). To this point, close-form formulas of the electric fields \(E_i\) are available from Eqs. (4), (5) but omitted here for brevity.

In the limit of thin electric double layers, the cross-sectional average fluid velocity \(\bar{u}_i\) in region \(i\) is given by \[9, 29, 39, 45\]

\[
\bar{u}_i = \mu_{eo,i} E_i - M_i P_i \tag{6}
\]

where \(\mu_{eo,i} = -\zeta_i \gamma_i / \eta_i\) is the electroosmotic mobility, \(M_i = R_i^2 / \delta \eta_i\) is the hydrodynamic conductivity, and \(P_i\) is the induced pressure gradient. Other symbols are the fluid permittivity \(\varepsilon = 305.7 \exp(-T/219)\varepsilon_0\), fluid viscosity \(\eta = A \exp(B/T)\), and zeta potential \(\zeta\) of the capillary wall where \(\varepsilon_0\) is the vacuum permittivity, \(A\) and \(B\) are the empirical constants (see Nomenclature for their values) \[6, 7\]. Hence, the mass continuity of the fluid flow and the zero pressure-drop across the entire capillary give rise to

\[
\rho_1 (\mu_{eo,1} E_1 - M_1 P_1) = \rho_2 (\mu_{eo,2} E_2 - M_2 P_2) \tag{7}
\]

\[
P_1 + P_2 \delta = 0 \tag{8}
\]

and \(P_1 = P_2\) since \(E_1 = E_2\). Here, we consider the temperature dependence of the fluid density as \(\rho_1 = \rho_0 / [1 + \gamma_0 (1 + \beta T) \Delta T]\) where \(\rho_0\) is the fluid density at \(T_0\), \(\Delta T = T_2 - T_0\), \(\gamma_0\) is the coefficient of thermal expansion of the fluid at \(T_0\), and \(\beta\) describes the temperature sensitivity of the coefficient of expansion itself. Introducing the new definitions of the electroosmotic mobility \(\mu_{eo,i} = -\zeta_i \gamma_i / \eta_i [1 + \gamma_0 (1 + \beta T) \Delta T]\) and the hydrodynamic conductivity \(M_i' = R_i^2 / 8 \eta [1 + \gamma_0 (1 + \beta T) \Delta T]\), Eqs. (7), (8) yield

\[
P_1 = \mu_{eo,1} E_1 - \mu_{eo,2} E_2 \tag{9}
\]

\[
P_2 = \frac{\mu_{eo,2} E_2 - \mu_{eo,1} E_1}{M_1' \delta + M_2'} \tag{10}
\]

As \(\delta\) is mostly larger than 1 in typical CZE with thermostating, the magnitude of \(P_1\) is higher than that of \(P_2\) so that the fluid velocity profile is more curved in the injection and detection regions (see Fig. 1a).

### 2.2 Separation efficiency

The separation efficiency in CZE is often expressed in terms of the theoretical plate number \(N\)

\[
N = L_{det}^2 / \sigma^2 \tag{11}
\]

where \(L_{det}\) is the distance from the capillary inlet (more specifically, the initial position of the injected sample) to the detector, and \(\sigma^2\) is the variance of the solute when passing through the detector. For 1-D sample transport along the flow direction, the value of \(\sigma^2\) is determined by integrating the effective dispersion coefficient \(D_{eff}\) over time

\[
\sigma^2(t) = \int_0^t 2D_{eff}(t') dt' \tag{12}
\]

where \(D_{eff}\) tends to a constant value at long times \[27, 28\]. This issue of time-dependent dispersion was numerically addressed by Potocke et al. \[46\] a decade ago. Recently, Ajdari et al. \[47\] demonstrated analytically that at time scales shorter than or comparable to that of molecular diffusion across the capillary diameter (typically on the order of seconds in a capillary of 100 \(\mu\m\) internal diameter), the different velocities in the cross-section increase the variance in a “ballistic” manner so that \(D_{eff}\) varies with time. We neglect, here, this transition period of \(D_{eff}\) and directly use the so-called Taylor–Aris dispersion coefficient \(K\) in a cylindrical channel \[27, 28\] which is, however, still a function of time as a result of the temperature and flow transients in the course of voltage ramping

\[
K(t) = D(t) + R_D^2 \frac{U_{pact}(t)}{48D(t)} \tag{13}
\]
where $u_{\text{parab}}$ denotes the average value of the parabolic component of the solute velocity over the cross-section. We acknowledge that the use of $K$ instead of the real $D_{\text{eff}}$ in Eq. (12) underestimates the variance of solute and thus overestimates the separation efficiency of CZE in Eq. (11). This deviation is, however, believed to be insignificant since the time that $D_{\text{eff}}$ takes effect is generally much shorter than the total analysis time in typical CZE.

For charged solutes, $u_{\text{parab}}$ in Eq. (13) is composed of the induced pressure-driven velocity due to the axial temperature gradients [31–34] and the parabolic electrophoretic velocity due to the radial temperature gradients [18–25]. Therefore, $u_{\text{parab},i}$ in region $i$ is given by [29]

$$u_{\text{parab},i} = -MP_i + \frac{1}{2} \omega_i \mu_{\text{ep},i} E_i$$

(14)

where $\mu_{\text{ep},i} = z_i e \delta \pi \eta a$ is the electrophoretic mobility of solute of radius $a$ and valence $z_i$, and $\omega_i = BU_i(T_i - T_0)R_i/2k_i(T_i^2 - T_0^2)$ is a nondimensional parameter characterizing the radial temperature nonuniformity [29].

Note that $k_{ho}$ here, reflects the variation of fluid thermal conductivity in different regions of the capillary. As $u_{\text{parab},i}$ results completely from the inherent Joule heating effects in CZE, we shall call the second term on the right hand side of Eq. (13) as the thermal dispersion. It is apparent that $u_{\text{parab},i}$ and thus the Taylor–Aris dispersion $K$ in Eq. (13) differ in the three regions of the capillary. Therefore, we have to distinguish both the temporal and spatial variations of $K$ in the total variance of solute $\sigma^2$ at the detector in CZE with an initial voltage ramp

$$\sigma^2(t_{\text{det}}) = \frac{1}{2} \int_0^{t_{1}} \left( D_1 + \frac{R_1^2 u_{\text{parab},1}^2}{4BD_1} \right) dt + \int_{t_{1}}^{t_{2}} \left( D_2 + \frac{R_2^2 u_{\text{parab},2}^2}{4BD_2} \right) dt + \int_{t_{2}}^{t_{3}} \left( D_3 + \frac{R_3^2 u_{\text{parab},3}^2}{4BD_3} \right) dt$$

(15)

where $D_i = \kappa_0 T_i/6 \pi \eta a$ is available from the Stokes–Einstein relation [43], and the time intervals $t_i$ are determined from the migration of solute zone whose center moves at the cross-sectional average speed [29]

$$L_1 = \int_0^{t_{1}} dt \left[ \mu_{\text{eo},1} E_{1} - M_1 P_1 + \mu_{\text{ep},1} (1 + \frac{1}{2} \omega_1) E_{1} \right]$$

(16)

$$L_2 = \int_{t_{1}}^{t_{2}} dt \left[ \mu_{\text{eo},2} E_{2} - M_2 P_2 + \mu_{\text{ep},2} (1 + \frac{1}{2} \omega_2) E_{2} \right]$$

(17)

$$L_{\text{det}} = L_1 + L_2 + \int_{t_{2}}^{t_{3}} dt \left[ \mu_{\text{eo},3} E_{3} - M_3 P_3 + \mu_{\text{ep},3} (1 + \frac{1}{2} \omega_3) E_{3} \right]$$

(18)

Specifically, $t_1$, $t_2$, and $t_{\text{det}}$ represent the times at which the solute enters region 2, region 3, and the detector (i.e., $t_{\text{det}}$) in CZE, respectively. It is important to note that the effect of initial voltage ramp on the separation efficiency is implicitly reflected by the temporal variations of $D_i$ and $u_{\text{parab},i}$ in Eq. (15). This issue will be clarified shortly.

### 2.3 Numerical method

As the terms with subscripts $i = 1–3$ in Eqs. (15)-(18) are all associated with the fluid temperature and thus the time in the course of voltage ramping, the trapezoidal rule is employed to solve numerically the integrals in these equations. Specifically, the electric field $E_i$ in each region of the capillary is first obtained from Eqs. (4), (5) from the time-dependent average electric field $E_{\text{avg}}$. Then, the fluid temperature $T_i$ in Eq. (2), fluid velocity $u_i$ in Eq. (6), the parabolic component of the average solute velocity in Eq. (14) and other terms among them are determined with respect to the migration time. Following that, the integrals in Eqs. (16)-(18) are updated every 0.25 s with the trapezoidal rule by dividing it into ten equal time steps, within which the migration time is compared to the voltage ramp-up time $t_{\text{ramp}}$ at every time step in order to call the appropriate parameters (i.e., either transient within the ramping or steady after the ramping) involved in the integration. Once Eqs. (16)-(18) are satisfied within a predefined tolerance, the migration times $t_1$, $t_2$, and $t_{\text{det}}$ are determined in order. Finally, the values of these times are substituted into Eq. (15) to calculate the variance of solute in Eq. (15) and the plate number of CZE in Eq. (11).

### 3 Results and discussion

In this section, we apply the proposed model to evaluate the Joule heating effects on separation efficiency in CZE with an initial voltage ramp. The ionic concentration of the electrolyte solution is assumed to be on the order of 10 mM with an electrical conductivity of $\kappa_0 = 0.15$ S/m at $T_0 = 298$ K [32, 33]. All other parameters necessary for the calculation are given in the Nomenclature unless otherwise indicated below.

Figure 2 shows the theoretical plate numbers (line with circles, refer to the left ordinate) for the solute of $a = 1$ nm and $z_a = +1$ in CZE with different voltage ramp-up times. The average electric field over the entire capillary length after the ramping is $E_{\text{avg}} \approx 60$ kV/m, where the steady state temperatures (i.e., after the initial voltage ramp ends) are $T_1 = T_3 = 323.6$ K and $T_2 = 300.5$ K, respectively. The improvement in separation efficiency is apparent in the presence of an initial voltage ramp. However, the plate number is not monotonically increased with the rise of ramping time. As demonstrated in Fig. 2, the plate number $N$ is almost a positively linear function of the
Figure 2. Effect of voltage ramp-up time on the theoretical plate number (line with circles) and the time (line with triangles) that the solute zone passes the detector, t_{det}. The average electric field is $E_{\text{avg}} = 60 \text{kV/m}$.

during time when less than 40 s. Following a quasiplateau in the range of 60–90 s, N drops linearly at even longer ramping times. The maximum value of N appears at the ramping time of 80 s or so, which is 60% larger than that without an initial voltage ramp. This trend is consistent with previous observations in both aqueous [37–39] and nonaqueous CZE [35, 36].

As discussed above, axial temperature gradients induce passively a disturbance to the EOF field, especially in the injection and detection regions (see the inset velocity profiles in Fig. 1a). Accordingly, the thermal dispersion is more pronounced in these two regions unless the wall zeta potential is suppressed by coating the capillary surface. This issue will be addressed later in this section. Compared to the abrupt application of the full voltage, the initial voltage ramp restricts the Joule heating to take effects gradually when the solute is migrating within the injection region. Therefore, the development of the axially nonuniform temperature distribution and simultaneously the induced pressure driven flows are delayed as well as that of the parabolic electrophoretic velocity. The resultant thermal dispersion is thus significantly decreased in the injection region. At the same time, however, the dispersion due to molecular diffusion is increased (while at a lower rate) because the solute takes more time to move out of the injection region. The variances from these two sources of dispersion are both displayed in Fig. 3 with respect to the voltage ramp-up time. One can see that the variance due to diffusion (line with triangles) is linearly increased with the ramping time. The variance due to thermal dispersion (line with circles) exhibits, however, a much more complicated relation to the voltage ramping time: it first drops linearly when the ramping time is less than 40 s, which agrees with the variation of plate number in Fig. 2; in the range of 50 s through 90 s it keeps dropping while at a continuously decreased rate; following that it drops linearly again at the lowest rate in the range of ramping time under investigation.

Another consequence of the application of an initial voltage ramp is the extended analysis time (i.e., the time that the solute passes through the detector, t_{det}) of CZE as demonstrated in Fig. 2 (line with triangles, refer to the right ordinate). Not surprisingly, t_{det} rises linearly with the voltage ramp-up time. We find that the coefficient of this linear relationship is 0.525 for the case demonstrated. In other words, a 100 s ramp-up time leads to a 52.5 s delay of t_{det}. Actually, both t_x (i.e., the solute enters the forced air-cooling region 2) and t_z (i.e., the solute enters the detection region 3) in Eq. (15) are increased in the presence of an initial voltage ramp.

Figure 3. Effect of voltage ramp-up time on the variance of solute at the detector due to molecular diffusion (line with triangles) and thermal dispersion (line with circles), respectively. The average electric field is $E_{\text{avg}} = 60 \text{kV/m}$.

Figure 4 compares the profiles of mean solute concentration $c$ over the capillary cross-section at different times with (solid lines) and without (dashed lines) an initial 60 s voltage ramp [34]

$$c = c_0 \left[ \text{erf} \left( \frac{w_0/2 - z - z_{\text{cont}}(t)}{\sqrt{2\sigma^2(t)}} \right) + \text{erf} \left( \frac{z + w_0/2 - z_{\text{cont}}(t)}{\sqrt{2\sigma^2(t)}} \right) \right]$$

(19)

where $c_0$ is the initially uniform concentration of the injected solute of width $w_0$, $z$ is the axial coordinate, and $z_{\text{cent}}(t)$ is the time-dependent position of the center of the solute zone that is determined from Eqs. (16)–(18). We assume in Fig. 4 that $c_0 = 1$ and $w_0 = 1 \text{mm}$ (or ten capillary internal diameters). With the abrupt application of the average electric field $E_{\text{avg}} = 60 \text{kV/m}$, the solute quickly moves to $z_{\text{cent}} = 4.18 \text{cm}$ in 12 s and the peak concentration $c_{\text{peak}}$ drops to 0.88 due to the significant diffusion and thermal dispersion in the injection region ($L_1 = 5 \text{cm}$).
Figure 4. Profiles of mean solute concentration over the capillary cross-section at different times with (solid lines) and without (dashed lines) an initial voltage ramp. The ramp-up time is 60 s and the average electric field is $E_{\text{avg}} = 60 \text{ kV/m}$. The injected solute concentration is $c_0 = 1$ of the width $w_0 = 1 \text{ mm}$ (or ten capillary internal diameters). The injection, forced air-cooling and detection regions are noted as I–III right above the abscissa.

Within the same period, however, the solute in CZE with the 60 s voltage ramping reaches barely $z_{\text{cent}} = 0.41 \text{ cm}$ but with $c_{\text{peak}}$ remaining unchanged. When the voltage ramping ends, the center of the solute zone moves to $9.58 \text{ cm}$ and $c_{\text{peak}}$ becomes 0.96. At the same time, the solute for the case of no voltage ramping arrives at $z_{\text{cent}} = 20.18 \text{ cm}$ with $c_{\text{peak}}$ = 0.78. In the latter, it takes the solute only 85 s (see the 83.5 s profile in Fig. 4) to get to the detector ($L_{\text{det}} = 28.5 \text{ cm}$) while $t_{\text{det}} = 117 \text{ s}$ is required for the case with voltage ramping. The eventual peak concentration is, respectively, 0.72 and 0.83 in the two cases under investigation.

Figure 5 compares the plate numbers for the same solute in CZE with (line with circles, refer to the left ordinate) and without (line with triangles, refer to the left ordinate) an initial voltage ramp at different electric fields $E_{\text{avg}}$. The voltage ramp-up time is fixed at 60 s. At low electric fields (e.g., $E_{\text{avg}} < 40 \text{ kV/m}$) Joule heating effects are insignificant. The difference in the steady state fluid temperatures between the injection and forced air-cooling regions (i.e., $T_1 - T_2$, see the dashed line with rectangles corresponding to the right ordinate) is less than 11 K. Therefore, the axial temperature gradients induced thermal dispersion is considerably lower than that due to diffusion. Under such a circumstance, the increase in the latter during the voltage ramp dominates the variation of the total dispersion. This explains why the plate number with voltage ramping is less than that without ramping at $E_{\text{avg}} < 40 \text{ kV/m}$ in Fig. 5. At the electric fields $E_{\text{avg}} \geq 40 \text{ kV/m}$, however, the improvement in the separation efficiency due to the voltage ramp becomes more and more pronounced because the thermal dispersion is comparable to or even larger than the diffusion. Figure 6
Figure 6. Ratio of plate number in CZE with and without an initial 60 s voltage ramp for solutes of different charges. The average electric field is $E_{\text{avg}} = 60 \text{ kV/m}$. 

Figure 7. Effect of the zeta potential $\zeta$ of the capillary wall on the ratio of plate number in CZE with and without an initial 60 s voltage ramp. The average electric field is $E_{\text{avg}} = 60 \text{ kV/m}$. 

Figure 8. Effect of voltage ramp-up time on the plate numbers in CZE predicted with the present model (solid line with hollow circles, refer to the left ordinate) and that considering only the radial temperature gradients (solid line with full circles, refer to the left ordinate). The dashed lines with hollow and full triangles (refer to the right ordinate) illustrate the migration time $t_{\text{det}}$ of the solute predicted from the aforementioned two models. The working parameters different from those given in the Nomenclature are: $R_l = 37.5 \mu\text{m}$, $R_w = 167.5 \mu\text{m}$, $R_p = 187.5 \mu\text{m}$, $k_l = 0.174 \text{ W} \cdot \text{m}^{-1} \cdot \text{K}^{-1}$, $k_w = 1.5 \text{ W} \cdot \text{m}^{-1} \cdot \text{K}^{-1}$, $k_p = 0.15 \text{ W} \cdot \text{m}^{-1} \cdot \text{K}^{-1}$, at $T_0 = 296 \text{ K}$ the electroosmotic mobility $\mu_{eo} = -3.7 \times 10^{-10} \text{ m}^2 \cdot \text{V}^{-1} \cdot \text{s}^{-1}$, electrophoretic mobility $\mu_{ep} = -1.23 \times 10^{-8} \text{ m}^2 \cdot \text{V}^{-1} \cdot \text{s}^{-1}$, fluid viscosity $\eta = 1.08 \times 10^{-2} \text{ kg} \cdot \text{m}^{-1} \cdot \text{s}^{-1}$, temperature coefficient of viscosity 0.023/K, electrical conductivity $k_0 = 0.05 \text{ S/m}$ and its temperature coefficient $\alpha = 0.0207/K$, coefficient of thermal expansion $\gamma_0 = 1.09 \times 10^{-3}/\text{K}$ and its temperature coefficient $\beta = 0.05/\text{K}$, and molecular diffusivity $D = 5.34 \times 10^{-16} \text{ m}^2/\text{s}$ [24, 25, 29, 35].

The ratio of plate number in CZE with and without an initial 60 s voltage ramp for solutes of different charges. The average electric field is $E_{\text{avg}} = 60 \text{ kV/m}$. 

presents the ratios of the plate numbers for solutes of $z_v = +1$, 0, and $-1$, respectively, with the voltage ramp to those without it, where they all exhibit a similar trend. The difference in the magnitudes of these ratios is mainly attributed to the different migration speed of solutes.

Another determining factor in the thermal dispersion is the zeta potential $\zeta$ of the capillary wall that hides in the definition of electroosmotic mobility (see Eqs. 9, 10). The influence of $\zeta$ on the ratio of plate number in CZE with and without an initial 60 s voltage ramp is demonstrated in Fig. 7. The applied electric field is fixed as $E_{\text{avg}} = 60 \text{ kV/m}$. Analogous to the effect of electric field, the application of voltage ramp actually reduces the plate number at $|\zeta| < 20 \text{ mV}$ because of the trivial magnitude of the induced pressure-driven flows. At higher values of zeta potential, the thermal dispersion gets dominant so that the plate number is amplified if an initial voltage ramp is applied to delay the development of axially nonuniform pressure-driven flows. Moreover, the higher the zeta potential is, the larger the ratio of the plate number achieves. For example, the separation efficiency at $\zeta = -90 \text{ mV}$ can be enhanced by nearly 120% in the presence of an initial 60 s voltage ramp. In practical CZE, however, the enhanced separation efficiency has been observed in both noncoated ($\zeta$ is estimated to be about $-50 \text{ mV}$) [36–39] and coated capillaries ($\zeta$ is suppressed to be close to 0 mV) [35] when a voltage ramp is applied. The latter case is examined below in more detail.

Figure 8 illustrates the plate numbers (line with hollow circles, refer to the left ordinate) in nonaqueous CZE with different voltage ramp-up times that are predicted from the proposed model at the conditions equivalent to Palo nen et al.’s experiment [35]. All parameters in the calcu-
oration are noted in the figure caption where the coefficient of thermal expansion of the electrolyte solution (15 mM NaAc + 15 mM Hac in EtOH) is $\gamma_0 = 1.09 \times 10^{-3}/K$ at $T_0$ and its temperature coefficient is $\beta = 0.05/K$. As the wall zeta potential calculated from the available electroosmotic mobility is only $-0.5$ mV [35], the thermal dispersion is reduced to that due solely to the parabolic electrophoretic velocity of the solute, especially in the forced air-cooling region where the cross-sectional temperature nonuniformity is the highest. The initial voltage ramp thus has a negligible effect on the thermal dispersion while that from diffusion is increased due to the extended migration time. The overall influence of the voltage ramping is to reduce the separation efficiency, which is, however, contrary to the observation in Palonen et al.’s experiment. It turns out that there might exist some other Joule heating originated phenomena responsible for the virtually enhanced separation efficiency, for example, the significant decrease and increase in the concentration of BGE at the junctions of injection/forced-air cooling and forced-air cooling/detection regions, respectively, as demonstrated in Gaš’s numerical analysis [30].

Figure 8 presents also the theoretical plate numbers (line with full circles, refer to the left ordinate) predicted from the model considering only the radial temperature gradients, i.e., assuming the forced air-cooling condition along the whole capillary. While these plate numbers follow the same trend as those predicted from the present model, the former are always 30% higher indicating an overestimation of the separation efficiency. As discussed above, there is hardly an EOF and hence the induced pressure-driven flow in the coated capillary. The thermal dispersion should therefore be approximately the same in both models. In other words, the deviation in the predicted plate numbers is mainly attributed to the different contribution of molecular diffusion in the two models. In the model with a uniform heat transfer condition, both the electric field ($E_{\text{avg}}$, dashed line in Fig. 1c) and the fluid temperature ($T_{\text{unfm}}$, dashed line in Fig. 1b) remain unvaried along the capillary column. In the present model with different heat transfer conditions, however, the electric field $E_2$ in the forced air-cooling region is larger than $E_{\text{avg}}$ so that the local fluid temperature $T_2$ is higher than $T_{\text{unfm}}$. While the electric fields $E_1$ and $E_3$ in the injection and detection regions are smaller than $E_{\text{avg}}$ due to the current continuity, the local fluid temperatures $T_1$ and $T_3$ are still both higher than $T_{\text{unfm}}$, because of the much lower heat dissipation of the free air-cooling relative to the forced air-cooling. Therefore, the molecular diffusion predicted in the present model is more significant than that in the model with a uniform heat transfer condition. This under-prediction is also evidenced by the longer migration time $t_{\text{mig}}$ in the latter model (dashed line with full triangles, refer to the right ordinate).

4 Concluding remarks

We have developed an analytical model to study the Joule heating effects on the separation efficiency in CZE with an initial voltage ramp. This model extends the one previously developed for the band broadening in CZE with axial temperature gradients in the inclusion of the temporal variations of temperature and flow fields and the consideration of the temperature dependence of fluid density. With the proposed model we demonstrate that the initial voltage ramping restricts the Joule heating effects when the solute is moving within the injection region. As a result of this delayed development of axially nonuniform temperature and flow fields, the thermal dispersion is significantly reduced resulting in enhanced separation efficiency although at the same time the molecular diffusion is increased. This enhancement is apparent in noncoated capillaries, which is consistent with the reported measurements in both aqueous and nonaqueous CZE [35–38]. In coated capillaries where the EOF is suppressed, however, the theoretical plate number predicted from the present model is reduced in the presence of an initial voltage ramp. This prediction is opposite to the observations in nonaqueous CZE [34]. The real reason underlying the improved separation efficiency in CZE with coated capillaries needs further investigation.

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5 References

6 Addendum

6.1 Justification of Eq. (1)

This addendum explains how we obtain Eq. (1) in the main text through the scaling analysis. The full energy equation for the fluid temperature in the presence of a time-dependent Joule heating source is given by

$$\rho C_p \left( \frac{\partial T}{\partial t} + \mathbf{u} \cdot \nabla T \right) = \nabla \cdot \left( k_1 \nabla T \right) + \kappa_0 \left[ 1 + \alpha(T - T_0) \right] |E|^2(t) \quad (A-1)$$

where $\rho$ and $C_p$ are, respectively, the density and the specific heat capacity of the fluid, and $\mathbf{u}$ signifies the velocity vector. With dimensionless variables and differential operators defined as

$$\tilde{\mathbf{u}} = \frac{\mathbf{u}}{V}, \quad \tilde{T} = \frac{T - T_0}{\Theta}, \quad \tilde{t} = \frac{t}{\tau_m}, \quad \tilde{T} = \frac{\nabla}{\Theta}, \quad \tilde{T}^2 = \frac{R_l^2 \nabla^2}{\Theta^2} \quad (A-2)$$

Eq. (A-1) becomes

$$\frac{\tau_c}{\tau_m} \frac{\partial \tilde{T}}{\partial t} + \text{Pe} (\tilde{\mathbf{u}} \cdot \nabla \tilde{T}) = \nabla \cdot \left( \frac{k_1}{\kappa_0} \nabla \tilde{T} \right) + \frac{\kappa_0 R_l^2 E^2(t)}{k_0 \Theta} \left( 1 + \alpha \tilde{T} \right) \quad (A-3)$$

where $\tau_c = R_l^2 \rho C_p / k_0$ is the characteristic time of thermal diffusion over the capillary cross-section with $k_0$ being the reference thermal conductivity (e.g., the fluid $k_1$ at room temperature), $\tau_m = \frac{L_{def}}{1 + \rho \kappa k_0 E_{avg}}$ the solute migration time in the absence of Joule heating and voltage ramping, $\text{Pe} = \frac{VR_l C_p}{k_0}$ the Peclet number based on the thermal diffusion, and $V$ and $\Theta$ are the reference velocity and temperature. In typical CZE with either aqueous [36, 37] or nonaqueous [35] BGE solutions, $\tau_c$ is on the order of milliseconds that is much shorter than the solute migration time $\tau_m$ (several to tens of seconds). Therefore, we can safely ignore the transient term in Eq. (A-3). However, we acknowledge that this neglect might cause some error in the time period comparable to $\tau_c$ at the very beginning of the voltage ramp, i.e., when

$$\frac{k_0 \frac{R_l^2 E^2(t)}{k_0 \Theta}}{E^2}\frac{\tau_m}{\tau_c} = \frac{\tau_c}{\tau_m} \frac{\partial \tilde{T}}{\partial t} + \text{Pe} (\tilde{\mathbf{u}} \cdot \nabla \tilde{T}) = \nabla \cdot \left( \frac{k_1}{\kappa_0} \nabla \tilde{T} \right) + \frac{\kappa_0 R_l^2 E^2(t)}{k_0 \Theta} \left( 1 + \alpha \tilde{T} \right) \quad (A-4)$$

where $t < \tau_m$ and $\Theta = k_0^2 E^2 \tau_c^2 / k_0$ has been defined with $E_0$ being the steady-state electric field after the voltage ramping. In addition, since a fully developed temperature

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field is assumed in each region of the capillary (i.e., $T = T(r, t)$) as well as the flow fluid (i.e., $u = u(r, t)$), the convective term in Eq. (A-3) vanishes despite $Pe = O(1)$. As such, Eq. (A-3) is reduced to

$$\vec{v} \cdot \left( k \nabla T \right) + \frac{\kappa_0 R^2 E^2(t)}{\Theta} \left( 1 + \Theta \right) = 0$$

(A-5)

which is the exactly the nondimensional form of Eq. (1) in the main text.

6.2 Nomenclature

6.2.1 General

- $a$: Radius of solute molecules, 1 nm
- $A, B$: Defined constants in fluid viscosity, $A = 2.761 \times 10^{-6}$ kg m$^{-1}$ s$^{-1}$ and $B = 1713$ K
- $D$: Diffusion coefficient
- $D_{eff}$: Effective dispersion coefficient
- $e$: Charge of a proton, $1.602 \times 10^{-19}$ C
- $E$: Applied electric field
- $E_{avg}$: Average electric field over the whole capillary column
- $h$: Surface heat transfer coefficient, 130 and $4000$ W m$^{-2}$ K$^{-1}$ for the still-air cooling and the forced-air cooling
- $k$: Thermal conductivity, 0.61, 1.38, and $0.15$ W m$^{-1}$ K$^{-1}$ for fluid (water), wall, and coating
- $k_B$: Boltzmann’s constant, $1.381 \times 10^{-23}$ J/K
- $L$: Capillary length, $L_1 = 5$ cm for the injection region, $L_2 = 22.5$ cm for the forced air-cooling region, and $L_3 = 2.5$ cm for the detection region
- $L_{det}$: Distance from the capillary inlet to the detector, 28.5 cm
- $M, M'$: Hydrodynamic conductivity
- $N$: Plate number
- $P$: Induced pressure gradient
- $r$: Radial coordinate
- $R$: Radius, 50, 160, and 180 µm for the internal wall, outer wall, and coating
- $T$: Temperature, 298 K ($T_0$ for ambient)
- $T_{unfm}$: Uniform fluid temperature for the case of uniform heat transfer condition
- $u$: Fluid velocity
- $U$: Overall heat transfer coefficient between the fluid and the ambient
- $V$: Reference fluid velocity
- $z_v$: Valence of ions

6.2.2 Greek symbols

- $\alpha$: Temperature coefficient of electrical conductivity, 0.02/K
- $\beta$: Temperature coefficient of the coefficient of thermal expansion, 0.04/K
- $\delta$: Defined nondimensional parameter in Eq. (5)
- $\varepsilon$: Permittivity, $305.7 \exp(-T/219) \times 8.854 \times 10^{-12}$ C V$^{-1}$ m$^{-1}$
- $\eta$: Dynamic viscosity given by $A \exp(B/T)$
- $\gamma_0$: The coefficient of thermal expansion of fluid at $T_0$, $2 \times 10^{-4}$/K
- $\kappa_0$: Electrical conductivity of fluid at $T_0$, 0.15 S/m
- $\lambda$: Defined parameter in Eq. (4)
- $\mu, \mu'$: Electromigration mobility
- $\omega$: Defined coefficient describing the radial temperature gradients
- $\Theta$: Reference fluid temperature
- $\sigma^2$: Variance of the solute concentration
- $\zeta$: Zeta potential, $-50$ mV

6.2.3 Subscripts

- $e_0$: Electroosmotic
- $e_p$: Electrophoretic
- $i$: Region in a capillary, $i = 1$–3
- $l$: Fluid
- $p$: Polyimide coating
- $pd$: Pressure-driven
- $w$: Wall

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