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Modelling of Microfluidic Channel Staging Dielectrophoretic Disjunction of Particles from Living Cells

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Abstract: Microfluidic channel form fluid manipulating units in Lab on chip systems by performing fluidic operations like transportation, sorting, mixing and separation of liquid samples by saving time and economy in a consistent way. A model of a microfluidic channel meant for separation of blood cells into red blood cells and platelets is designed and modelled using Comsol Multiphysics. The approach exploits the effect of an induced Dielectrophoretic (DEP) force on particles moving through a microfluidic channel driven by non-uniform electric field supplied by serial array microelectrodes. The tragectories of blood cells through the microchannel is modelled by applying an actuating voltage of ±3 V and ±5 V. The non-uniform electric field distribution and the DEP force inside the microchannel causes separation of blood cells. We succeeded to plot the tragectories of separated red blood cells and platelets under the influence of DEP force. The size-sensitive separation of particles from blood cells using a microchannel in the presence of non-uniform electric filed is modelled and simulated by changing the strength of applied electric field.

Keywords: Dielectric particle disjunction; Dielectrophoretic force; DNA analysis; Lab on chip; Microfluidic channel; Size sensitive separation.

1. INTRODUCTION

A class of miniaturized devices capable of processing a micro volume of fluid samples is termed as Lab on chip system. The role of such miniaturized devices is lies in their potentiality of parallelizing biomedical tests and laboratory work in less time and low analysis processing charge in a manner competitive to bench-top instruments. Lab on chip technology focuses on the fabrication of hybrid devices is by means of integrating the fluidics, electronics and various sensorics onto a single microchip [1-5]. In addition to their quantifying potentialities, these microchip devices can be function as fluidic processing units for sorting, mixing, or separation of liquid samples. Among the lab-on-chip devices, a microchip so called biochip, primarily dedicated for liquid sample processing but also designed for the analysis of solutions of amino acids, macromolecules, proteins, nucleic acids, or cells and viruses. The lab-on-chip devices mimics the integrated chips in electronics, biochemists, scientists, and medical doctors currently apply the potentiality of these devices in the context of biochemical synthesis, analysis and screening. The main applications of such biochips have emerged, from the detection of infectious diseases and diagnostics to the assessment of food quality. Several on-chip medical assessments include cell analysis, cytometry, blood analysis, nucleic acids amplification, genetic mapping, enzymatic assays, peptide analysis, protein separation, toxicity analysis and bioassays, drug delivery etc. Technical limitations such as size reduction, sample input rates, power consumption, but also chip reliability and biocompatibility shall all be accounted in the design of lab-on-chip devices.

Lab-on-chip devices have become very attractive nowadays as they force the development of personalised devices for point-of-care treatments [6]. Microfluidics challenged the era of Lab on chip technology by manipulating micro volume of fluids in these biochips carrying all biochemical processes performed in centralised laboratories in a short time with less cost. Lab on chip systems composed of microfluidic channels, micro sensors and actuators which paves a consistent way for miniaturization, integration, automation of micro devices. Many microfluidic biochips for biomedical analysis like blood cell filtration, separation and fractionation [7-10] and DNA protein analysis [11-14], have already been developed based on the processes like sedimentation, centrifugation, hydrodynamic methods, electrophoresis, dielectrophoresis and magnetophoresis.

By exploiting the behavior of dielectric particles in a non-uniform electric field [15] we designed and modelled a microfluidic channel for a biochip driven by serial array of microelectrodes to perform size-sensitive disjunction of dielectric particles from living cells using Dielectrophoretic (DEP) force. For demonstrating the working of the microchannel we chose mixed blood cells as sample and set an electric potential of ±V volt on the micro electrodes to control the sample flow through the microchannel. As the first part of modelling of the structure the spatial gradient of non-uniform electric field in the

frequency domain for the designed structure has been simulated using Comsol Multiphysics, and then we modeled splitting of platelets and red blood cells (RBCs) in this microfluidic structure.

2. MICROFLUIDIC CHANNEL DESIGN

The model of microfluidic channel that we have designed for a biochip separates dielectric particles from living cells. Figure 1(a) shows the two dimensional geometry of designed structure of microfluidic channel that forms fluid processing unit in a biochip. It consists of two inlet1 and inlet2, for mixing and injecting blood cells with carrier fluid into the microchannel. Each inlet is designed to have a height of 180×10^{-6} m and 40×10^{-6} m. The inlet1 carries living cells say blood cells and inlet2 supplies carrier fluid. We have simulated the working of the present micro device for two different operating voltages such as ±3 V or ±5 V. The inflow velocity for inlet2 has been set as 450×10^{-6} m/s which is greater than that of inlet1 say 120×10^{-6} m/s. A serial array of square microelectrode has a dimension of 30×10^{-6} m configured on either side of microchannel act as micro actuators to perform the disjunction of blood cells inside the microchannel. Each microelectrode has an alternating polarity of either V+ or V- volt. Motion through a non-uniform electric field, creates a DEP force on these dielectric particles causes a DEP separation of blood cells into platelets and red blood cells. The separated cells can be ejected out through outlets in which outlet1 and outlet2 have the same dimension as that of inlet.

3. SIMULATION METHODOLOGY

This model evaluates the disjunction of dielectric particles from blood cells, when they pass through a microchannel with a non-uniform electric field distribution. The non-uniform electric field created by microelectrodes embedded on either side of the microchannel induces a Dielectrophoretic (DEP) force on the suspended dielectric cells in the blood sample due to interaction of the particle induced dipoles with the spatial gradient of the electric field. When the electric field is computed in the frequency domain, the DEP force expressed in Equation (1) contributes to the total force acting on the particles [16]

$$F_{ext} = 2\pi r^3 \varepsilon_m real\left(\frac{\varepsilon_p - \varepsilon_c}{\varepsilon_p + 2\varepsilon_c}\right)\nabla|E_{rms}|^2 \quad (1)$$

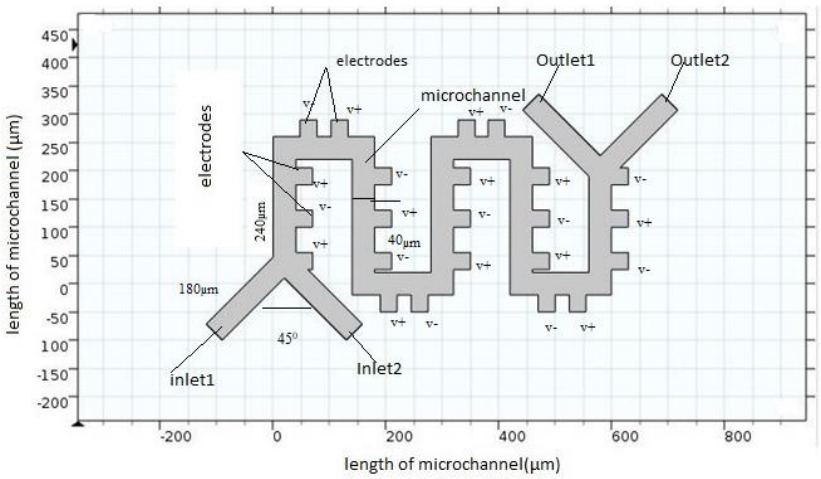

Figure 1(a). Two dimensional geometry of the modeled microchannel

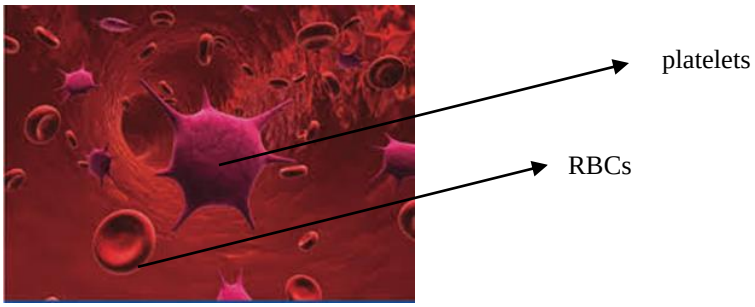

Figure 1(b). Structure of red blood cells and platelets

where ε_c is the complex relative permittivity of the carrier fluid, ε_p is the complex relative permittivity of the particle and E_{rms} is the root mean square electric field. For fields that are computed in the frequency domain, the complex permittivity can be expressed as

$$\varepsilon = \varepsilon + \frac{i\,\sigma}{\omega} \tag{2}$$

where ε is the permittivity, σ is the conductivity and ω is the angular frequency of the electric field. This expression has been useful for approximating the DEP behaviour of particles such as RBCs. The shape of real red blood cells are biconcave disks having diameter in the range of 6-8 μm and that of platelets are biconvex discoid structures having a diameter of 2-3 μm (Figure 1(b)). Both these particles contain an inner part and outer layers means membrane. The thickness of inner and outer regions of blood cells is different. Because of the dielectric nature of these particles, DEP force causes polarisation in these particles while placing in a non-uniform electric field. It causes different values of dielectric constants or permittivity for inner and outer portions of the blood cells. In this simulation study we replaced both RBCs and platelets by a homogeneous particles comprising of an interior particle (its permittivity is same as that of original particle) surrounded by thin layer of dielectric shells. The dielectric particles in a non-uniform electric field can be replaced by the dielectric shells and the complex permittivity of the shell can differ from the complex permittivity of the rest of the particle. When computing the DEP force, the complex permittivity of the particle is replaced by the equivalent complex relative permittivity ε_{eq} [17] as

$$\varepsilon_{eq} = \varepsilon_s \frac{\left(\frac{r_0}{r_i}\right)^3 + 2\left(\frac{\varepsilon_p - \varepsilon_s}{\varepsilon_p + 2\varepsilon_s}\right)}{\left(\frac{r_0}{r_i}\right)^3 - 2\left(\frac{\varepsilon_p - \varepsilon_s}{\varepsilon_p + 2\varepsilon_s}\right)} \tag{3}$$

where r_0 and r_i are the outer and inner radii of the shell, respectively, $\mathcal{E}_p$ and $\mathcal{E}_s$ are the complex relative permittivity of the particle and complex relative permittivity of the outer shell. For this model, the shell parameters for platelets and RBCs are obtained from the literature [18-21]. In this simulation, we have used three physics interfaces available in Comsol Multiphysics like Fluid Flow module, to model fluid flow inside the microchannel, AC Electric Currents module to model the electric field in the microchannel, and Particle Tracing for Fluid Flow (Particle Tracing Module) to compute the trajectories of red blood cells and platelets under the influence of drag force and DEP forces. Using these interfaces, we have followed three important steps to model the microfluidic separation of blood cells. The three important steps are:

1. Solved the steady state fluid dynamics and frequency domain (AC) electric potential.
2. Used a Time Dependent evaluation which utilises the solution from step 1 and estimates the particle trajectories in the presence of electric field that separates mixed blood cells into platelets and RBCs.
3. Plots the trajectories of blood cells without applying an external electric field.

4. RESULTS AND DISCUSSION

For this micro device, the blood cell separations with and without applying the electric potential to the microchannel have been simulated using Comsol Multiphysics considering the effect of a DEP force field. When no electric field is applied, only drag force due to carrier fluid drives the whole blood cells so they follow the same path and exit through the same outlet. Figure 2 shows the trajectories of RBCs without applying the electric field. By first step of the simulation, a non-uniform electric field distribution inside the microchannel is obtained after applying an electric potential of ±3 V. We have repeated the simulation for the same device by changing the value of electric potential into ±5 V. Figures 3(a) and 3(b) show the non- uniform electric field distribution inside the microchannel obtained by solving electric potential in the frequency domain.

As the second step of the study we obtain the trajectories of separated blood cells inside the microchannel under the influence of DEP force. The effect of DEP force is such that it separates RBCs and platelets due to their differences in their dielectric properties, traces different paths, finally platelets reaches out through outlet2 and RBCs through outlet1 of the microfluidic device. When we changed the value of electric potential, separated path traced by dielectric particles are almost same. Figures 4(a) and 4(b) show the trajectories of separated platelets and red blood cells inside the microchannel when an electric field of ±3 V and ±5 V is applied. Platelets are displayed in blue and red blood cells are displayed in red. Figures 4(a) and 4(b) clearly indicate the action of DEP force on particle separation in blood cells. There is a slight difference the electric field distribution that we obtained for ±3 V and ±5 V. Due to that small difference electric field, gradient the path of platelets gets deviated to the increased electric field distribution. A DEP force is nothing but a force exerted on a dielectric particle when it is subjected to a non-uniform electric field. An induced polarization in the dielectric particles causes the DEP force which is proportional to the gradient of the electric potential. The DEP force is sensitive to the size, shape, and dielectric properties in the blood cells, so platelets and RBCs get separated due to the difference in their size, relative permittivity and electrical conductivity.

Another application of this model is in the field of DNA and protein analysis. A single stranded DNA mixed with a buffer solution can be feed to the microchannel through any one of the inlet. Operating the device by changing the frequency of electric field will result in the DEP trapping of the molecules. The pulling out the molecules will be in the direction of higher electric field gradient. Using this idea, we can apply the above designed microchannel for separating phosphates and nucleotides in DNA. The present model of microchannel can be realised by fabricating a three dimensional structure of polymer

microfluidic device using Poly Dimethyl Siloxane (PDMS) based on the design mentioned above. We can choose a fabrication method so called soft photolithography, so that a very thin layer of microelectrodes made up of gold can be easily deposited as a serial array on either side of PDMS layer. More systematic process is needed when a two dimensional model of microchannel is converted into a three dimensional structure with a higher particle separation efficiency.

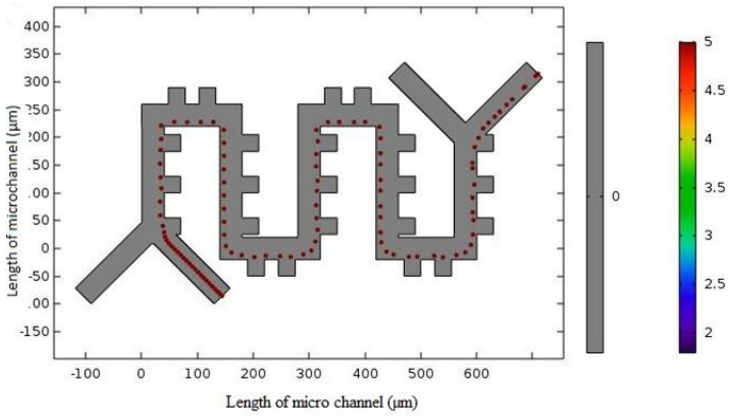

Figure 2. The trajectories of blood cells without applying the electric field, V=0

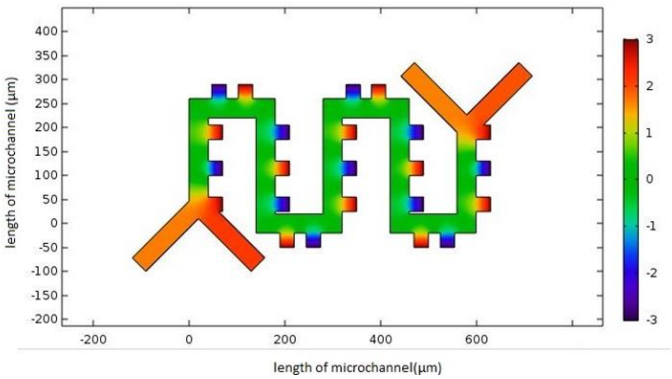

Figure 3(a). The non-uniform electric field distribution inside the microchannel when ±3 V is applied

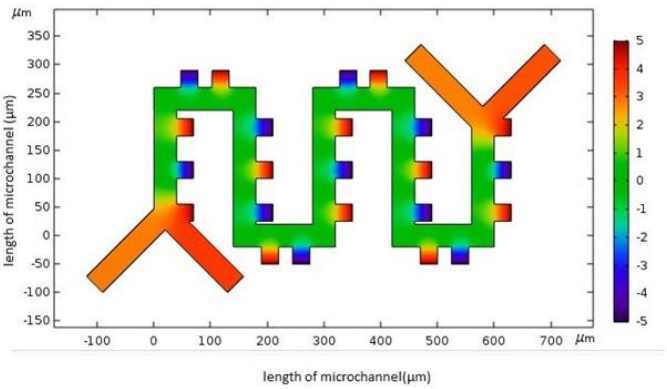

Figure 3(b). The non-uniform electric field distribution inside the microchannel when ±5 V is applied

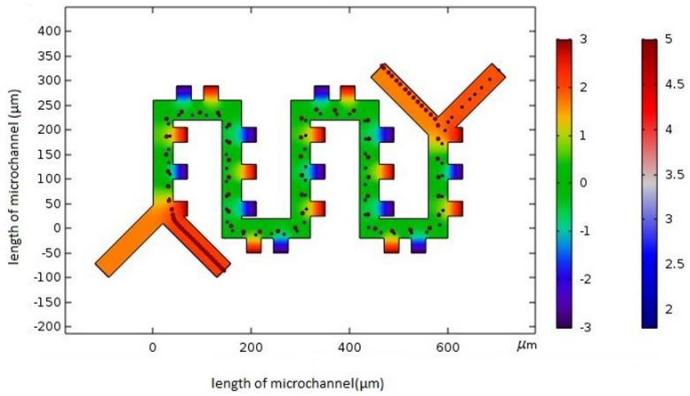

Figure 4(a). The disjunction blood cells into platelets and red blood cells in a DEP force field when an electric potential of ±3 V is applied

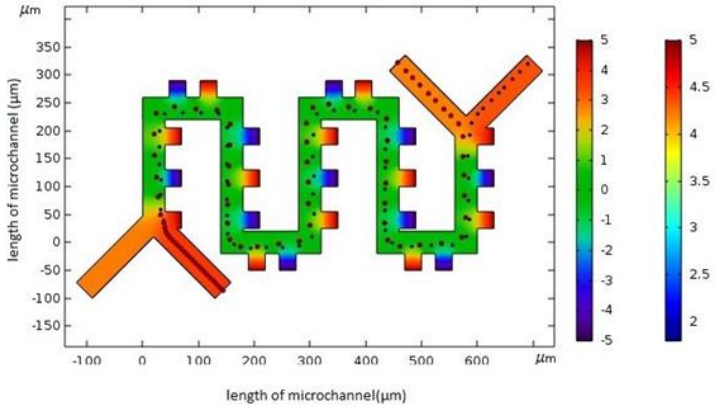

Figure 4(b). The disjunction of blood cells into platelets and red blood cells in a DEP force field when an electric potential of ±5 V is applied

5. CONCLUSIONS

By this model we design a microchannel for a biochip for size sensitive separation of dielectric particles from living cells. The present model of microfluidic channel can form a noteworthy part of a lab on chip system for performing biochemical process like separating platelets from blood cells, nucleotides from DNA or separating amino acids from proteins etc. These biochips can be developed into personalised devices for counting or measuring strength of the dielectric parts in living cells based on their sizes. This will be helpful for the personal diagnosis of various kinds of diseases decided by these parts of living cells saving the economy and time in large extend.

6. ACKNOWLEDGEMENTS

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