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Microfluidic Manipulation for Biomedical and Biohealth Applications

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***Abstract*—**Automation and control of biological samples and solutions at the microscale is a major advantage for biochemistry analysis and biological diagnostics. Despite the known potential of miniaturization in biochemistry and biomedical applications, comparatively little is known about fluid automation and control at the microscale. Here, we study the electric field effect inside a fluidic channel and proper electrode structures with different patterns proposed to form forward, reversal, and rotational flows inside the channel. The simulation results confirmed that the ac electro-thermal flow is efficient for the control and automation of high-conductive solutions. In this research, the fluid pumping and mixing effects were numerically studied by solving physic-coupled electric, temperature, hydrodynamic, and concentration fields inside a microchannel. From an experimental point of view, the electrode structures are deposited on a silicon substrate and bonded to a PDMS microchannel to form a microfluidic chip. The motions of fluorescent particles in pumping and mixing modes were captured by using a CCD camera. By measuring the frequency response of the fluid and exciting the electrodes with the proper voltage, the fluid motions (including pumping and mixing effects) are observed inside the channel through the CCD camera. Based on the results, there is good agreement between the experimental and simulation studies.

***Keywords*—**Microfluidic, nano/micro actuator, AC electrothermal, Reynolds number, micropump, micromixer, microfabrication, mass transfer, biomedical applications.

I. Introduction

THE successful approach in Micro-Electro-Mechanical industry was a signal to apply the integration mechanism into the other biochemistry and bio-analysis field [1]-[4]. Low sample consul and fast analysis make the micro-devices useful for portable bio and chemistry analysis [5], [6]. The control and automation of fluid at micro-scale is an important issue for integration of biological applications where fluid mediums with different ionic strength (such as deionized water, biochemistry/buffers buffer and etc.) are used as medium fluid to do a special analysis [7], [8]. The behavior of fluid inside the micro-channel can be considered as laminar and creeping flow. The fluid behavior can be explained by dimensionless Reynolds number, where $Re = \rho_0 U_0 d_h/\mu_0$ [9], [10]. The viscose effects at microscale are dominate factors [11], and that is why the fluid control and automation is challengeable at micro-scale. Therefore, active actuation mechanisms such as DC and AC electrokinetic [12]-[14], magnetic force [15] and surface acoustic force [16] is used to increase the inertial effects inside a microchannel. DC electrokinetic force needs very high electric field and it is not advantageous for the most practical applications [17], [18]. AC electroosmotic flow benefits from low driving voltage and it is only useful for low ionic strength mediums such as DI-water.

In this research, a microfluidic channel and an electrokinetic excitation mechanism is modeled to study the simulation and experimental effect of ac electrokinetic mechanism on conductive mediums. The multiphysic governing equations containing the electrical, thermal and fluid dynamic equations are solved inside the microchannel. In order to control and automation of biofluids inside the channel, both the numerical and experimental investigations for the interactions between the fluid and electric field is studied in this study.

II. Material and Methods

By applying an electric field to the electrodes immersed in an electrolyte, three important mechanisms can occur. a) When the applied electric field frequency (f), is well below that of the electrolyte charging frequency ($\tau_q^{-1}=\sigma/\varepsilon$) [19], all of the applied electric field will consume for the screening effect by the counter ions and nothing else happens. b) When the applied electric field frequency is comparable to the electrolyte charging frequency, there is not sufficient time to completely screen the electrodes. Therefore, a part of applied electric field will be used for screening effect and the remaining part will be dropped over the electrolyte. If a tangential electric force applies to the fluid medium, the charges at the electrode and electrolyte interface (electric double layer) will experience a significant force. Consequently, these double layer charges pull the bulk fluid along and a secondary flow generates inside the channel [20]. The flow direction forms from the screened portion towards the unscreened portion. The thickness of electrical double layer (EDL) is determined as Debye length [17], [19].

$$\lambda_D = \sqrt{\frac{\varepsilon\varepsilon_0 k_b T}{2n_i^0 z_i^2 e^2}} \quad (1)$$

where, k_b is the Boltzmann constant, n_i^0 is bulk concentration of ion i, ε is the dielectric constant of solution, z_i is valence of ion i, ε_0 is the permittivity of vacuum, T is the absolute temperature, and e is the initial charge [4]. Based on (1), the AC electroosmotic flow is not efficient for the fluids with high salt medium [18]-[20]. c) By applying high frequency electric fields, there is not sufficient time for the counter ions to screen

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the surface of the electrodes and the whole of the electric field will be dropped over the electrolyte. This case causes the local temperature to rise inside the fluid. A temperature gradient field ∇T induces inside the conductive solution by applying electric potential to the electrode pieces with different size. In the presence of thermal gradient, the conductivity and permittivity properties of electrolyte solution change and then as a result, bulk fluid motions form around the electrodes which is called ac electro-thermal flow [21], [22]. The interaction of electrodes and electric potential and also the bulk fluids' ionic strength is responsible for the generated AC electro-thermal flow. Based on the Joule's law ($W=\sigma E^2$), the generated temperature rise inside the channel increases by increasing the ionic strength of the electrolyte [19]. It should be noted that for conductive solutions, the AC electroosmotic effect will lose its efficiency, because of poor electric double layer formation [18], [19].

A. Microdevice Design

The physical design of the microdevice for control and microfluid automation is shown in Fig. 1. A pair of electrodes are located at the bottom of channel and the loaded fluid transports inside the channel by applying AC electric potential over the electrodes. the direction of fluid transportation can be changed by employing different electrode patterns.

B. Microchip Fabrication Process

The fabrication process flow for the electrode structures and Polydimethlsiloxane (PDMS) microchannel are visualized in Figs. 2 (A) and (B). As the first chip, the electrode structures were deposited and structured by sputtering and dry etching process, respectively.

The electrode structures are deposited on a silicon/silicon-dioxide substrate. Several chips with different electrode structures are designed for fluid manipulation and control process (Fig. 2 (C)). As the second chip, a mold for PDMS microchannel is fabricated, deep reactive ion etching method is employed for bare silicon etching and making the mold. PDMS is cured over the mold, then removed from the mold and bonded to the electrode chips as biochip device. The geometrical dimensions of electrodes' gap and the channel are also shown in Fig. 2.

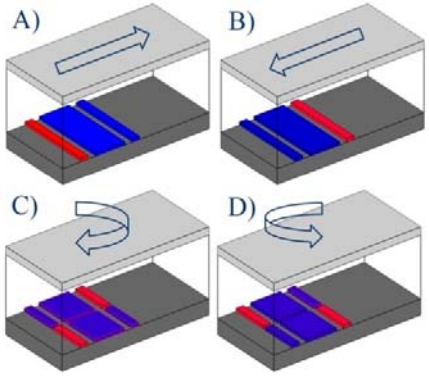

Fig. 1 Schematic illustration of electrode patterns for fluid control at microscale, A) Directional flow; B) Reversal flow; C) Clockwise rotational flow; D) Anti-clockwise rotational flow

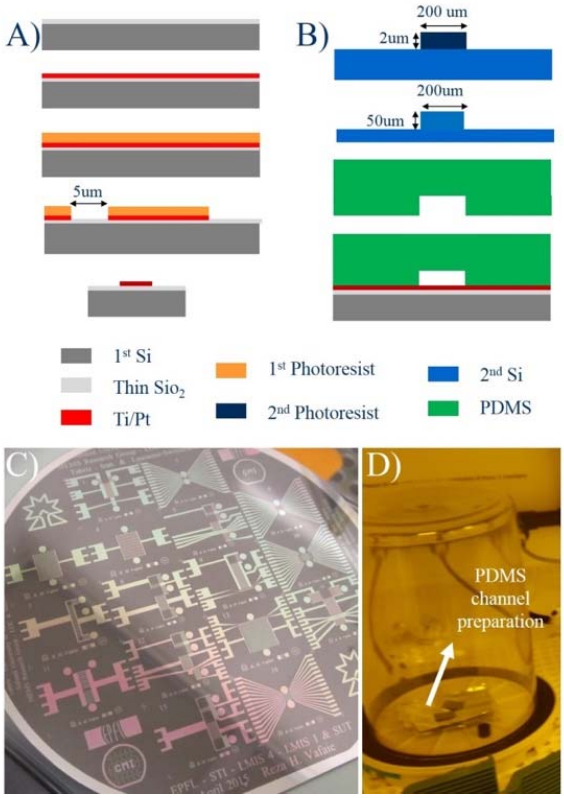

Fig. 2 Fabrication process; A) Process flow for electrode deposition on Si/SiO2 substrate as 1st chip, B) Process flow for Si-mold to form PDMS mirochannel. C) A silicon wafer with 16 different chips for fluid control at microscale; D) PDMS chip preparation as microfluidic channel

C. Physical Equations

The transport and control of a conductive solution involve simultaneous coupling of the electric field, E, temperature field, T and fluid flow field, U. since the magnetic field effect is negligible, electric field can be expressed by electric voltage φ and electric conductivity σ [17], [23]:

$$E = -\nabla\varphi, \tag{2}$$

$$\nabla.(\sigma\nabla\varphi) = 0, \tag{3}$$

As discussed earlier, the electric properties variation with temperature can be expressed by [23]:

$$\sigma(T) = \sigma(T_0)(1+\beta(T-T_0)),$$
$$\beta = \frac{1}{\sigma(T_0)}\left(\frac{\partial\sigma}{\partial T}\right)|T_0 = 2\%/K \tag{4}$$

$$\varepsilon(T) = \varepsilon(T_0)(1+\alpha(T-T_0)),$$
$$\alpha = \frac{1}{\varepsilon(T_0)}\left(\frac{\partial\varepsilon}{\partial T}\right)|T_0 = -0.4\%/K \tag{5}$$

As result of an inhomogeneous electric field, the temperature gradient arises inside the fluid; the temperature field can be formulized by energy balance equation [23]:

$$\rho_m c_p \overline{v}.\nabla T + \rho_m c_p \frac{\partial T}{\partial t} = k\nabla^2 T + \sigma|E|^2, \tag{6}$$

The potential and temperature fields are coupled with Incompressible-Navier-Stokes equations to describe the fluid motion. It should be noted that the body force originating from ac electro-thermal phenomenon is taken into account in Navier-Stokes equation [18], [23]:

$$\nabla \bar{u} = 0, \tag{7}$$

$$\rho_m \left[\frac{\partial \bar{u}}{\partial t} + \vec{u}\nabla\bar{u}\right] - \mu\nabla^2\vec{u} + \nabla p = f_{ET}, \tag{8}$$

$$< F_{ET} >= -0.012\nabla T.\frac{\varepsilon|E|^2}{1+(\omega\tau)^2} + 0.001\nabla T.\varepsilon|E|^2, \tag{9}$$

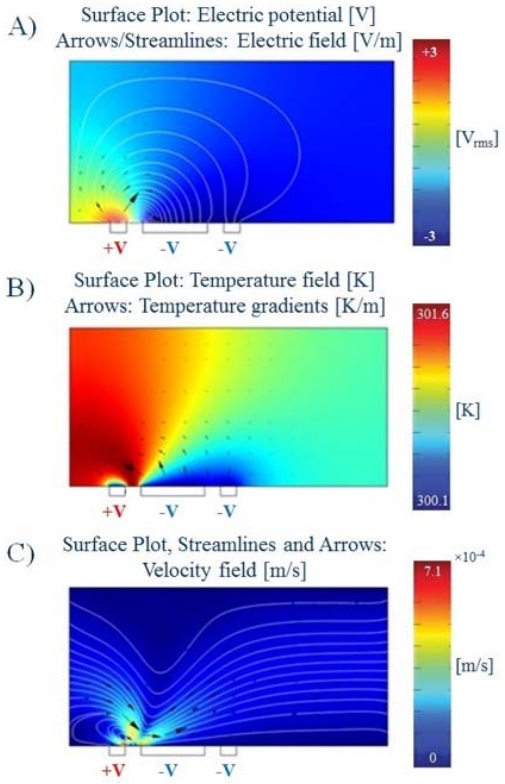

Fig. 3 FEM simulation results for fluid transportation and control, A) Electric potential distribution; B) Temperature field; C) Fluid motion, streamlines and arrows indicates the fluid velocity direction and magnitude

III. Results and Discussion

A. Simulation Results

Finite-element-method (FEM) simulation analyses were carried out with COMSOL Multiphysics Software to investigate the bulk fluid motion effects for pumping and mixing purposes. The proposed electrode structures were patterned in the bottom of the microchannel to investigate the flow motion for the electrolytes with high ionic strength medium, where the AC electro-thermal flow is dominant. Fig. 3 shows the pumping flow generated inside the channel by applying voltage to the electrode pattern A. The temperature field study shows that the generated temperature rise inside the channel is below 2 K, which is not trouble making for biological applications. By using the patterns C and D the device is able to generate vortex effect for mixing purposes. The fluid sample A (red color) and regent solution B (blue color) with two different species concentration (C_A = 1 mol.m^{-3} and C_B = 0 mol.m^{-3}) inserted into the microchannel. The concentration distribution inside the channel is illustrated in Fig. 4.

B. Experimental Test

A printed circuit board (PCB) is designed for providing the electrical signals to the electrodes and the biochip is mounted on the chip holder part. The motions of fluorescent particles were captured by using a CCD camera. The experimental test setup is indicated in Fig. 5 (A).

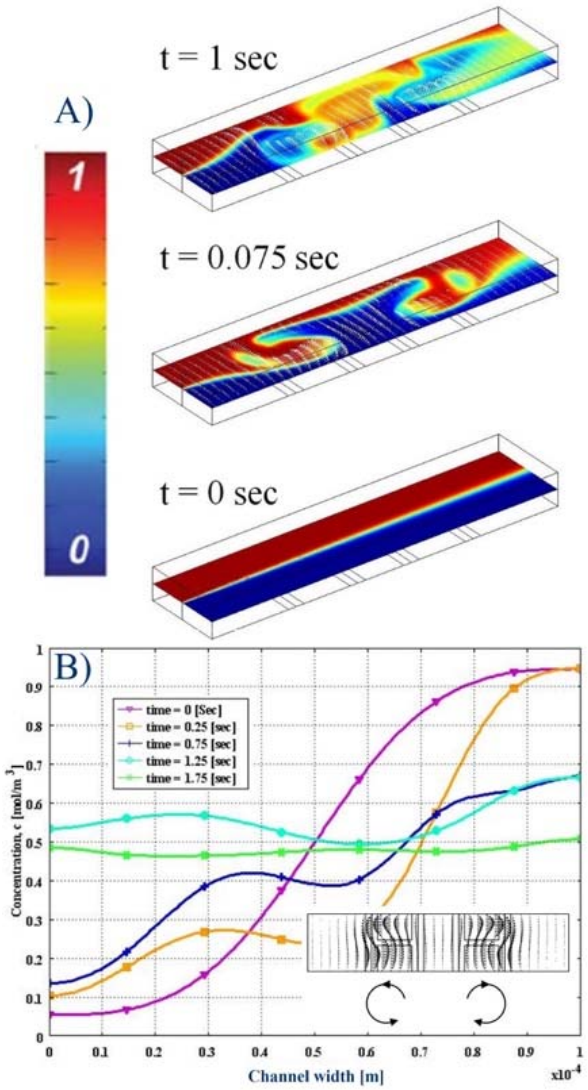

Fig. 4 A) Concentration distribution of the sample and reagent inside the microchannel; B) The concentration profile at outlet of the channel for different times

In order to study the fluid motion of biological samples inside the proposed PDMS microchannel, the water with high conductive medium were mixed with fluorescent particles and inserted from the input hole of the channel. The electrical

property and frequency response of the fluid is measured by using electrochemical impedance spectroscopy and the proper actuation voltage applied to the electrodes. For high ionic strength electrolyte (like most biological buffers) the electrical behavior of the fluid is similar to resistive and as a result the AC electrothermal effect is dominant and the ac electroosmotic flow will be negligible. A proper electric field is applied to the electrode structures and fluid motion starts near the electrodes, where the flow direction is based on the electric field lines. By increasing the number of electrode pairs, net flow velocities observe inside the channel. The particle motion and trajectories of the fluorescent particles are shown in Fig. 5 (B). measuring the pumping velocity magnitude shows that there is a good agreement between the experimental and simulation study.

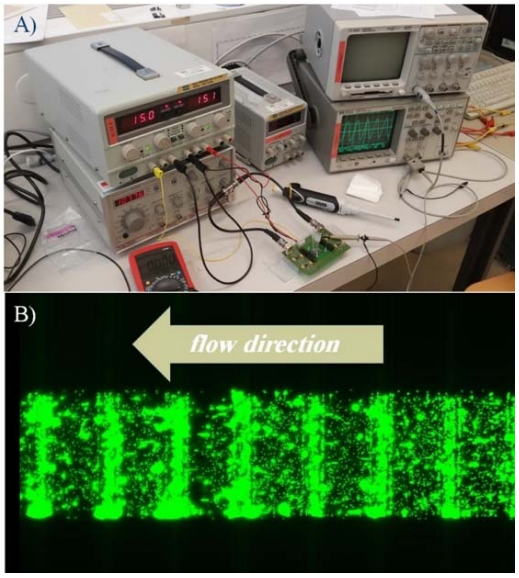

Fig. 5 A) Experimental setup: illustrating microfluidic chip on a chip holder, and electronic devices for actuation; B) Particles motion due to ac electrothermal pumping effect, (0.2 S/m water, +/−4 Vrms and 400 kHz)

IV. Conclusion

To conclude, the high ionic strength fluid motion is observed inside the microchannel by exciting the electrodes with high frequency electric potential. The fluid control and automation at microscale is achieved by electrode engineering and generating forward, reversal and rotational flows. The characteristics of electric, temperature, concentration and fluid velocity fields were analyzed by using FEM simulation study. Fluorescent particles experimentally seeded with water solution (as biological buffer) to investigate the fluid motion and micro-manipulation inside the microchannel. The measurement of the electrical property of electrolyte and the frequency response knowledge gained from this study helps us to control and automate the fluids at micro-scale.

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References

[1] Ebensberger, Y. C., Lausen, T. and Thewes, R., 2018, September. Design of a High Accuracy Spatially Distributed Temperature Sensor Array for CMOS Lab-on-Chip Applications. In ANALOG 2018; 16th GMM/ITG-Symposium(pp. 1-5). VDE.

[2] Alam, M., Golozar, M. and Darabi, J., 2018. Modelling and simulation of particle-particle interaction in a magnetophoretic bio-separation chip. Physics of Fluids, 30(4), p.042001 .

[3] Chen, X. and Zhang, L., 2018. Review in manufacturing methods of nanochannels of bio-nanofluidic chips. Sensors and Actuators B: Chemical, 254, pp.648-659.

[4] Cui, X., Liu, Y., Hu, D., Qian, W., Tin, C., Sun, D., Chen, W. and Lam, R.H., 2018. A fluorescent microbead-based microfluidic immunoassay chip for immune cell cytokine secretion quantification. Lab on a Chip, 18(3), pp.522-531.

[5] Mozaffari, M. H., Ebnali-Heidari, M., Abaeiani, G. and Moravvej-Farshi, M.K., 2018. Designing a miniaturized photonic crystal based optofluidic biolaser for lab-on-a-chip biosensing applications. Organic Electronics, 54, pp.184-191.

[6] Shwetha, M., Reddy, N. K., Pattnaik, P. K. and Narayan, K., 2018, June. Design and analysis of silicon ring resonator for bio-sensing application. In Optical Design and Engineering VII (Vol. 10690, p. 106902R). International Society for Optics and Photonics.

[7] Whitesides, G., 2018. Microfluidics in Late Adolescence. arXiv preprint arXiv:1802.05595.

[8] Yu, F., Kumar, N. D. S., Choudhury, D., Foo, L. C. and Ng, S. H., 2018. Microfluidic platforms for modeling biological barriers in the circulatory system. Drug discovery today.

[9] Liu, G., Ma, X., Wang, C., Sun, X. and Tang, C., 2018. Piezoelectric driven self-circulation micromixer with high frequency vibration. Journal of Micromechanics and Microengineering, 28(8), p.085010.

[10] Hadjiaghaie Vafaie, R., 2018. A high-efficiency micromixing effect by pulsed AC electrothermal flow. COMPEL-The international journal for computation and mathematics in electrical and electronic engineering, 37(1), pp.418-431.

[11] Gambhire, S., Patel, N., Gambhire, G. and Kale, S., 2016. A Review on Different Micromixers and its Micromixing within Microchannel. International Journal of Current Engineering and Technology, 4, pp.409-413.

[12] Prabhakaran, R. A., Zhou, Y., Zhao, C., Hu, G., Song, Y., Wang, J., Yang, C. and Xuan, X., 2017. Induced charge effects on electrokinetic entry flow. Physics of Fluids, 29(6), p.062001.

[13] Wu, Y., Ren, Y., Tao, Y. and Jiang, H., 2017. Fluid pumping and cells separation by DC-biased traveling wave electroosmosis and dielectrophoresis. Microfluidics and Nanofluidics, 21(3), p.38.

[14] Rashidi, S., Bafekr, H., Valipour, M. S. and Esfahani, J. A., 2018. A review on the application, simulation, and experiment of the electrokinetic mixers. Chemical Engineering and Processing-Process Intensification, 126, pp.108-122.

[15] Yu, H., Ye, W., Zhang, W., Yue, Z. and Liu, G., 2015. Design, fabrication, and characterization of a valveless magnetic travelling-wave micropump. Journal of Micromechanics and Microengineering, 25(6), p.065019.

[16] Gao, Y., Tran, P., Petkovic-Duran, K., Swallow, T. and Zhu, Y., 2015. Acoustic micromixing increases antibody-antigen binding in immunoassays. Biomedical microdevices, 17(4), p.79.

[17] Ramos, A., García-Sánchez, P. and Morgan, H., 2016. AC electrokinetics of conducting microparticles: A review. Current Opinion in Colloid & Interface Science, 24, pp.79-90.

[18] Yang, F., Kuang, C., Zhao, W. and Wang, G., 2017. AC electrokinetic fast mixing in non-parallel microchannels. Chemical Engineering Communications, 204(2), pp.190-197.

[19] Ramos, A., Morgan, H., Green, N.G. and Castellanos, A., 1998. Ac electrokinetics: a review of forces in microelectrode structures. Journal of Physics D: Applied Physics, 31(18), p.2338.

[20] Vafaie, R. H., Mehdipoor, M., Pourmand, A., Poorreza, E. and Ghavifekr, H.B., 2013. An electroosmotically-driven micromixer modified for high miniaturized microchannels using surface micromachining. Biotechnology and bioprocess engineering, 18(3), pp.594-605.

[21] Ng, W. Y., Goh, S., Lam, Y. C., Yang, C. and Rodríguez, I., 2009. DC-biased AC-electroosmotic and AC-electrothermal flow mixing in microchannels. Lab on a Chip, 9(6), pp.802-809.

[22] Feldman, H. C., Sigurdson, M. and Meinhart, C. D., 2007. AC electrothermal enhancement of heterogeneous assays in microfluidics. Lab on a Chip, 7(11), pp.1553-1559.
[23] Vafaie, R. H., Ghavifekr, H. B., Van Lintel, H., Brugger, J. and Renaud, P., 2016. Bi-directional ACET micropump for on-chip biological applications. Electrophoresis, 37(5-6), pp.719-726.