Anal. Chem. **2007,** *79,* 3862−3866

Electroosmosis-Based Nanopipettor

Chang Kyu Byun, Xiayan Wang, Qiaosheng Pu, and Shaorong Liu*

Department of Chemistry and Biochemistry, Texas Tech University, Lubbock, Texas 79407

Decreasing the volume of reagent solutions consumed in each assay is an effective means to reduce the overall cost in high-throughput analysis laboratories. Recently, increasing attention has been paid to investigate the behavior of individual cells. If one wishes to transfer solution to or from a single cell, a picoliter pipettor is needed since the entire cell volume is commonly less than 1 nL. While pressure ejection and iontophoresis have been used to deliver picoliter volumes of solutions, these techniques cannot yield routine pipettors which perform both solution "picking up" and "dispensing" functions. The state-of-the-art pipettors can handle liquids down to ∼100 nL, although the pipetting accuracy and precision deteriorate considerably from microliters to nanoliters. If one wishes to pipet reagents of less than 100 nL, new pipettors need to be developed. Electroosmosis has been utilized to pump solutions at flow rates of nanoliters to approximately picoliters per second, which is ideal for nanopipettors. The issue is how to arrange fluidic/electrical connections so that pipetting functions can be performed conveniently. In this paper, we present the results of our initial attempt to develop an electroosmosis-based nanopipettor. The first version of this pipettor consists of a microfabricated electroosmotic (EO) flow pump, a polyacrylamide grounding interface, and a nanoliter-to-picoliter pipet tip. The detailed configuration and fabrication process of the pipettor are discussed. An excellent feature of an EO-driven pipettor is that it has no moving parts. Good reproducibilities (RSD = 6% at 140 pL, 2% at 950 pL, and 2% at 13 nL) and accuracies (9% at 0.13 nL, 4% at 1.0 nL, and 3% at 10 nL) of this pipettor have been demonstrated to aliquot/transport nanoliter-to-picoliter solutions.

One of the most frequently performed tasks in an analytical laboratory is to transport samples and reagents from one place to another. Often, minimizing the volumes of sample/reagent consumed in each assay is an effective means to reduce the overall analysis cost, which leads to a demand for small volume (e.g., nanoliter) pipettors. Recently, increasing attention has been paid to investigate the behavior of individual cells. If one wishes to transfer solution to or from a single cell, a picoliter pipettor is needed since the entire cell volume is commonly less than 1 nL. Pressure ejection[1−5] and iontophoresis[6−8] are capable of delivering solutions down to picoliters. The former technique employs a pulse of positive pressure to push a small volume of solution out of a fine tube into a targeted location (e.g., a single neuron), while the latter utilizes an electric field to electrophoretically drive a charged drug substance across a barrier (e.g., a skin) into a fluid stream (e.g., a blood circulation system). Instruments based on these technologies have been commercially manufactured.[9,10] However, because none of the above techniques can be used to accurately pick up solutions (a basic function of a pipettor), one cannot develop a pipettor out of these technologies. The state-of-the-art pipettors (e.g., Rainin pipet) are capable of handling liquids down to 100 to ∼200 nL, with an accuracy of ±12% at 200 nL,[11] and no commercial pipettors are available to accurately pick up, aliquot, and transport solutions of less than 100 nL.

Nanoliter pipettors were reported and used in research laboratories decades ago.[12] The first nanoliter pipettor was developed by Prager et al. in 1965.[12] The essential component of this pipettor is a piece of capillary which defines the pipettor volume. As the capillary is dipped into a solution, the liquid is pulled up filling the capillary by capillarity force. To dispense the liquid, an air pressure is applied to the back end of the capillary to blow the solution out to a targeted place. Depending on the dimension of the capillary, this pipettor can have a volume (but only a fixed volume) from a fraction of a nanoliter to hundreds of nanoliters.[12] Obviously, one shortcoming of this pipettor is the inconvenience to tune the pipetted volume accurately. In addition, it is required that a sample solution can create sufficient upward capillarity force so that the solution can be pipetted. More recently, a syringe-based nanopipettor was described.[13] The pipettor was formed by tightly connecting a segment of capillary to a Hamilton syringe. When the plunger of the syringe is pulled to a preset position, a known negative pressure (vacuum) is created and a solution is aspirated into the capillary under this vacuum. By

* To whom correspondence should be addressed. Fax: 806-742-1289. E-mail: shaorong.liu@ttu.edu.

(1) Smith, T. G., Jr.; Cunningham, M. F. *Med. Biol. Eng. Comput.* **1983**, *21*, 138−144.
(2) Gerhardt, G. A.; Palmer, M. R. *J. Neurosci. Methods* **1987**, *22*, 147−59.
(3) Hanani, M. *J. Basic Clin. Physiol. Pharmacol.* **1997**, *8*, 57−71.
(4) McCaman, R. E.; McKenna, D. G.; Ono, J. K. *Brain Res.* **1977**, *136*, 141−147.
(5) Poulain, P.; Carette, B. *Brain Res. Bull.* **1981**, *7*, 33−40.
(6) Junginger, H. E.; *Adv. Drug Delivery Rev.* **2002**, *54*, S57−S75.
(7) Kalia, Y. N.; Naik, A.; Garrison, J.; Guy, R. H. *Adv. Drug Delivery Rev.* **2004**, *56*, 619−658.
(8) Pikal, M. J. *Pharm. Res.* **1990**, *7*, 118−126.
(9) http://www.harvardapparatus.com; http://www.eppendorf.com.
(10) http://www.vyteris.com.
(11) http://www.rainin.com/pdf/ab15.pdf.
(12) Prager, D. J.; Bowman, R. L.; Vurek, G. G. *Science* **1965**, *147*, 606−608.
(13) Lorieau, J.; Shoemaker, G. K.; Palcic, M. M. *Anal. Chem.* **2003**, *75*, 6351−6354.

10.1021/ac062457i CCC: $37.00
Published on Web 04/12/2007

selecting an appropriate aspiration time, a desired volume of solution is pipetted. Precisions of less than ±5% were reported.[13] However, the pipetted volume will deviate if the viscosity of the sample solution varies.

In the microarray community, numerous technologies such as TopSpot, NanoJet, PipeJet, and DWP, etc. have been invented to transfer nanoliters of solutions onto solid surfaces.[14] While these methods are successfully used for surface spotting, they are not suitable for accurate solution aliquoting/transportation.

Electroosmotic (EO) flow has been employed to pump solutions in capillaries and microchannels, and various pumps have been developed.[15−20] EO pumps have several unique features such as low stable flow rates, no moving parts, and convenience in adjusting the flow rate and flow direction. These features should enable us to develop an excellent nanoliter-to-picoliter pipettor based on electroosmosis. Because EO flow goes with electric current, the solution outlet end is usually connected to an electrode. This arrangement will be practically inconvenient.

In this work, we develop an electrical grounding interface to solve the above problem. The interface is a piece of capillary filled with cross-linked polyacrylamide that allows continuity of electricity but inhibits fluid flow across the interface. Referring to Figure 1, when a negative electric field is applied from the HV to the GND reservoirs, an upward EO flow is generated in the pump channels. Owing to the polyacrylamide interface that blocks the flow, the EO flow will aspirate a sample solution into the pipet tip to perform the "picking up" function. Similarly, when a positive electric field is applied, a downward EO flow is created and will push the sample solution out of the pipet tip to perform the "dispensing" function. We have previously reported the use of a Nafion membrane as a grounding interface,[15,19,20] and other groups have utilized nanoporous membranes[16] and packed columns[21,22] to build the interface. However, because these materials preferentially permit one kind of ion (e.g., cations) to pass through, ion enrichment and ion depletion (IEID)[23] will occur at the interface, resulting in deteriorated pipetting accuracy and precision. Polyacrylamide overcomes this problem, since both cations and anions can pass through polyacrylamide impartially.

EXPERIMENTAL SECTION

Materials. Acrylamide, bis([*N*,*N*′-methylene bisacrylamide]), bifunctional reagent [(3-methacryloxypropyl)-trimethoxysilane], TEMED (*N*,*N*,*N*′,*N*′-tetramethylethylenediamine), and APS (ammonium persulfate) were obtained from Bio-Rad Laboratories (Hercules, CA). Other chemicals were from Fisher Scientific International Inc. All solutions were prepared using ultrapure water purified by a NANO Pure Infinity Ultrapure water system (Barnstead, Newton, WA). Bare fused silica capillaries were purchased from Polymicro Technologies (Phoenix, AZ).

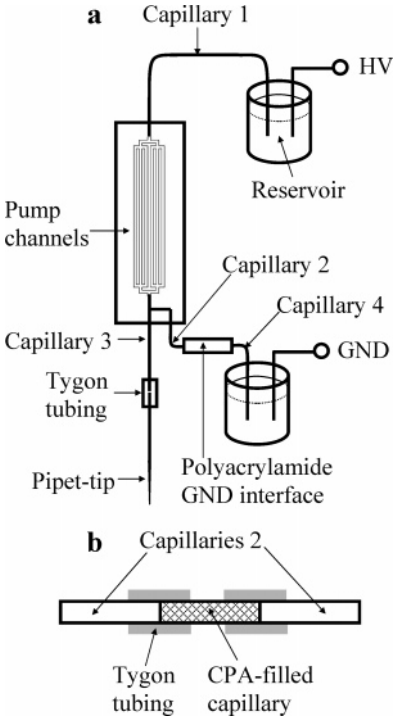

Figure 1. Schematic diagram of an EO-driven pipettor: (a) schematic configuration of an EO-driven pipettor and (b) detailed structure of a polyacrylamide grounding interface. HV, high voltage; GND, ground/grounding; CPA, cross-linked polyacrylamide.

Laser-Induced Fluorescence Detector. The detector is a confocal laser-induced fluorescence (LIF) detection system that has been described previously.[24,25] Briefly, a 488 nm beam from an argon ion laser (LASERPHYSICS, Salt Lake City, UT) was reflected by a dichroic mirror (Q505LP, Chroma Technology, Rockingham, VT) and focused onto a microchannel through an objective lens (20× and 0.5 na, Rolyn Optics, Covina, CA). Fluorescence from the microchannel was collimated by the same objective lens and collected by a photosensor module (H5784-01, Hamamatsu, Japan) after passing through the dichroic mirror, an interference band-pass filter (532 nm, Carlsbad, CA), and a 2 mm pinhole. The output of the photosensor module was measured using an NI multifunctional card DAQCard-6062E (National Instruments, Austin, TX). The data were acquired and treated with a program written in-laboratory with Labview (National Instruments, Austin, TX).

Manufacturing of a Polyacrylamide Grounding Interface. A 10 cm long capillary (360 μm o.d. and 100 μm i.d.) was cut, and its inner wall was cleaned by flushing the capillary with 1.0 M NaOH for 45 min, DI water for 15 min, and acetonitrile for 15 min. After the capillary was dried with N_2, the inner wall was reacted with a solution containing 0.4% (v/v) 3-(trimethoxysilyl)-propyl methacrylate and 0.2% (v/v) acetic acid in acetonitrile at room temperature for 1 h. Then, a degassed solution containing

(14) Daub, M.; Kaack, R. M.; Gutmann, O.; Steinert, C. P.; Niekrawietz, R.; Koltay, P.; Heij, B.; Zengerle, R. *Mater. Res. Soc. Symp. Proc.* **2004**, *820*, R6.6.1−R6.6.11.
(15) Dasgupta, P. K.; Liu, S. *Anal. Chem.* **1994**, *66*, 1792−1799.
(16) Lazar, I. M.; Karger, B. L. *Anal. Chem.* **2002**, *74*, 6259−6268.
(17) Zeng, S. L.; Chen, C. H.; Mikkelsen, J. C.; Santiago, J. G. *Sens. Actuators, B* **2001**, *79*, 107−114.
(18) Chen, L. X.; Ma, J. P.; Tan, F.; Guan, Y. F. *Sens. Actuators, B* **2003**, *88*, 260−265.
(19) Liu, S.; Pu, Q. S.; Lu, J. J. *J. Chromatogr., A* **2003**, *1013*, 57−64.
(20) Pu, Q.; Liu, S. *Anal. Chim. Acta* **2004**, *511*, 105−112.
(21) Paul, P. H.; Arnold, D. W.; Rakestraw, D. J. In *Micro Total Analysis Systems '98*; Harrison, D. J., van den Berg, A., Eds.; Kluwer Academic Publishers: Boston, MA, 1998; pp 49−52.
(22) Paul, P. H.; Arnold, D. W.; Neyer, D. W.; Smith, K. B. In *Micro Total Analysis Systems, 2000*; van den Berg, A., Olthuis, W., Bergveld, P., Eds.; Kluwer Academic Publishers: Boston, MA, 2000; pp 583−590.
(23) Pu, Q.; Yun, J.; Temkin, H.; Liu, S. *Nano Lett.* **2004**, *4*, 1099−1103.
(24) Lu, J. J.; Liu, S. *Electrophoresis* **2006**, *19*, 3764−71.
(25) Pu, Q.; Liu, S. *Anal. Chim. Acta* **2004**, *511*, 105−112.

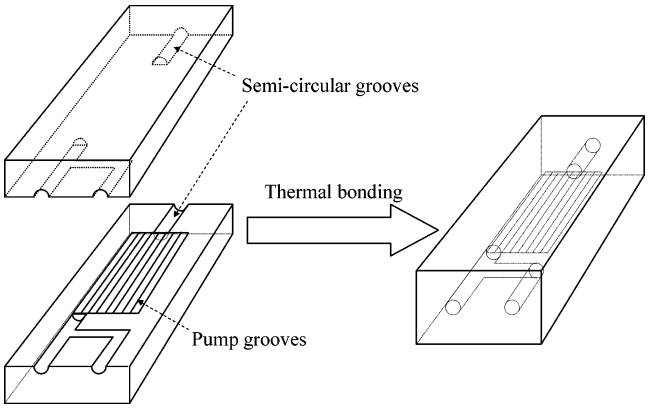

Figure 2. Schematic process to fabricate the pump part of an EO-driven pipettor.

2 to ~12 %T (%T stands for the total weight concentration acrylamide and bis in the solution), 3 to ~7 %C (%C represents bis concentration relative to acrylamide), 0.2% (v/v) TEMED, and 0.1% APS was pressurized into the capillary and remained inside the capillary at 4 °C overnight. After ~1 cm of the capillaries at both ends were cut off and discarded, 50 mM sodium tetraborate was electrophoretically driven through the polyacrylamide inside the remaining capillary until a stable current was obtained. The above capillary was cut into ~1 cm pieces, and each piece serves as a polyacrylamide grounding interface.

Measurement of the Electrical Resistance of a Polyacrylamide Grounding Interface. After the interface was equilibrated with 50 mM sodium tetraborate, a high voltage was applied across the capillary, and the current was measured. To facilitate the current measurement, a 98.8 kΩ resistor was incorporated between the ground electrode and the ground reservoir, and the voltage across the resistor was monitored constantly. Dividing the voltage by the resistance yields the current across this resistor. The same current also passed through the interface capillary. The resistance of the interface was calculated by dividing the voltage on the interface capillary (the total voltage minus the voltage on the 98.8 kΩ resistor) by this current.

Fabrication of an EO Pump Chip. A three-photomask process was used to make this device. The procedure of fabricating round channels on a chip was described previously.[26,27] Briefly (referring to Figure 2), one photomask was utilized to yield the semicircular grooves on the top wafer, the second photomask for the semicircular grooves on the bottom wafer, and the third photomask for the parallel shallow pump grooves. The radius of the semicircular grooves was ca. 190 μm, and the dimensions of the pump channels (24 in parallel) were 30 mm (length) × 200 μm (width) × ~1.5 μm (depth). The pump channels were evenly distributed with a center-to-center distance of 300 μm between two adjacent ones. The EO pump chip was produced after two wafers were aligned and thermally bonded.

Assembly of an EO-Driven Pipettor. Referring to Figure 1a, capillaries 1−3, having an i.d. of 150 μm, an o.d. of 375 μm, and lengths of 10, 2, and 12 cm respectively, were inserted into the round channels of the pump chip and secured in positions with silicone adhesive. The pipet tip was another piece of capillary (~12 cm long, 375 μm o.d., and 100 μm i.d.) with a taped tip (~1 cm long). The taped tip was formed by pulling the capillary under a butane torch. At the very end of the tip the capillary had an o.d. of ~7 μm and an i.d. of ~5 μm. The pipet tip was coupled with capillary 3 through a segment of Tygon tubing. The polyacrylamide interface was incorporated between capillaries 2 and 4 as depicted in Figure 1b. Capillary 4 had an i.d. of 150 μm, an o.d. of 375 μm, and lengths of 5 cm, but its i.d. can be increased and its length can be decreased in the next version of pipettors. During pipetting, a high voltage was applied to the free ends of capillaries 1 and 4 via two reservoirs containing 50 mM sodium tetraborate.

Pipettor Operations. The pipet tip was prefilled with 50 mM sodium tetraborate by pumping the pump solution to the tip. Two operation modes were tested. Under operation mode A, a negative HV (e.g., −3.5 kV) was applied to capillary 1 for an extended period of time to aspirate ~500 nL of sample solution into the pipet tip. The tip was rinsed by dipping it into and lifting it from a vial containing DI water three times. Then, various aliquots of the solution were dispensed to different containers. Under operation mode B, a negative HV was applied to the pipettor temporarily to aspirate a desired amount of solution. The tip was rinsed by dipping it into and lifting it from a vial containing DI water three times. The polarity of the HV was then switched (often the magnitude did not change) to dispense the solution. Normally, a dispense time of ~10% longer than the pipetting time was used to enable all aspirated solutions to be dispensed.

Calibration of the Pipettor. To calibrate the pipettor, we prepared a series of standard fluorescein solutions (from 6.0 nM to 5.0 μM) in 2.0 mM sodium tetraborate. These solutions were pressurized through a capillary, and the relative fluorescence intensities from the capillary were measured using an LIF detector. Very good linear relationship was obtained ($r^2 = 0.999$ from 6.0 nM to 1.0 μM and $r^2 = 0.997$ from 6.0 nM to 5.0 μM). Then, a given volume ranging from ~0.1 to ~300 nL of a fluorescein stock solution was transferred using the EO-driven pipettor to a vial containing a known volume (250 μL to 5 mL) of 2.0 mM sodium tetraborate. The fluorescence intensity of the resulting solution was measured following the same procedure as for the standard solutions, and the fluorescein concentration was calculated from the calibration curve. On the basis of the dilution factor and the solution volume in the vial, the volume of stock solution transferred was calculated.

RESULTS AND DISCUSSION

The electrical resistance of the polyacrylamide ground interface is preferred to be low, because the voltage on the interface extends to the pipet tip, which is normally unwanted. Figure 3 presents the effect of %T and %C on electrical resistance. All the measurements were performed using ~8 cm long (375 μm o.d. and 100 μm i.d.) capillaries, and the data points shown in Figure 3 were normalized to 1 cm long capillaries. Owing to some random factors of the polymerization, resistance value exhibited some fluctuations. In general, the resistance did not change much from 3 %T to ~9 %T, and decreased slightly from ~9 %T to 12 %T. Further increasing %T resulted in bubble formation in polyacrylamide due to the heat generated from the polymerization reaction. Under the same %T, the resistance decreased slightly with the %C.

In this work, we used 9 %T−3 %C and 10 %T−5 %C more often than any other compositions. Under these conditions, the resist-

(26) Liu, S. *Electrophoresis* **2003**, *24*, 3755−3761.
(27) Liu, S.; Guttman, A. *TrAC, Trends Anal. Chem.* **2004**, *23*, 422−431.

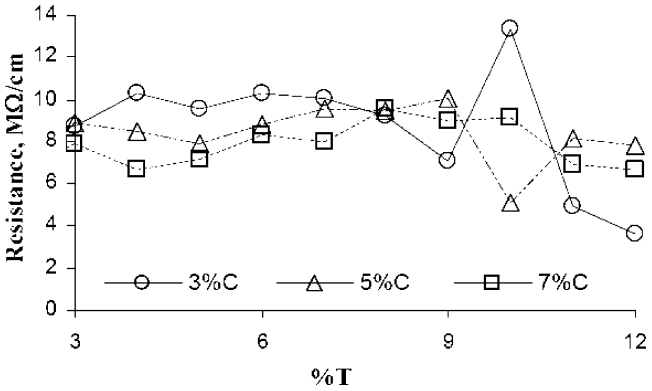

Figure 3. Effect of %T and %C on resistance of the polyacrylamide interface. All the measurements were performed using ~8 cm long (375 μm o.d. and 100 μm i.d.) capillaries loaded with polyacrylamide. The polymer phase was equilibrated with 50 mM sodium tetraborate. The data points shown in Figure 4 were normalized to 1 cm long capillaries.

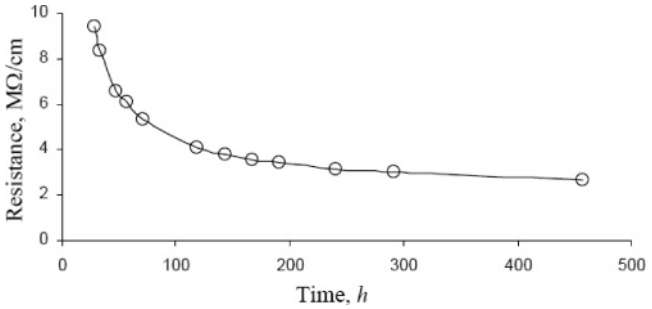

Figure 4. Resistance of a polyacrylamide interface as a function of time. The time on the *x*-axis represents the duration in which 50 mM sodium tetraborate is present in the polyacrylamide.

ance of the polyacrylamide in the interface was ~6 MΩ. We also measured the resistance of the pump channels filled with 50 mM sodium tetraborate, and the resistance was found to be ~700 MΩ. That is, less than 1% of the total voltage was on the interface. This number may be further reduced by increasing the diameter and decreasing the length of the interface capillary.

When polyacrylamide was stored in 50 mM sodium tetraborate, we noticed its decreasing resistance with time (see Figure 4). After about a week, its resistance reached ~3.5 MΩ/cm, compared to ~2.0 MΩ/cm when a capillary of the same size was loaded with 50 mM sodium tetraborate solution without polyacrylamide. To check whether the polymer was hydrolyzed, we applied a pressure of up to 4000 psi to the capillary using a Shimadzu HPLC pump, but no apparent flow was detected. Interestingly, if the polymer was re-stored in DI water, its resistance was gradually recovered to ~70% of its original value. The resistance measurements were, of course, performed after the polymer was equilibrated with 50 mM sodium tetraborate. At this moment, we do not have a convincing explanation for this phenomenon.

A taped pipet tip was important to achieve high pipetting accuracies. In this experiment, a 100 μm i.d. capillary was used to make the tip. It will be problematic to use this capillary directly to pipet solutions at subnanoliter levels, because there will be a short solution segment (~130 μm for 1 nL) at the tip with a large opening (100 μm diameter). During tip rinsing, a significant portion of sample will be lost. This situation was significantly improved after using a tip-taped capillary. With the use of an ~5

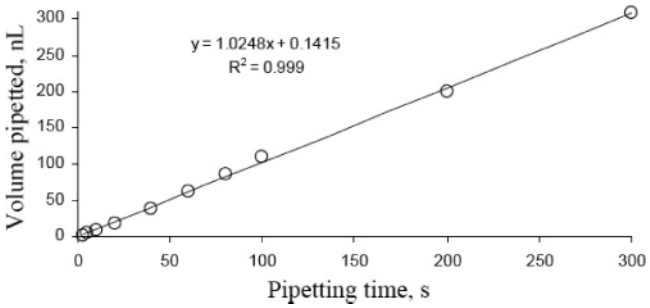

Figure 5. Relationship between pipetted volume and pipetting time. The total applied voltage was 3.5 kV. The pipettor was operated under mode B.

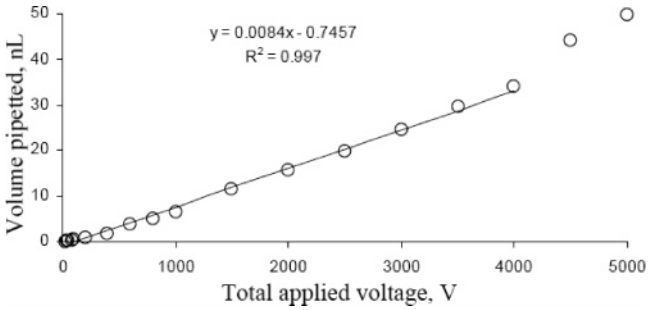

Figure 6. Relationship between pipetted volume and total applied voltage. The pipetting time was 30 s. The pipettor was operated under mode B.

μm i.d. tip as an example, 100 pL of solution will have a length of ~5.1 mm. In combination with a shrunk opening, sample loss is effectively prohibited.

With the use of a sharp (e.g., ~1 μm o.d.) pipet tip with its outer surface hydrophobically derivatized, little solution will adhere to the tip and tip rinsing may be avoided. This would simplify the pipettor operation considerably. In our lab, there is an ongoing project to explore such feasibility.

Figure 5 presents an excellent linear relationship ($r^2 = 0.999$) between pipetted volume and pipetting time. It should be pointed out that all linear coefficients were within 0.999−1.000 when the total voltage applied to the pipettor was less than 3.5 kV. At higher voltages, the linear coefficient decreased progressively with an increasing voltage due to the growing Joule heating. The effect of Joule heating is further evidenced by the data presented in Figure 6. From 20−4000 V, the pipetted volume and the applied voltage had a reasonably good linear relationship ($r^2 = 0.997$), but an exponential curve clearly showed up as the voltage continuously increased.

In this experiment, our main focus was to demonstrate the feasibility of an EO-driven pipettor to pipet nanoliter-to-picoliter liquids, and little effort was invested in reducing the Joule heating. Obviously, Joule heating can be mitigated by decreasing the electrolyte concentration of the pump solution, by reducing the pump channel depth (an increased number of channels may be needed to compensate the diminished pump rate), by effectively cooling the pump device, etc.

Once the pipettor is calibrated, a desired volume is pipetted by selecting an appropriate combination of a pipetting time and a total applied voltage. Under the experimental conditions used in this work and a total voltage of less than 3.5 kV, the pipetted

volume is directly proportional to the product of the pipetting time by the total applied voltage.

To prepare for pipetting, the pipet tip was prefilled with a 50 mM sodium tetraborate solution. Under operation mode B, some pump solution was dispensed to the target solution. This is acceptable in this experiment because only fluorescein solutions were pipetted. In practical applications, the pump solution might be incompatible with the sample or/and reagent solution. A proper intermediate solution or a small air bubble may be aspirated to isolate the pump solution from the sample or/and reagent solution.

A stable pump rate is critical to achieve a high pipetting reproducibility. In capillary electrophoresis, it is notorious that EO flow can fluctuate considerably. The fundamental reasons that cause this fluctuation are changed inner wall surface conditions and varied pump solution compositions. Joule heating also contributes to the unstable EO flow. As long as these parameters are maintained constant, a stable EO flow can be achieved. Capillary 3 (see Figure 1a) was used to prevent sample/reagent solutions from entering pump channels so that the surface properties of the pump channels were unaltered. To effectively inhibit surface contamination by sample/reagent solutions, it is recommended that the internal volume of this capillary should be at least 2 times as much as that of the pipet tip capillary. A high concentration (50 mM) of sodium tetraborate was employed to resist the composition (especially the pH) change against the electrolysis during pipetting/dispensing and the adsorption of CO_2 from the air. A total voltage of less than 3.5 kV was applied to the pipettor to avoid excessive Joule heating.

To assess the pipettor reproducibility, we pipetted a small volume of a fluorescein stock solution and diluted it in a given volume of 2.0 mM sodium tetraborate (operation mode B). The fluorescein concentration of the resulting solution was measured using an LIF system. This process was repeated for 8−10 times, and the relative standard deviations (RSD) of these measurements were 6% ($n = 8$) at 140 pL, 2% ($n = 8$) at 950 pL, and 2% ($n = 10$) at 13 nL. These numbers included also the uncertainties from the LIF measurements. Under operation mode A, the RSDs were generally better than but close to those under operation mode B, i.e., RSD = 5% ($n = 8$) at 140 pL.

To evaluate the pipettor accuracy, a small air bubble was introduced into the capillary tip, and a microscope was used to measure the bubble positions before and after a pipetting/dispense action. The microscope was equipped with a background grid with a resolution of 10 μm. This test revealed accuracies of 9% at 0.13 nL, 4% at 1.0 nL, and 3% at 10 nL. The accuracies were normally smaller than 3% at higher volumes (up to 300 nL).

CONCLUSIONS

We have for the first time developed an EO-driven nanopipettor and demonstrated its feasibility to pipet nanoliter-to-picoliter liquids with good accuracies and reproducibilities. Good linear relationships exist between pipetted/dispensed volume and pipetting/dispensing time and between the volume and the voltage applied to the pipettor. Although the volume range demonstrated is from ~100 pL to ~300 nL, this range can be extended considerably. For example, the upper limit can be boosted to microliters by increasing the depth of the pump channels or the number of pump channels, or simply by raising the pipetting time. Meanwhile, the lower limit can be easily decreased by reducing the depth of the pump channels or the number of pump channels, or by diminishing the voltage applied to the pipettor. Another important specification of an EO-driven pipettor is its wide volume range of a single pipettor, i.e., ~100 pL to ~300 nL for the pipettor described in this paper. Because the major body of the pipettor is composed of a microfabricated chip and the associated capillaries, these pipettors can be highly parallelized with a common HV power supply. Combined with computer control, such a tool can have great impact on high-throughput assays. We have an ongoing project to use this pipettor to precisely deliver and pipet fluids to/from the inside of a single cell. Low-micrometer or submicrometer pipet tips (fabricated using Sutter P-2000 Micropipette Puller, Novato, CA) are being used for this application, and the results will be published elsewhere.

ACKNOWLEDGMENT

This work is partially supported by NIH (1 RO1 GM078592-01), NSF (CHE-0514706), and the Texas Advanced Research Program.

Received for review December 29, 2006. Accepted February 27, 2007.

AC062457I