Analysis of Sample Transport in Capillary Electrophoresis Microchip using Full-Scale Numerical Analysis

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ABSTRACT

An implicit finite-volume numerical scheme has been developed to solve the three-dimensional transport equations along with fully-coupled ionization equilibria in acid/base systems. The scheme solves conservation equations for mass and momentum while satisfying the electroneutrality condition in a sequential fashion until convergence is achieved. The electric field is computed based on current conservation formulation. We employ this computational analysis/design tool to study the time evolution of a sample containing several analytes in a capillary electrophoresis microchip. The phenomena of sample stacking and tailing due to conductivity differences and the effect of degree of ionization are analyzed and compared with experimental data of Ermakov and Righetti [1].

Keywords: Electrophoresis, ionization, microfluidics, CFD-ACE+, stacking

1 INTRODUCTION

Capillary Electrophoretic (CE) devices have been successfully fabricated on microchips for biological/chemical sensing applications. Miniaturization of these devices has advantages of compact size, integrated functions of separation and detection, low cost due to batch production and potential parallel analysis. However, design, fabrication and commercialization of this technology requires understanding of fundamental physical mechanisms associated with transport of various species and fluid flow in the presence of electric fields. Numerical analysis can provide insight into the interactions between various physical processes and improve the design of such microdevices.

Migration of charged species in a liquid solution under the influence of electric field is known as electrophoresis. Modeling of this phenomenon has been pursued by many researchers over the years and includes the study of multicomponent mixture systems and proteins [2-4]. Mosher et. al. [5] have summarized various efforts in this field. The implementation of this work has the potential of providing MEMS designers an analysis tool that will help them to understand physico-chemical processes in three-dimensional electrophoretic systems. This modeling effort is an extension of our work presented at MSM2000 [6] and that of Giridharan and Krishnan [7]. The computer simulations accurately describe convection, electromigration, diffusion, acid/base ionization equilibrium and electric field. Simulation results are compared with the experimental and simulation data of Ermakov and Righetti [1].

2 MATHEMATICAL MODELING

2.1 Governing Equations

We assume that an aqueous solution contains monovalent acids (HA_n) and bases (B_m) for which association-dissociation reactions can be represented by

$$HA_n \Leftrightarrow A_n^- + H^+ \qquad n = 1,2,3,\ldots N \tag{1}$$

$$H^+B_m \Leftrightarrow B_m + H^+ \qquad m = 1,2,3\ldots M \tag{2}$$

$$H_2O \Leftrightarrow H^+ + OH^- \tag{3}$$

where A_n^- and H^+B_m are the conjugate bases. These reactions are described by the association/dissociation equilibrium constants and degrees of dissociation. Given the concentration of various acids and bases, and their equilibrium constants, at any given time, the system should satisfy the electroneutrality condition.

The generalized transport equation for ionic species is expressed as:

$$\frac{\partial C}{\partial t} + \nabla \bullet (z\mu EC + VC - D\nabla C) = 0 \tag{4}$$

where z is the valence of the ion, μ is the mobility, $\mathbf{V}$ is the velocity vector, $\boldsymbol{E}$ is the electric field vector, C is the molar concentration of the analyte, and D is the diffusion coefficient. To compute the electric field $\boldsymbol{E}$, we need to solve the continuity equation for current

$$\nabla \cdot j = 0 \tag{5}$$

where j is the flux that can be described by generalized Ohm's law.

2.2 Initial and Boundary Conditions

All the walls are assumed insulated and a no-flux boundary condition is applied. Voltages are specified at the inlet and outlet of the channel. The pH value and acid/base concentrations of the buffer solution are defined as initial conditions. Location and concentration of the sample are also initially defined.

3 PROBLEM DESCRIPTION

The coupled nonlinear partial differential equations (1) to (5) were solved using CFD Research Corporation's advanced multi-physics commercial software package, CFD-ACE+. The implicit finite-volume technique discussed in [8] is used to solve the governing equations. The geometry considered in this case was a capillary tube similar to one used in the experimental and computational studies of Ermakov and Righetti [1]. An isothermal condition was assumed since the experiments were performed in the range of 26-28°C. A weak monovalent picric acid was chosen as sample species. Buffer solution consisted of 20 mM acetic acid titrated with NaOH to a pH of 5.0. The concentration of the sample species was varied from 0.02-10 mM. Table 1 provides a summary of the various input data for the computer simulations.

Analyte	pK	μ (10^{-8} m^2/Vs)
Acetic Acid	4.75	4.24
NaOH	14	5.19
Picric Acid	0.38	3.15

Table 1: Input Data for Computer Simulation [1]

An electric potential of 0 V is applied at the inlet while 10,000 V is applied at the outlet. Initially, the capillary tube is filled with the acetate buffer and a sample volume of 20.6 nl was introduced into the system. The simulation was performed in a transient manner over a long period of time.

4 RESULTS AND DISCUSSIONS

In Figure 1, the contour levels of the sample at two time intervals, (t = 1 and 6 minutes), for three different initial concentrations, (C_o = 0.02, 1.0 and 1.0 mM) of the sample are shown. At low concentration, there was not much dispersion and the sample stayed narrow and focussed. As the initial concentration increased, we observed

- The sample dispersed more as it traveled downstream towards the anode
- The difference in the electrical conductivity between the sample and the buffer created a nonuniform electric field that led to sample stacking. The sample attained a triangular shape at larger concentration as shown in Figure 1 (f) while maintaining a Gaussian profile at lower concentration as shown in Figure 3.

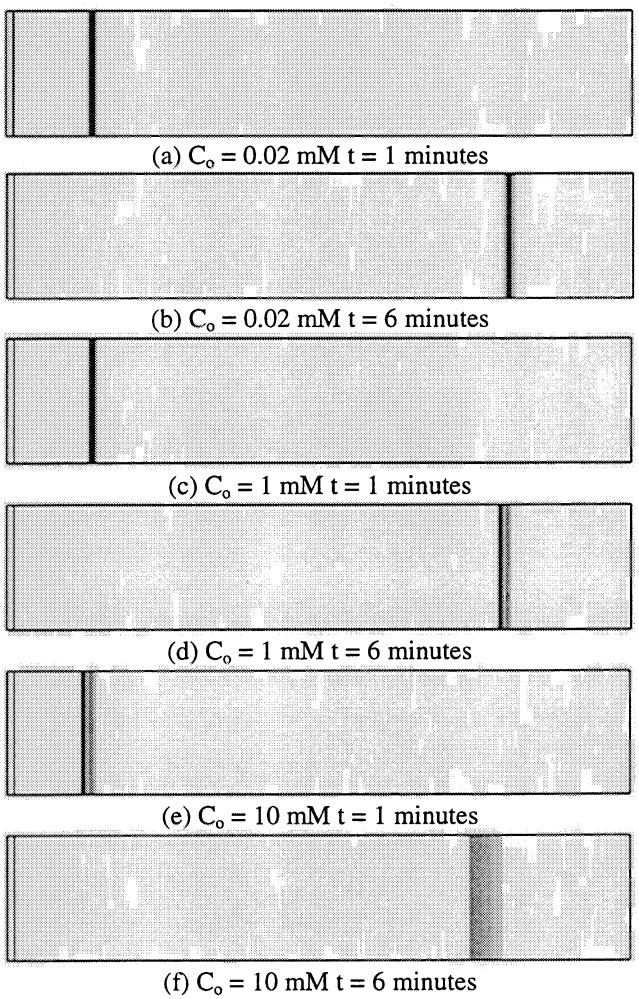

Figure 1: Contour Levels of Sample (Picric Acid) Concentration is Shown at 1 and 6 minutes into the Simulation for Initial Concentrations of 0.02, 1.0 and 10 mM. CFD-ACE+ Simulations Predicted that as the Concentration of the Sample Increased, the Stacking Effect due to Variation in Electrical Conductivity Between the Sample and Buffer Became Significant.

In Figure 2, the contour levels of pH value of the system at two different time intervals are shown for various sample initial concentrations (C_o = 0.02, 1.0 and 10 mM). The darker region represents a lower pH (more acidic) value. As expected, when C_o increased, the system became more acidic in the regions where the sample was present. This change in pH introduced significant variations in the electrical conductivity that further enhanced the stacking phenomenon.

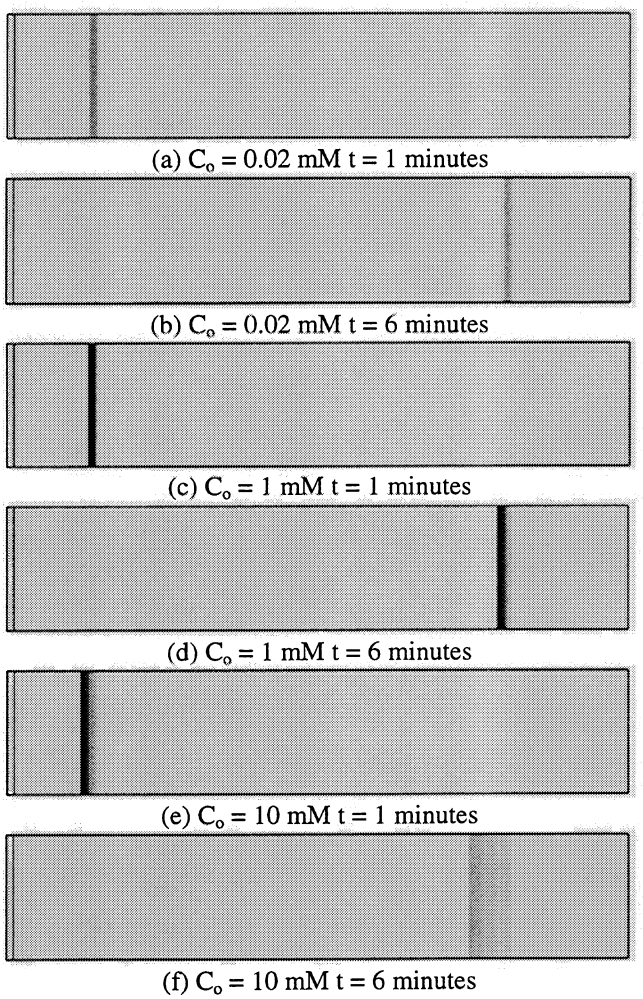

Figure 2: Contour Levels of pH is Shown At 1 and 6 Minutes into Simulations for Initial Concentrations of 0.02, 1.0 and 10.0 mM. CFD-ACE+ Simulations Predicted that as the Concentration of the Sample Increased, the System Became More Acidic Where the Sample was Present. The Darker Regions Correspond to a pH Value Less than the Initial Value.

An electropherogram, taken at the location 30 cm from the inlet as predicted by the computer simulation was compared with the experimental data [1] in Figure 3. From the figure, we observed that there was a good qualitative and quantitative agreement in shape of the concentration profile, the migration time and the maximum concentration of the sample. With a sample concentration of 0.02 mM, which is very low compared to that of the buffer, the sample tended to maintain a Gaussian profile with the maximum concentration almost the same as that of the initial concentration. This suggests that the system is subjected to diffusional dispersion only. At higher concentration, (C = 1.0 mM), the conductivity difference between sample zone and background electrolyte caused sample stacking and the sample shape became triangular as observed in experiments [1].

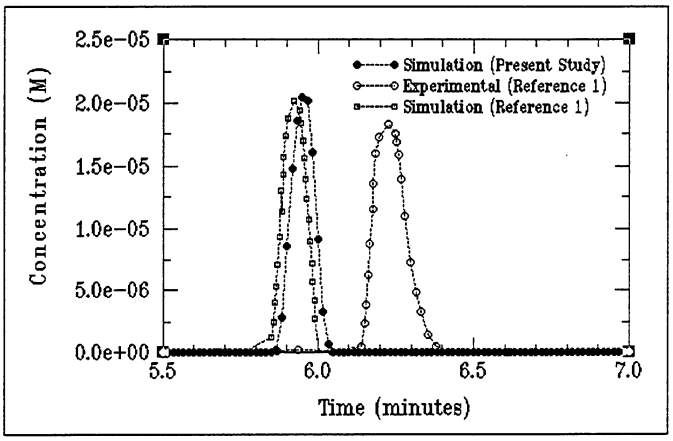

Figure 3: Comparison of Experimental (Sergey and Righetti, 1994) and Computational (Present Study and Sergey and Righetti, 1994) Electropherogram for Picric Acid with an Initial Concentration of 0.02 mM.

In Figure 4, the electric field is plotted along the axis of the channel for various C_o at t = 6 minutes. The electric field was relatively undistorted at low concentration, however, became highly distorted as C_o increased. This again suggests that the variations in the electrical conductivity can not be ignored at higher concentration when acid/base ionization is taken into consideration in the analysis.

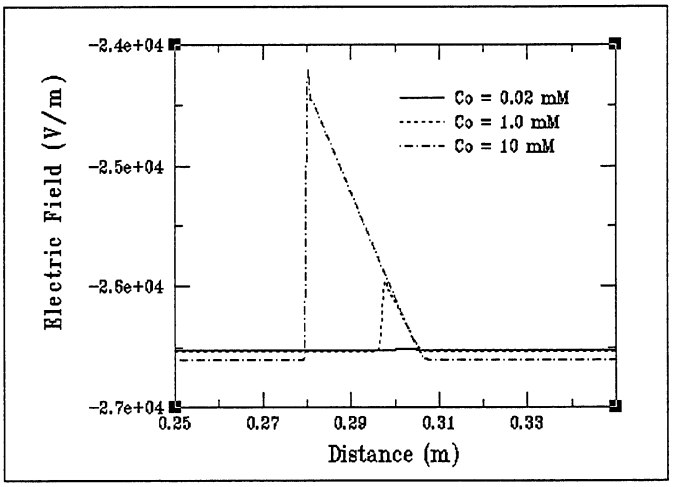

Figure 4: Electric Field Along the Axis of the Channel is Shown at Different Initial Concentration of the Sample.

5 CONCLUSIONS

In this work a model has been developed for simulating transport of a species in a CE microchip under the influence

of electric field. The model simulates the physico-chemical phenomena such as electromigration, convection, diffusion and acid/base equilibrium reactions. This multi-physics simulation tool should aid the CE microchip designers to understand various physical processes that are significant in the MEMS/biomicrosystems. The simulation tool has been tested and validated against published data from Reference [1]. The model predicted that the initial concentration of the sample was an important parameter that could influence the shape of the plug as it migrated under applied electric field. Sample stacking was also predicted to occur at higher concentrations due to the difference in the conductivity between the sample and the background electrolyte. Similar phenomena have been observed in previous experimental studies [1]. The model also predicted that diffusional dispersion dominated at lower concentration, while electromigration dispersion became important at higher concentrations of the sample. The ability to predict these effects will help MEMS designers in the optimization of microchip design based on the trade-off between compactness and separation performance.

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