

Potential for Use of Liquid Crystals as Dynamically Tunable Electrophoretic Media

Durgesh S. Vaidya, S. L. Diamond, J. M. Nitsche, and David A. Kofke

Dept. of Chemical Engineering, State University of New York at Buffalo, Buffalo, NY 14260

When two solutes have dissimilar structures, they move through an electrophoretic medium with different mobilities and, therefore, different speeds. This phenomenon is used to separate the charged components of a mixture. In a conventional electrophoretic separation, the velocities and diffusion coefficients of all solutes are constant because the transport properties of the medium are static, remaining unchanged over the length of the column and over the duration of separation. Here, we examine the question of how an electrophoretic separation might benefit from the use of a *dynamic* separation medium—one with the transport properties that can be tuned to values specified by the user.

Liquid crystal (LC) polymers appear to be good candidates for tunable media, as their microstructure can be externally controlled. In particular, on application of a transverse external field, they undergo a transition from a configuration with randomly oriented side chains ("random," r) to a configuration in which all side chains are aligned perpendicular to the axis of the column ("aligned," $\perp$). There are then two principal values for the diffusion coefficient and migration velocity of a solute, viz., D_r , v_r , and $D_\perp$, $v_\perp$. D_r is the diffusion coefficient in the random mode (m^2/s), and $D_\perp$ is the diffusion coefficient in the aligned mode (m^2/s). If the external field itself is made position-dependent, the diffusion coefficient of the solute can be modulated in space. Moreover, azobenzene-based LC polymers with response times as low as 200 μs have recently been synthesized (Ikeda and Tsutsumi, 1995), which suggests that it should also be feasible to modulate the solute velocities and diffusivities in time as well.

This note summarizes a general theoretical study of electrophoretic separations in dynamic media. The emphasis is not a demonstration of the separation of specific solutes such as amino acid systems or DNA fragments, but rather a presentation of broad guidelines for solute separations in tunable media.

Moving Front

The one-dimensional electrophoretic motion of solutes j in dilute solution is through a column of length L (m) governed by transport equations of the general convective-diffusive form

$$\frac{\partial c_j}{\partial t} = \frac{\partial}{\partial x} \left[D_j(x, t) \frac{\partial c_j}{\partial x} \right] - \frac{\partial}{\partial x} [v_j(x, t) c_j], \quad (1)$$

subject to initial conditions that depend on the details of sample injection. Both the solute diffusivities D_j and the electrophoretic velocities v_j (m/s) are functions of axial position x (m) and time t (s) (c is the concentration of solute, Kg/m^3). Their spatial and temporal variations are influenced by the external modulation of the microstructure of the electrophoretic medium. It is through these variations that we seek to enhance separations.

A detailed optimization analysis of the transport equations suggests that tuning of the medium be performed in a way that creates "fronts"—regions where the microstructure undergoes an abrupt change from one principal configuration to the other (Vaidya, 1997a); the result is a piecewise constant distribution of transport properties. Intermediate values (if attainable) of solute diffusivities and velocities are not desirable for optimal operation.

The precise locations of the fronts in the optimal separation protocol depend on details of the evolving solute concentration profiles, which may be impossible to obtain in practice. However, it is likely that the number of such fronts will remain constant over significant time periods, and that they will move across the column as the separation proceeds. It is also likely that the speeds at which they move, although varying in time, will remain close to (and probably between) the convective velocities of the solutes in the random and aligned configurations of the medium. Thus, the separation protocol that we choose to examine here consists of a single front that moves with a prescribed constant velocity v_f .

In practice, the front will not be a perfectly singular surface; rather, the transition from the random to the aligned configuration of the medium will occur over a small but finite width $2\epsilon_f L$ ($\epsilon_f \ll 1$). The transition zone thus extends from $\xi = -\epsilon_f$ to $\xi = \epsilon_f$, where ξ is a dimensionless coordinate measured from the midpoint $L_f(t)$ (m) of the transition zone of the front, viz., $\xi = [x - L_f(t)]/L$. The seemingly small distinction between a discontinuous and a thin, smooth front has a profound impact on the scaling of the solute concentration profiles (Vaidya et al., 1997a).

It has been shown (Vaidya et al., 1997a) that when the front moves with a constant velocity v_f that is intermediate between the solute velocity v_r in the random phase and $v_\perp$ in the aligned phase, there is progressive accumulation, or focusing, of the solute at the front. The focusing does not continue indefinitely, but instead reaches a steady state where the incoming convective flux relative to the front is balanced by the outgoing diffusive flux arising from the high concentration gradients. Specifically, the concentration distribution forms a Gaussian peak centered at the point—different for each solute—where the velocity of solute j relative to the front vanishes, and with a standard deviation given by (Vaidya et al., 1997a)

$$\sigma_{j,s} = \sqrt{\frac{\phi_{j,0}}{Pe b_j}} \quad (2)$$

$\sigma_{j,s}$ is the standard deviation of steady-state Gaussian distribution of solute j made dimensionless with respect to L . The quantities $\phi_{j,0}$ and b_j represent the dimensionless diffusivity and magnitude of the dimensionless velocity gradient at the point of vanishing relative velocity for each solute, and Pe is the Peclet number (dimensionless) associated with the flow; $\phi_{j,0}$ is $\mathcal{O}(1)$, b_j is expected to be $\mathcal{O}(1/\epsilon_f)$, and Pe is typically $\mathcal{O}(10^5)$. Interestingly, the steady-state profile is independent of the initial distribution; it depends only on the transport properties of the medium and the solute.

The primary conclusion is that, with a judicious choice of speed for the moving front, different solutes will (1) get their band-widths sharpened, and (2) come to rest at different locations depending on their transport properties. This feature of dynamic media can be exploited to formulate enhanced separation protocols.

Separation Protocols

System characterization

We begin by defining appropriate nondimensional groups as measures of differences between two solutes 1 and 2. The solute that is faster in the random mode is designated as solute 1, and the properties of both solutes are normalized using the properties of solute 1. Thus, we introduce

$$\alpha = \frac{D_{\perp,1}}{D_{r,1}}, \quad \beta_j = \frac{D_{r,j}}{D_{r,1}}, \quad \gamma_j = \frac{D_{\perp,j}/D_{r,j}}{D_{\perp,1}/D_{r,1}} \quad (3)$$

The quantity α (dimensionless) is a measure of the reference anisotropy offered by the medium, β_2 is the relative diffusivity of the solutes, and γ_2 is the relative anisotropy. In what follows, we have assumed that the electrophoretic velocity of each solute is proportional to its diffusivity as is true for small, dilute, and noninteracting species. We do not expect the qualitative features of the results to change dramatically for cases where this assumption does not hold. All solute concentration profiles have been calculated by using the numerical scheme QUICKEST (Leonard, 1979), which is especially suited to high- Pe problems.

Pre-processing protocol

The existence of the steady state described above implies that the locations and widths of the focused solute peaks will

have limiting values for two-solute systems. Therefore, there exists a limiting steady-state value for the resolution that can be achieved. This effect differs from the case of nondynamic media, where the longer the column (or elution time), the higher the resolution achieved at the exit. The limiting resolution can be shown to be (Vaidya, 1997b)

$$Rs_s = \frac{1}{2} \sqrt{\frac{Pe}{\beta_f}} \frac{\left[\frac{a_1}{b_1} - \frac{a_2}{b_2} \right]}{\left[\sqrt{\frac{1}{b_1}} + \sqrt{\frac{1}{b_2}} \right]} \quad (4)$$

where

$$a_j = \left\{ \frac{\beta_j}{(1-\alpha)} [\beta_f(1-\alpha\gamma_j) - \alpha(1-\gamma_j)] \right\} - \beta_f \quad (5)$$

Here β_f is the dimensionless velocity of the front ($v_f/v_{r,1}$). High resolution in the steady state requires the use of a wide front which, however, extends the time needed to reach the steady state. A hybrid approach is to focus solutes until they sharpen to about half the limiting value of resolution, and then to remove the front, allowing the sharpened peaks to evolve under constant conditions. This procedure constitutes what we term the preprocessing protocol, the results of which are illustrated in Figure 1 for the case where $Pe = 10^5$, $\alpha = 0.5$, $\beta_2 = 0.9$, $\gamma_2 = 0.89$, and $\epsilon_f = 0.01$. The front is initially placed at the mean position of the initial distribution (viz., at $x/L = 0.05$), and is maintained for a time interval $\tau = 0.1$. Figure 1a shows the resulting focusing of the solutes into thin bands. Subsequently, the front is removed and the solutes are allowed to migrate through the column operating entirely in the random mode. Figure 1b compares the resolution in this dynamic mode with that obtained for the conventional operation in a uniformly random mode throughout the entire duration of solute migration. It is seen that the dynamic operation achieves a resolution of 2 (a value characterizing full separation) in about one-third the time required by conventional (nondynamic) operation.

Sieving protocol

In the previous section, solute 1 was faster than solute 2 in the random and aligned modes. On the other hand, if solute 1 is faster than solute 2 in the random-microstructure mode, but slower than solute 2 in the aligned-microstructure mode, then a cyclic sieving protocol can be imposed whereby the solutes are separated in a column of substantially smaller physical length than that required by conventional unidirectional flow. In terms of the dimensionless variables defined earlier, the requirement that solute 2 be faster than solute 1 in the aligned medium translates to the inequality

$$\alpha < \alpha\beta_2\gamma_2 < \beta_2 \quad (6)$$

In the forward cycle of the sieving protocol, a random configuration is imposed for an interval $\Delta\tau_f$. (τ is dimensionless time.) Solute 1 being faster than solute 2 in this mode, moves ahead, leading to partial separation. In the backward cycle, the aligned mode is imposed and the polarity of the axial field is reversed so that the solutes migrate in the opposite

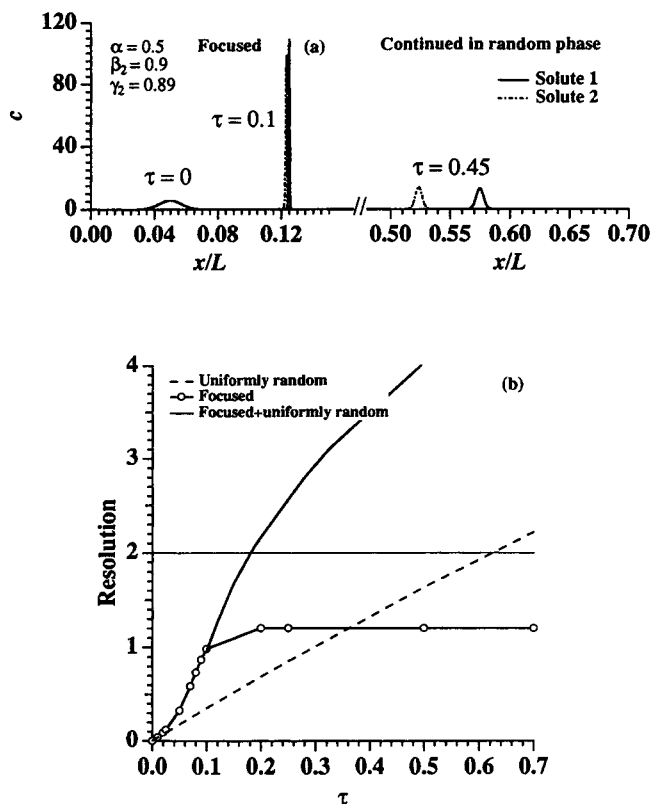


Figure 1. Results of pre-processing protocol for $Pe = 10^5$, $\alpha = 0.5$, $\beta_2 = 0.9$, $\gamma_2 = 0.89$, and $\epsilon_f = 0.01$.

(a) Concentration profiles of solutes 1 and 2. The front was placed at the mean position of the initial distribution ($x/L = 0.05$), and maintained for $\tau = 0.1$. Subsequently, the front was removed and the solutes were allowed to migrate with the column operating in random-microstructure mode. (b) Comparison of resolution using the preprocessing protocol with uniformly random mode. The circles denote the evolution of the resolution in the presence of a moving front. If the front is removed at $\tau = 0.1$, it leads to better separation.

direction for a time interval $\Delta\tau_b$. In this mode, solute 2 is faster than solute 1, and owing to the reversal of motion moves further away from solute 1, incrementing the degree of separation. The duration of the backward cycle is increased such that solute 1 recovers all the distance traversed in the forward cycle that is, $\Delta\tau_b = \Delta\tau_f/\alpha$. On repeating this cycle many times, the solutes are separated within a considerably smaller physical length (Figure 2).

In the sieving mode, it is worth noting that there may be some residual migration of solutes along the length of the column. This phenomenon is due to infinitesimal errors that build up over the large number of cycles, and are discussed in greater detail in Vaidya (1997b).

The sieving protocol resembles the Flow Counterbalanced Capillary Electrophoresis proposed by Culbertson and Jorgenson (1994), but, unlike their protocol, the backward cycle also contributes to separation, and there is no band-broadening due to parabolic velocity profiles owing to the pressure gradient (as opposed to reversed electric field) used in the backward cycle.

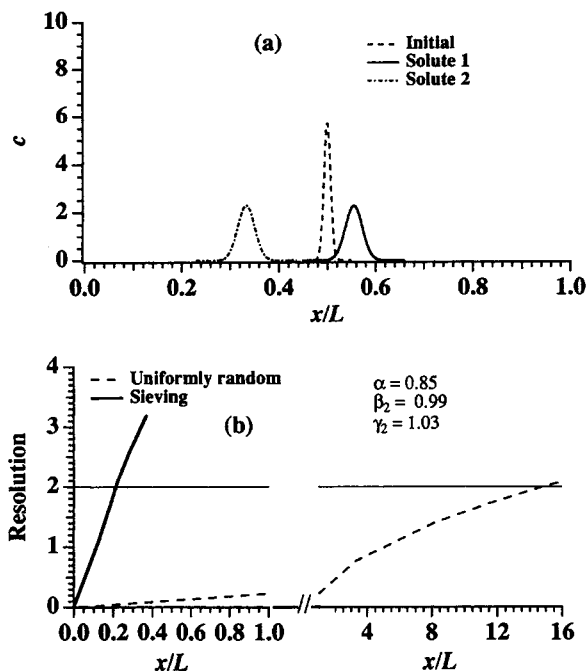


Figure 2. Results of sieving mode protocol for $\alpha = 0.85$, $\beta_2 = 0.99$, and $\gamma_2 = 1.03$.

The forward cycle time $\Delta\tau_f$ is 0.01. (a) Concentration profiles at the end of 750 cycles; (b) comparison of the physical length required for achieving resolution.

Summary

The preceding theoretical analysis suggests that the ability to dynamically tune the properties of an electrophoretic medium offers clear advantages in being able to focus and control the distribution of solutes.

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