Capillary Electrophoresis in Nanofluidic Channels

Paul J. Atzberger*+, Frederic Gibou+, and Sumita Pennathur+

+ Department of Mechanical Engineering
* Department of Mathematics
University of California Santa Barbara
6712 South Hall, Goleta, CA 93117.

Last update to manuscript PDF was on April 14, 2011; 9:33pm.

ABSTRACT

We investigate electrokinetic transport of nanoparticles and biomolecules in nano-scale channels exhibiting novel features in comparison to microscale channels. Recent experimental work provides information about how the mobility and diffusivity depend sensitively and non-monotonically on pH, ionic valence, and channel size. We discuss a TIRFM platform in which single quantum dot nanoparticles are used to probe in three dimensions single-particle transport through nanochannels. We also discuss studies at the ensemble level of both nanoparticles and biomolecules (e.g. oligoucleotides). We focus particularly on theoretical investigations toward explaining these experimental findings. We study as ionic concentration and valence are varied the role of particle proximity to the channel walls, the role of the electric double layer structure around the wall and particles with possible overlap, and the role of solvent hydrodynamic coupling.

Keywords: nanofluidics, nanochannel, capillary electrophoresis, statistical mechanics, computational fluid dynamics

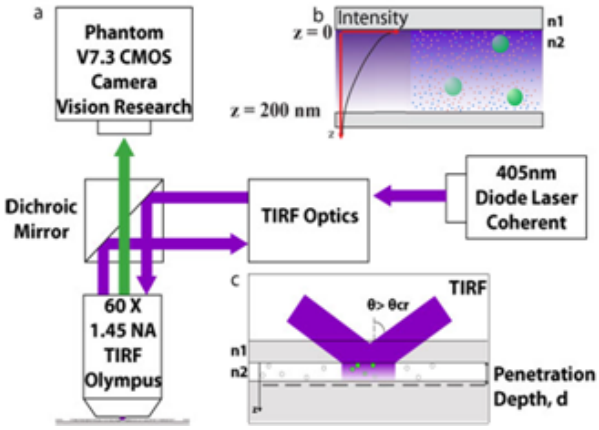

Figure 1: : (a) Schematic of optical TIRFM setup with nanoparticles confined by the channel within the evanescent wave. (b) The evanescent wave intensity is used to obtain measurement of the z-component of the nanoparticle position. This is used to obtain a time-averaged distribution function for the full three-dimensional positions sampled by individual confined nanoparticles.

1 Experimental Results

Our group is using primarily two experimental approaches to investigate electrokinetic transport within nano-channels. The first is Total Internal Reflection Fluorescence (TIRF) to probe at the single-particle level the electrokinetic transport of quantum dot nanoparticles confined within the nanochannel [4]. The TIRF yields measurements of three dimensional single-particle time-averaged distributions across the channel height, transverse displacement, and axial position. Since transverse and axial motions occur over longer time scales than diffusion across the channel height, significant transverse and axial Brownian diffusion of individual quantum dots can be observed in these experiments [4]. Quantitative analysis of these measurements provides useful information about the effective accessible volume of the nanochannel, rate of axial transport, and dispersion. By varying the ion concentrations and valence, these measurements also offer information about the role played by the Electrical Double Layer (EDL) and interactions between the nanoparticle probes and the channel walls, see Figure 1.

Electrokinetic transport in nanochannels of larger analytes (DNA oligonucleotides 1 - 100 bps) is also being investigated using measurements of cross-sectional through-put in the nanochannel. The resulting electropherograms exhibit interesting features when compared to microscale channels [3]. It is found that better resolution is attained in separating oligonucleotides in the nanochannel relative to microscale channels, see Figure 3. It is also found that EDL related effects appear to play an important role in the separation efficacy and the rate of axial transport. In fact, for larger Debye lengths an interesting non-monotonic behavior is observed where the longer oligonucleotides actually exhibit a higher through-put than shorter oligonucleotides [3], see Figure 2.

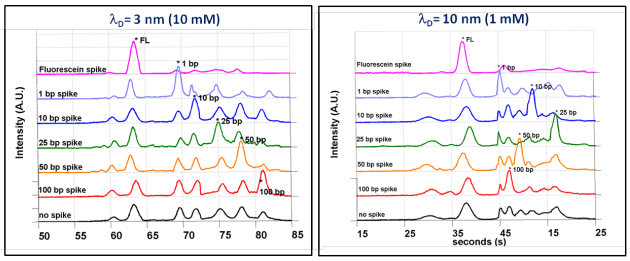

Figure 2: Electrokinetic transport in a nanochannel of 100nm of oligonucleotides for different lengths ranging from $1 - 100$bps (top to bottom). (left) For a Debye length $\lambda_D = 3$nm the peak arrival time increases monotonically in the number of base pairs (bps). (right) For a Debye length $\lambda_D = 10$nm the peak arrival time exhibits a non-monotonic behavior. For example, the 100bps oligonucleotides arrive at an earlier time than 25bps oligonucleotides.

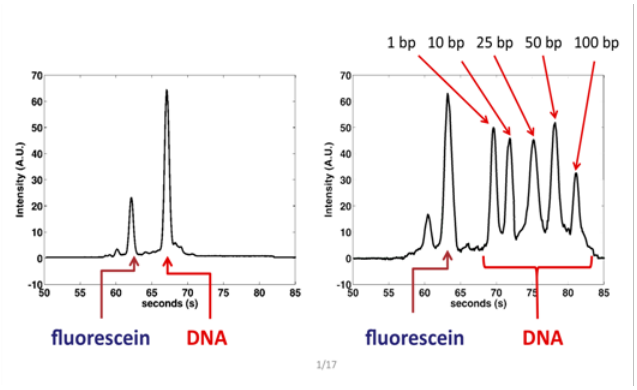

Figure 3: Electropherograms showing the separation of flourescein and five different length strands of oligoncuelotides in a microfluidic channel (left) and nano-fluidic channel (right). In the microchannel, only two peaks are visible, corresponding to free solution flourescein, with all the different length oligonucletoides convoluted into one peak. The DNA does not separate into individual peaks because in the microchannel they have similar electrophoretic mobilites. In contrast, all five different lengths of oligonucelotides separate in the nanochannel.

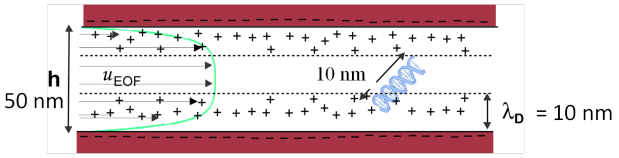

Figure 4: Electrokinetic Transport in a Nanochannel.

2 Theoretical Investigations

For nanochannels it is important to consider a number of physical effects that are typically neglected in studies of microscale channels. New effects come into relevance in nanochannels given the comparable size of the channel diameter, the electrical double layers (EDLs), and the analyte particle size. This results in effects including the possible overlap of the EDLs of the analyte particle and wall, analyte-wall steric interactions, and adsorbtion/desorption kinetics. The electro-osmotic hydrodynamic flow is also expected to deviate from a plug-flow across the channel, see Figure 4.

An interesting challenge in the study of nanochannels is the non-linear coupling between the electrostatics, hydrodynamics, and analyte configurations. To investigate the role of these effects, we propose a detailed theoretical model of electrokinetic transport within a nanochannel taking into account the Brownian motion of analyte particles, the particle-wall sterics, the ionic concentrations (EDLs), and the solvent hydrodynamics driven by the ions and analyte particles.

We investgate this detailed model by developing new computational methods for the simulation of electrokinetic transport of a finite number of analyte particles within a nanochannel. We perform simulation studies to study the relative contributions of these physical effects. We make comparisons to reduced theoretical descriptions and to our experimental observations.

2.1 Electrokinetic Transport Model

We now describe our system of equations for taking into account the Brownian motion of analyte particles, the particle-wall sterics, the ionic concentrations (EDLs), and the solvent hydrodynamics driven by the ions and analyte particles. The system is described in terms of the following fundamental degrees of freedom

$$\begin{aligned} (\mathbf{X}, \theta) &: \text{Particle Rigid Body Configuration} \\ c_k(\mathbf{x}, t) &: \text{Ionic Species Concentration} \\ \mathbf{u}(\mathbf{x}, t) &: \text{Solvent Fluid Velocity} \\ \Phi[\mathbf{c}, \mathbf{X}, \theta] &: \text{Total Energy} \end{aligned}$$

The electrostatics are modeled by the equations

$$-\nabla \cdot \epsilon \nabla \phi = q(\mathbf{x}, t)$$

$$
\begin{aligned}
q(\mathbf{x},t) &= q_{\text{ion}}(\mathbf{x},t) + q_{\text{wall}}(\mathbf{x},t) + q_{\text{prt}}(\mathbf{x},t) \\
q_{\text{ion}}(\mathbf{x},t) &= \sum_k q_k c_k, \qquad q_{\text{wall}}(\mathbf{x},t), \qquad q_{\text{prt}}(\mathbf{x},t)
\end{aligned}
$$

The electrical potential is given by ϕ. The charge distribution in space is given by $q = \sum_k q_k$ where $k \in \{\text{ion}, \text{wall}, \text{prt}\}$. The q_k give the local contributions arising from the ions, channel wall, and analyte particles. The $\epsilon = \epsilon(x)$ gives the local permittivity used to account for differences in the electrical properties in space within the ion-solvent fluid and within the analyte particle volume.

The ionic concentration fields are governed by

$$
\begin{aligned}
\frac{\partial c_k}{\partial t} &= -\nabla \cdot \mathbf{J}_k \\
\mathbf{J}_k &= -D_k \nabla c_k - \alpha_k \nabla \Phi c_k + u c_k \\
\Phi &= \phi + \psi + E_{\text{electrodes}}.
\end{aligned}
$$

The ions are subject to the potential Ψ given by

$$
\psi = \psi_{\text{st}} + \psi_{\text{wl}} + \psi_{\text{pr}}
$$

This incorporates in the ion description a potential energy for the ion concentration field that accounts approximately for ion-excluded volume, interactions with the wall and analyte particle, and the electric field produced by the electrodes.

The solvent hydrodynamic flow within the channel and around the rigid particles is taken into account using the Stokes equations

$$
\begin{aligned}
\mu \Delta \mathbf{u} &= -\nabla p + \mathbf{f} \\
\nabla \cdot \mathbf{u} &= 0 \\
\mathbf{u} &= 0, \qquad \mathbf{x} \in \partial\Omega_{\text{wall}} \\
\mathbf{u} &= V_\ell, \qquad \mathbf{x} \in \partial\Omega_{\text{particle } \ell} \\
\mathbf{f} &= \sum_k \alpha_k \nabla \Phi c_k.
\end{aligned}
$$

In practice, for fixed analyte particle configuration, these equations are solved to steady-state to obtain instantaneous ionic concentration fields c_k and hydrodynamic field $\mathbf{u}$.

The analyte particles are treated as rigid bodies. They have overdamped translational and rotational stochastic dynamics

$$
\begin{aligned}
\frac{d\mathbf{X}}{dt} &= -\Gamma_{\text{hyd}}^{-1} \mathbf{F} + \mathbf{g}_{\text{thm}} \\
\frac{d\theta}{dt} &= -\Lambda_{\text{hyd}}^{-1} \tau + \mathbf{h}_{\text{thm}}.
\end{aligned}
$$

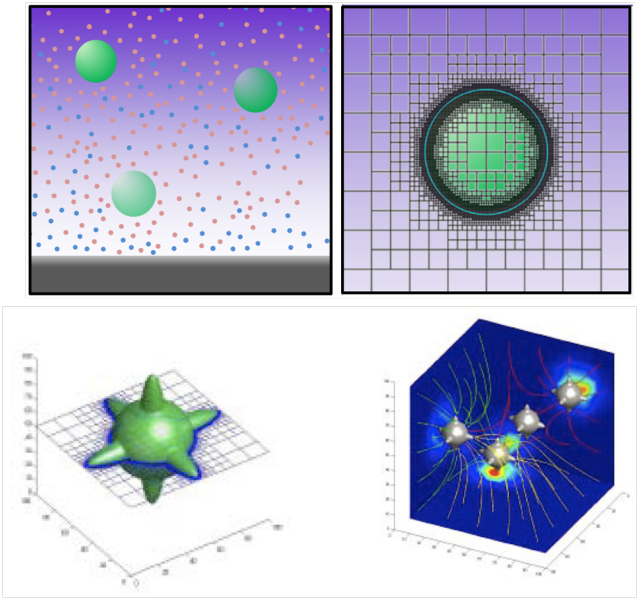

Figure 5: Computational Methods

The forces $\mathbf{F}$ and torques τ are computed from the electrostatic potential and hydrodynamic fields. The effective hydrodynamic coupling tensors are determined from the solution $\mathbf{u}$ of the Stokes flow for the domain defined by the analyte particles and nanochannel geometry.

To account for translational and rotational diffusion of the analytic particles we use the fluctuation-dissipation principle to drive the dynamics with a stochastic forcing term that is a Gaussian process with δ-correlation in time and with covariances

$$
\begin{aligned}
\mathbf{g}_{\text{thm}} &= Q \frac{d\mathbf{B}_t}{dt} \\
\langle \mathbf{g}_{\text{thm}}(s) \mathbf{g}_{\text{thm}}^T(t) \rangle &= Q Q^T \delta(t-s) \\
Q Q^T &= 2 k_B T \Gamma_{\text{hyd}}^{-1}.
\end{aligned}
$$

Similarly, for $\mathbf{h}_{\text{thm}}$.

To investigate the behaviors of this detailed model computational methods are developed to solve the electrostatic and hydrodynamic fields within the domain determined by the analyte particle configurations and nanochannel geometry. To cope with this complex geometry Adaptive Mesh Refinement (AMR) methods along with efficient iterative solvers have been developed, [2], see Figure 5. The hydrodynamic coupling tensors and stochastic driving fields of the analyte particles are computed in practice using a variant of the recently introduced Stochastic Eulerian Lagrangian Method (SELM), [1], see Figure 5.

This approach allows for simulation-based investigations of electrokinetic transport for analyte particles having different geometries, ion concentrations corresponding to different Debye lengths and valences, and

nanochannel geometries. This approach allows for characterization of the role of the hydrodynamic coupling and transport, the role of EDL structure and overlap, and the role of translational/rotational Brownian diffusion of the analyte particles.

3 Summary

A detailed theoretical model of electrokinetic transport within nanochannels is presented. This detailed model is explored using new computational methods to study the relative contributions of the EDLs overlap, steric effects, Brownian motion of analyte particles, and the induced solvent hydrodynamics. Comparisons are made with reduced models and with experimental observations.

4 Acknowledgements

The authors acknowledge supported from the W.M. Keck Foundation and the Institute for Collaborative Biotechnologies.

REFERENCES

[1] Atzberger, P. J. ,"Stochastic Eulerian Lagrangian Methods for Fluid Structure Interactions with Thermal Fluctuations," J. Comp. Physics, Vol. 230, 2821-2837, 2011.

[2] Min, C. and Gibou, F., A second order accurate projection method for the incompressible Navier-Stokes equations on non-graded adaptive grids, J. Comp. Physics, Vol. 219, 912-929, 2007.

[3] Free-Solution Oligonucleotide Separation in Nanoscale Channels, S. Pennathur et al., Anal. Chem., 79, 8316-8322, 2007.

[4] Wynne, T. M, Dixon, A. H, Pennathur, S., Nanofluidic fTIRF Nanoparticle Characterization Tool (preprint), 2011.