Numerical Simulation of Field Amplified Sample Stacking in Microfluidic System

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ABSTRACT

When an external electric field is applied to a system in which the conductivity in the sample zone is lower than that of running buffer, one establishes a protocol, namely field amplified sample stacking (FASS). The physical process of this pre-concentration technique is quite complex because of the interaction of convection, diffusion, electrophoresis and electroosmosis. We have developed a numerical simulation method that solves the transport phenomenon associated with sample stacking in microchip-based separation system. The model is based on thin double layer approximation where the electrostatic force is only salient in a very thin double layer adjacent to the charged surfaces. The electrokinetic equations describing the electrophoresis as well as electroosmosis are solved numerically in conjunction with fluid flow and electrostatics. Results for some typical sample stacking with one or two interfaces in the presence of electroosmosis are presented and compared with experiments.

Keywords: Field amplified sample stacking, dispersion, numerical method

1 INTRODUCTION

Sensitivity to low analyte concentration is a challenging issue toward the design and development of robust miniaturized microfluidic biochips. The use of electrokinetics to pre-concentrate chemical or biological samples is becoming more and more popular in a wide variety of areas in both micro- and nano-technology such as integrated DNA chips. When an external electric field is applied to a system in which the conductivity in the sample zone is lower than that of running buffer, the migration velocity of charged species in the region of lower conductivity exceeds that of high conductivity, due to higher electric field strength they experienced. As a result, the species will accumulate at the interface between regions of different electric conductivities, forming very thin bands in which the concentrations are much higher than those of the original sample. This establishes a protocol, namely field amplified sample stacking (FASS) see, figure 1. The physical process of this pre-concentration is quite complex because of interaction of convection, diffusion, electrophoresis and electroosmosis etc. In particular, electroosmosis may cause undesirable effects such as sample broading due to Taylor dispersion [3]. The reduction of important characteristics such as resolution and sensitivity due to dispersion should be appropriately addressed when FASS is used.

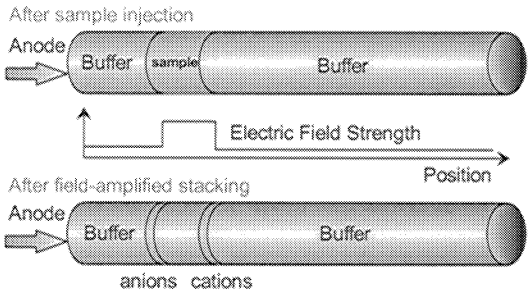

Figure 1: Schematic illustration of physical mechanism that leads to FASS.

In this paper we discuss a numerical methodology that solves the transport phenomenon associated with sample stacking in microchip-based separation systems. The model is based on thin double layer approximation where the electrostatic force is only pronounced in a very thin layer adjacent to the charged surface. The electrokinetic equations describing the electrophoresis as well as electroosmosis are solved numerically in conjunction with fluid flow and electrostatics. The entire theory is applicable to both fully ionized electrolyte solutions as well as acid, base and ampholyte solutions in which rapid association and dissociation of species may occur [1]. Results are presented for typical FASS configurations involving either one or two interfaces. It is found that the simulation method is capable of predicting sample evolution which is in qualitative agreement with experimental observation.

2 GOVERNING EQUATION

2.1 Governing equations

We consider the transport of charged species mixture in the presence of applied electric field. The species are dissolved in electrolyte of different ionic strength. Although we developed a theory for fully ionized electrolyte in this paper, it is straightforward to extend our approach to weakly ionized acid, base or ampholyte solutions. We assume that the double layer thickness formed at charged surfaces is thin so that the mobility of species is approximated by Smoluchowski for-

mula and the effect of electrostatic force is equivalent to a slip boundary condition [4]. The zeta potential of any charged surface is assumed to be relatively low compared with thermal energy so that linearized Poisson-Boltzmann equation describes the potential distribution within the double layer. We also assume that the system is dilute and no chemical reaction occurs. The mass conservation leads to

$$\frac{\partial c_i}{\partial t} + \frac{\partial J_{ij}}{\partial x_j} = 0 \tag{1}$$

where J_{ij} is flux of species i in j direction and is defined by Nernst-Planck equation

$$J_{ij} = u_j c_i - D_i \frac{\partial c_i}{\partial x_j} - z_i c_i \omega_i \frac{\partial \phi}{\partial x_i} \tag{2}$$

Here c_i, D_i, z_i and ω_i are concentration, diffusivity, valency and electrophoretic mobility of the specie i, respectively, $\boldsymbol{u}$ is the fluid velocity and ϕ is the electric potential. The motion of background electrolyte is described by Navier-Stokes equation for the incompressible Newtonian fluid flow

$$\rho \frac{\partial u_i}{\partial t} + \frac{\partial u_i u_j}{\partial x_j} = -\frac{\partial p}{\partial x_i} + \mu \frac{\partial^2 u_i}{\partial x_j \partial x_j} + \epsilon \kappa^2 \zeta \frac{\partial \phi}{\partial x_i} \tag{3}$$

$$\frac{\partial u_i}{\partial x_i} = 0 \tag{4}$$

where ρ is density, p is hydrodynamic pressure, κ^{-1} is Debye-Huckel thickness, ϵ is dielectric constant of the medium and ζ is zeta potential. The last term on the right hand of equation is the electroosmotic volumetric source term which arises due to the interaction of charged wall and the ions in the solution. We assume that the external electric field is sufficiently weak that it is decoupled with potential distribution within the double layer. Therefore the electric potential due to the applied electric field is described by steady state conduction equation

$$\frac{\partial J_i^e}{\partial x_i} = 0 \tag{5}$$

where $\boldsymbol{J}^e$ is the electric current density defined by

$$J_i^e = -\sigma \frac{\partial \phi}{\partial x_i} + \sum_{j=1}^{N} F z_j \frac{\partial D c_i}{\partial x_j} + u_i F \sum_{j=1}^{N} z_j c_j \tag{6}$$

Here σ is electrical conductivity and F is Faraday constant. The electrical conductivity is calculated from species composition

$$\sigma = F \sum_{j=1}^{N} z_j^2 c_j \omega_j \tag{7}$$

2.2 Numerical Method

Due to the nonlinear behavior of the governing equation, analytic solution is not available for general configurations and operating conditions. The coupled equations (1), (3) and (5) are solved using finite volume method [5]. The simulation domain is divided by finite number of cells and the temporal term in the governing equations is discretized by Crank-Nicolson scheme with second order accuracy. The spatial discretization adopts second-order upwind scheme. The resulting linear algebraic equations are solved by a conjugate gradient steepest (CGS) method in iterative manner with prescribed relative error. Test and validation of the method are performed for a variety of simplified problems such as electroosmosis in a channel, transport of charged species by electrophoresis etc.

3 RESULTS AND DISCUSSION

In this section, results of some typical FASS problems are discussed. We first consider sample stacking in a system shown in figure 1 in which two interfaces are involved. In this case, the sample contains both anions and cations. The purpose of this simulation is to illustrate how anions and cations migrate in opposite directions and stack at the interface. We neglect electroosmotic flow (EOF) to eliminate the sample dispersion due to EOF. The simulation parameters are listed below:

	D (m^2/s)	ω (m^2/V s)	C_0 (moles/m^3)
A++	10^{-10}	10^{-9}	10^{-8}
B–	10^{-10}	2×10^{-9}	2×10^{-8}
A+	10^{-10}	2×10^{-9}	10^{-6}
B-	10^{-10}	3×10^{-9}	10^{-6}

Table 1: Diffusivity, mobility and initial concentration of each species in the simulation.

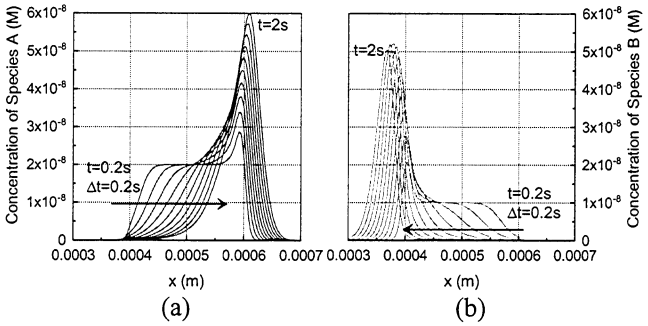

Figure 2: Simulation results illustrating how stacking occurs when the sample contains both cations and anions. In Figure (a), positively charged cations migrate toward anode (right) and accumulate at the right interface, while in (b) negatively charged anions accumulate near left interface.

The simulation domain is a simple 2D channel of 1mm long and 50μm high. The buffer is composed of species A+ and B- and the sample contains species A++ and B–. Initially the sample spans from x=0.4mm to 0.6mm. The applied electric field is 42.7V/cm. The time-dependent con-

centration profile of sample is shown at an increment of 0.2s starting with the initial condition. The figures clearly illustrate how cation (Specie A++) and anion (Specie B–) stack at the interface between sample and the running buffer. We define a stacking ratio γ as [2]

$$\gamma(t) = \frac{c_{\text{stacked}}}{c_{\text{intial}}} \tag{8}$$

In the present simulation $\gamma = 3$ for species A++ and $\gamma = 5.1$ for species B– were observed at $t = 2$s.

As discussed before, stacking of species arises from variations in migration rates due to different electric field species experience. Figure 3 shows the electric field variation along the channel. The strength is very high in the low conductivity region where the sample is located and is very low and almost uniform in high conductivity buffer region. As a result, the species will be concentrated at the interface, leading to a highly concentrated band as time evolves. The concentrated sample is in favor of producing a stronger signal for detection in a electrophoretic separation based device.

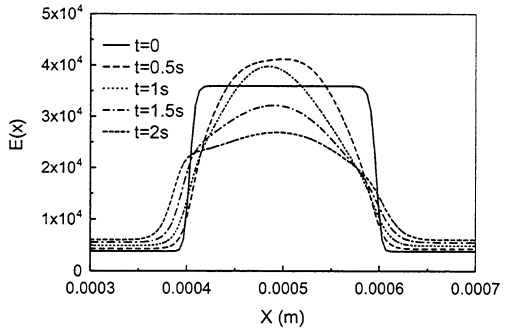

Figure 3: Distribution of electric field at t=0, 0.5, 1, 1.5 and 2 second.

In practice the walls of channel or tube are charged with certain zeta potential. The ions in the electrolyte are attracted to the surface forming a thin double layer that will response to external electric field. This will create an electroosmotic flow (EOF) that further complicates the stacking phenomenon, as shown in figure 4. In order to obtain an initial approximate solution of the scalar fields in this flow, we have assumed that the EOF mobility is constant and does not depend on local concentrations of charged species. The electroosmotic mobility of 4×10^{-9} (m^2/V s) is applied to the walls of the channel in this simulation. As discussed by[3], the variations in the electroosmotic flow will generate internal pressure gradient that induces sample dispersion. In the present case, the variation in the EOF is caused by variations in the electric field, due to stacking. Dispersion of species in this case is very similar to classic Taylor dispersion due to a pressure driven flow in a channel [4].

Results of actual pressure distribution at various times are shown in Figure 5. The pressure distribution is almost piecewise linear along the channel and the turning points migrate as the sample moves due to the electroosmosis.

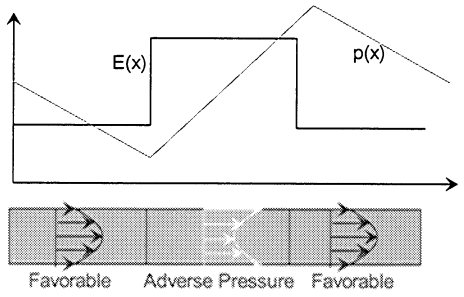

Figure 4: Schematic illustration of stacking under the influence of electroosmotic flow.

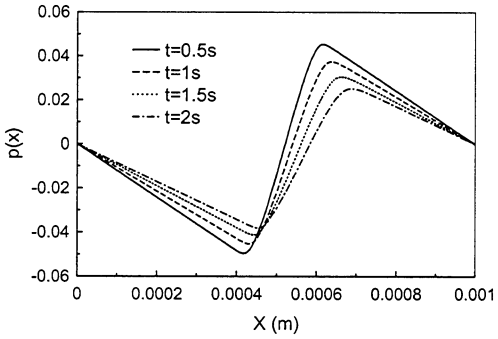

Figure 5: Schematic illustration of stacking under the influence of electroosmotic flow. $E(x)$ and $p(x)$ represent electric and pressure fields, respectively.

Sample transport under the influence of EOF is shown in Figure 6. Note that due to the EOF, migration of both cations and anions are affected. A stacking ratio of 2.5 and 4 at $t = 2$s were observed for Species A+ and B-, respectively. The reduction of peak concentration will be more pronounced as initial γ increases. This suggests that an optimal γ exists for best performance of staking.

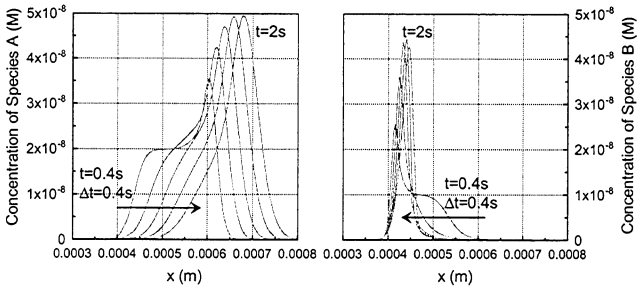

Figure 6: Schematic illustration of stacking under the influence of electroosmotic flow.

The numerical results are here compared to the experimental performed at Stanford University. The schematic of the system is shown in Figure 7. The sample is prepared in low conductivity buffer (shown in gray) and the high conductivity buffer is then electrokinetically driven from the buffer well, on left, towards the sample well, on the right. It is anticipated that the sample will stack at the interface between the two electrolytes.

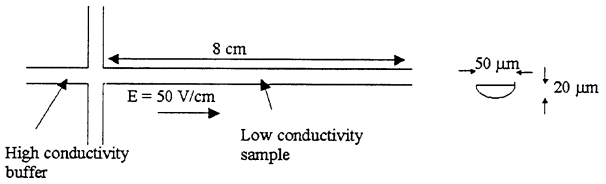

Figure 7: Schematic of single-step stacking device.

Three species can be used in this model problem and the required parameters are listed below

	D (m^2/s)	ω (m^2/V s)	charge
A+	10^{-9}	5.19×10^{-8}	1
B-	7×10^{-10}	3.06×10^{-7}	-1
C–	5×10^{-10}	3.01×10^{-8}	-2

Table 2: Diffusivity, mobility and number of charged of each species in the simulation.

The hydrodynamic properties of the electrolyte are those of water. The EOF mobility is set to 7×10^{-10} m^2/(V s). The initial concentration is set to

$$c_A = 0.5c_{A0}(\gamma + 1 - (\gamma - 1)\text{erf}(a(x - s))) \quad (9)$$

$$c_C = c_{C0}(1 + \text{erf}(a(x - s))) \quad (10)$$

$$c_{A0} = 10^{-3} \quad (11)$$

$$c_{C0} = 10^{-6} \quad (12)$$

in which $\gamma = 4$ is the ratio of buffer concentration in the background high conductivity and to that in the low conductivity sample.

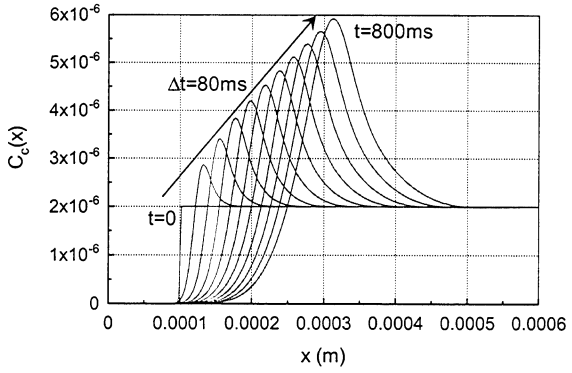

Figure 8: Concentration of stacked sample as a function of time.

We apply 50V/cm electric field along the channel and simulate the evolution of sample transport. We first assume that there is an infinite supply of the sample, and the interface moves across the horizontal channel. The concentration of species C is plotted along the channel for different time steps in figure 8. It clearly demonstrates the stacking of species at the interface. The peak value is almost linear as observed during experiments due to the mismatch of EOF along the channel, the sample will disperse as stacking takes place. Contours of concentration of C are shown in figure 9. We compared the simulation results with those of experiment in figure 9. The results agree qualitatively with experimental data.

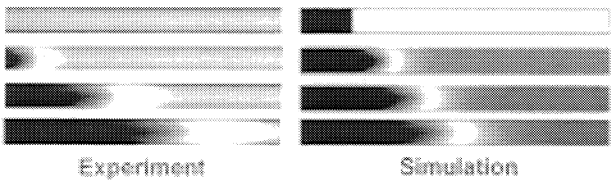

Figure 9: Comparison of experimental and simulation results for sample concentration contours. Light and dark colors represent high and low concentrations, respectively.

In summary, we have developed a numerical method for simulating FASS in capillary electrophoretic system. The method can be extended to account for rapid association and dissociation of species in weakly ionized systems [6]. The dispersion due to varying zeta potential on the wall need refined model to correlate zeta potential and the species concentration. In contrast to FASS protocol where species reside in buffer of lower conductivity, one can construct a simple pump if the species locates in buffer of higher conductivity since the results lower electric migration suppresses the separation in this region. As a result, all species will translate with uniform rate by EOF.

ACKNOWLEDGMENT

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