Fundamental Understanding of Nanofluidics for Advanced Bioseparation and Analysis

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Research Area and Objective: This research is in the area of investigating the unique physical phenomena associated with nanoscale structures and utilizing them for an engineering purpose. Specifically, our scientific goal is to render an accurate description of biomolecular structural changes, reaction, and transport in nanochannels as a function of built-in as well as externally applied potentials. The understanding of such fluid and molecular transport is imperative for the development of a new generation of devices for efficient separation of proteins in the context of their application to proteomics, environmental science, and advanced diagnostics. The technological and scientific outcome from this research will enable high throughput separation, purification, identification, and determination of structure-function relationships of biomolecular species and biomolecular complexes.

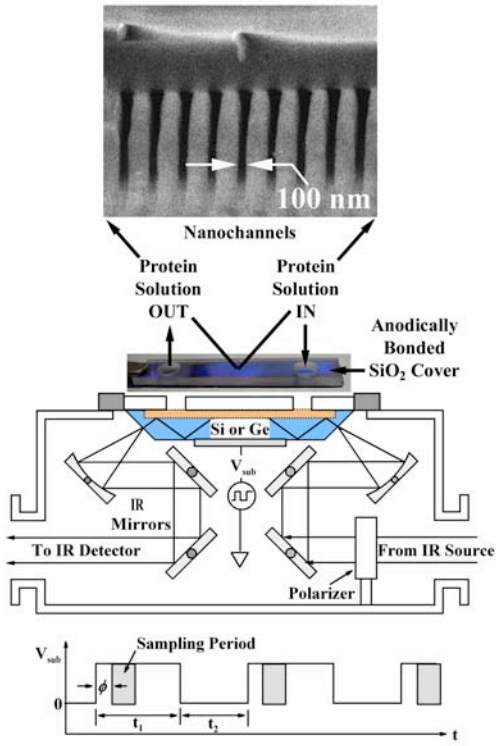

Figure 1: Architecture of NWA-FTIRS to probe molecular transport in nanochannels. This experimental setup also interrogates the double layer by modulating the potential applied to the substrate in FET configuration and monitoring the changes in IR absorbance with 500-nsec resolution.

Employed Experimental Methods: In order to study the molecular flow and its manipulation in nanochannels, we have developed two experimental platforms: (1) hybrid micro/nanofluidic "T-chip"[2, 3] that provides access for scanning laser confocal fluorescence microscopy (SL-CFM) and electrochemical impedance spectroscopy (EIS) and (2) multiple-internal-reflection (MIR) infrared waveguide with integrated nanochannels to conduct both SL-CFM and nanomachined–waveguide-assisted Fourier transform infrared spectroscopy (NWA-FTIRS). See Refs. 2 and 3 for the description of the 1st platform. Figure 1 shows the 2nd platform. Both platforms are fabricated on Si wafers, using interferometric lithography (IL)[4-7], conventional plasma etching, and anodic bonding of a glass ceiling. Approximately 10^5 nanochannels are imbedded into the Si substrate to allow multiplexed, high-throughput separation of biomolecules. The width, depth, and length of the channels are on the order of 10-100 nm, 1 μm, and 1 cm, respectively. To move the fluid along the micro/nanochannels by electroosmosis, two different electrical potentials are applied to the inlet and outlet of the experimental platform. A third electrical potential is applied, in the field-effect-transistor (FET) configuration, [8, 9] to the Si channel walls to control the ζ-potential and therefore the flow speed and

direction.

Notable Results: For the purpose of initial transport studies and visualization, fluorescent dyes (Alexa 488 and Rhodamine B) are chosen. Utilizing the previously described experimental platforms, we have focused on the electrokinetic transport of these fluorescent dyes in a range of pH and ionic strength with the application of transverse "gate" bias in the FET configuration.[‡] During the 2004-2005 period, we have discovered the following:[10]

- The average flow velocity of dye molecules, their relative position in the nanochannels, and wall adsorption can be probed by NWA-FTIRS, in conjunction with SL-CFM, provided that the channel width is substantially less than the IR wavelength.
- The gate potential effectively controls the electroosmotic flow of dye molecules: i.e., acceleration, deceleration, and reversal of flow direction. The flow control can be enhanced by an order of magnitude in speed with an isolated gate surrounding a short longitudinal segment of the nanochannels.
- The leakage current that typically flows through thin thermal SiO_2 surrounding the channels, when the gate potential is applied, can be reduced by a number of means, including the insertion of a Si_3N_4 layer between thermal SiO_2 and the Si channel walls. However, the leakage current cannot be eliminated.
- Effective separation of charged molecules can be achieved over a shorter distance than in capillaries by over 2 orders of magnitude.

In parallel with the experiments, we have conducted theoretical modeling and analysis[11, 12] of the transport in nanometer sized channels. Most of the analysis preformed so far is for slit-shaped plane parallel channels. The effect of gate potential is included in the consideration. Using the weak double layer overlap approximation, we have derived analytical expressions for the transport processes and presented a simple model for the effect of gate potential on the ζ-potential. Through the theoretical development, we have shown that

- The transport of fluid becomes a nonlinear function of the electrokinetic ζ-potential for small channels with overlapping double layers.
- The current along the channels increases with the ζ-potential. The lowest possible value for the electrical current in a nanochannel occurs at $\zeta = 0$. Hence, the electrical current in the fluidic FET could be decreased to a non-zero, minimum value. Asymmetric electrolytes lead to an asymmetry in the shape of the current vs. ζ-potential curve. Divalent counterions, when compared to monovalent counterions, increase the conductivity.
- The ζ-potential depends nonlinearly on the gate potential. However, the extent of this dependence and therefore the ability to manipulate the electrokinetic potential are limited.
- Charged molecular species, when surrounded by charged channel walls of the same polarity, are electrostatically forced toward the center of the channels, following the streamlines with greater velocity and leading to additional acceleration in comparison to neutral molecules.

Using the method of matched asymptotic expansion, we have also developed an analytical model for the potential distribution and electroosmotic flow in a cylindrical capillary with arbitrarily high surface potential.

[‡] U.S. provisional and utility patent applications were filed on July 19, 2004 and 2005, respectively.

Near Term Activities and Direction: We will utilize the combined experimental and theoretical understanding to achieve efficient, high-throughput protein separations. A number of separation strategies, such as isoelectric focusing and isotachophoresis, will be employed. The fluidic FET device architecture will be altered to accommodate these experimental strategies applied to nanochannels.

References

[1] For further information about this project, send an email message to meister@unm.edu.

[2] A. Garcia, L.K. Ista, D. Petsev, M.J. O'Brien, P. Bisong, A.A. Mammoli, S.R.J. Brueck, G.P. López, "Electrokinetic Molecular Separation in Nanoscale Fluidic Channels," *Lab on a Chip* **5,** 1271 (2005).

[3] M.J. O'Brien, P. Bisong, L.K. Ista, E.M. Rabinovich, A.L. Garcia, S.S. Sibbett, G.P. Lopez, S.R.J. Brueck, "Fabrication of an Integrated Nanofluidic Chip Using Interferometric Lithography," *J. Vac. Sci. Technol. B* **21,** 2941 (2003).

[4] S.H. Zaidi, S.R.J. Brueck, "Multiple-Exposure Interferometric Lithography," *J. Vac. Sci. Technol. B* **11,** 658 (1993).

[5] S. Zaidi, S.R.J. Brueck, "Nanoscale Fabrication by Interferometric Lithography," *Proc. SPIE* **3740,** 340 (1999).

[6] L.F. Johnson, G.W. Kammlott, K.A. Ingersoll, "Generation of periodic surface corrugations," *Appl. Opt.* **17,** 1165 (1978).

[7] E.H. Anderson, C.M. Horwitz, H.I. Smith, "Holographic lithography with thick photoresist," *Appl. Phys. Lett.* **43,** 874 (1983).

[8] R.B.M. Schasfoort, S. Schlautmann, L. Hendrikse, A. van den Berg, "Field-effect flow control for microfabricated fluidic networks," *Science* **286,** 942 (1999).

[9] R. Karnik, R. Fan, M. Yue, D. Li, P. Yang, A. Majumdar, "Electrostatic Control of Ions and Molecules in Nanofluidic Transistors," *Nano Lett.* **5,** 943 (2005).

[10] T.C. Gamble, Y.-J. Oh, A. Garcia, A. Neumann, D.N. Petsev, C.F. Ivory, C.-H. Chung, S.R.J. Brueck, G.P. Lopez, S.M. Han, in *Study of Molecular Transport in Nanofluidic Channels by Integrated Multiple Internal Reflection Infrared Waveguide*, AVS 52nd International Symposium & Exhibition, Boston, MA, 2005.

[11] D.N. Petsev, "Theory of transport in nanofluidic channels with moderately thin electrical double layers. Effect of the wall potential modulation on solutions of symmetric and asymmetric electrolytes," *J. Chem. Phys.*, submitted (2005).

[12] D.N. Petsev, G.P. Lopez, "Electrostatic potential and electroosmotic flow in a cylindrical capillary filled with symmetric electrolyte: analytic solutions in thin double layer approximation," *J. Colloid Interface Sci.*, accepted (2005).