Design and Simulation of a BioMEMS Leukocyte Counter with Concurrent Processing

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Abstract

Cell counting (such as white blood cells, red blood cells) is a popular technique being used in blood testing for disease diagnosis. It can give important indication about the health condition of a patient, and give hints for doctors to effectively diagnose disease. In this poster, a BioMEMS (Bio-Microelectromechanical Systems) cell counter with concurrent processing is proposed. It has presorting stage to separate out red blood cells, white blood cells and/or other cells of interest from the microfluidic flow of blood sample. The cells are then passed to branching stage to divide it into multiple braches. Each branch allows cells to pass through the microchannel in series. The cell counting is achieved by electrical impedance sensing. By introducing concurrent counting based on branching, it leads to faster throughput and improved efficiency. The proposed BioMEMS cell counter is designed and simulated in COMSOL. Simulation results verified the correct counting function of the cell counter device.

Introduction

Microfluidic Leukocyte counters are promising devices in blood disease treatment due to their advantages of low cost, portability, and accuracy in healthcare. Previously, cell counters based on the mechanism of optical, electrical, acoustic or magnetic mechanisms have been demonstrated to count and analyze cells in micro-fluid structure. For the electrical detection, the sensing methods can be categorized by current sensing, voltage sensing and impedance sensing. The current and voltage sensing signals are sometimes affected by the voltage supply and external driving circuit, which may bring some inaccuracy into the measurement results. Different from the voltage sensing and current sensing, the impedance sensing Leukocyte counters are independent of circuit configuration, and the measured impedance can be also used to characterize the Leukocyte size information. This can be used to distinguish lymphocytes from erythrocytes and platelets. The Leukocyte counter based on impedance sensing can be categorized into DC and AC method. For AC method, the measurement results are sometimes affected by the impedance matching of the circuit and also affected by the electrode position, consequently, leading to low accuracy. This problem can be solved by DC impedance Leukocyte counter, which can be also called resistive sensing. Recent studies have demonstrate the advantages of impedance Leukocyte counter using a pair of electrodes in besides the micro-fluid channel, However, this structure may be influenced by the velocity of the fluid, the concentration and electrical conductivity of the liquid. In order to solve this problem, we designed and numerically verified a differential-structure bio-MEMS leukocyte counter device based on DC impedance sensing technique.

Conceptual Design

As shown in Fig.1, the geometry numerical modeling of the proposed Differential Structured Bio-Microelectromechanical Leukocyte Counter Device consists three components, namely, the micro-fluid channel, two pairs of electrodes and cells array. The left and right hand sides of micro-fluid channel are designed as inlet and outlet of solutions. Terminals 1- 2 and terminals 3-4 form two pairs electrodes, among which terminal 2 and 4 are defined as the grounding electrode. 1 and 3 are defined as positive electrode supplied by 1 V DC voltage. The voltage can be adjusted to smaller value to reduce the bubbles caused by electrolyzation. The geometry are parametrically established to provide user friendly interface to further structural optimization.

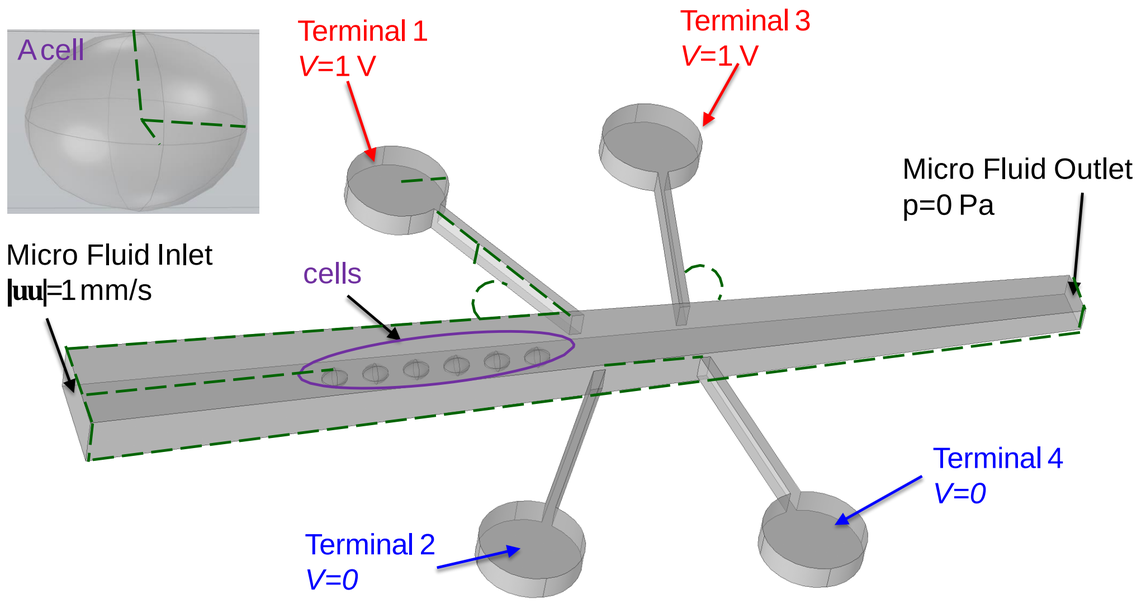

Figure 1. Adjustable Geometry of Differential Structured Bio-Microelectromechanical Leukocyte Counter Device (Note: all the geometry marked by _ _' are parametrically adjustable)

Governing Equations

Since the incompressible liquid in micro-fluid channel usually moves at relatively slow velocity, the inertial terms can be neglected. Thus, the fluid dynamics in the micro-fluid channel is assumed to be governed by Incompressible form Naiver-Stokes equations without inertial term as:

$$\nabla[-p\mathbf{I} + \mu(\nabla\mathbf{u} + \nabla\mathbf{u})^{\mathrm{T}}]=0 \quad \text{Naiver}$$

$$\rho\nabla(\nabla\mathbf{u})=0 \quad \text{Stokes}$$

p[Pa] is the fluid pressure;
$\mathbf{I}$ [I]is the unit matrix;
μ[Pa*s]is the dynamic viscosity
$\mathbf{u}$[m/s] is the fluid velocity field;
ρ[kg/m^3] is the density;

The current in the electrodes, solutions and cells are governed by Ohm's Law and current conservation.

$$\nabla\mathbf{J} = 0 \quad \text{Current Conservation}$$
$$\mathbf{J}=\sigma\mathbf{E} \quad \text{Ohm's Law}$$
$$\mathbf{E}=-\nabla V \quad \text{Electric field definition}$$

V [V] is the voltage potential;
$\mathbf{J}$ [A/m^2]is the current density;
σ [S/m]is the electrical conductivity
$\mathbf{E}$ [V/m] electric field;

Results and Discussions

The model is solved by stationary MUMP solver based on fully coupled method with assumption of quasi-static problem. Parametric study is applied to simulate the leukocyte moving process. The differential structured are optimized structure derived from the conceptual design in Fig.1.

- We see from Fig.2 and Fig.3 that the fluid velocity and pressures are affected by the leukocyte. Velocity field and pressure are enhanced around the cell.

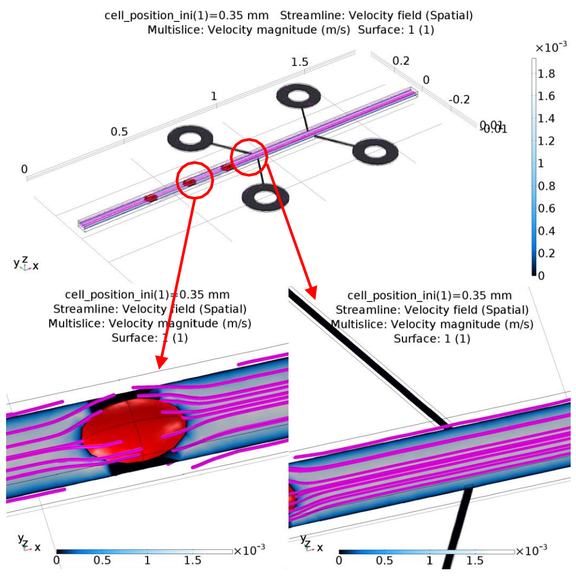

Fig. 2. The fluid velocity field with inset figures indicated by red arrows.

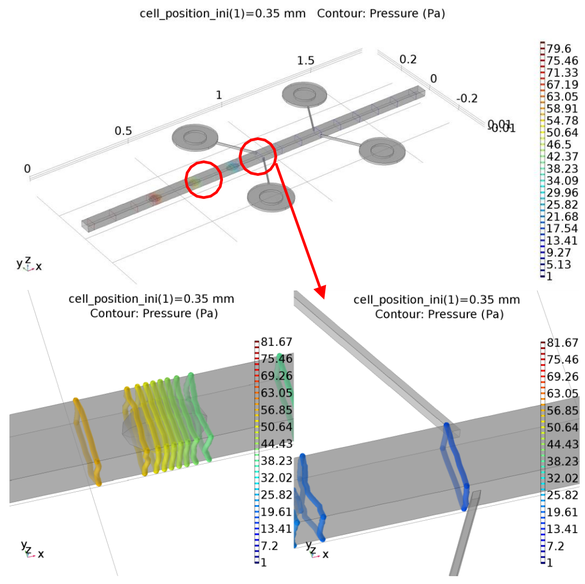

Fig. 3. The fluid pressure contours with inset figures indicated by red arrows.

- The electric potential and electric field distribution in Fig. 4 and Fig.5 indicate that, the electric potential is relatively smooth in the channel but the electric field are enlarged at edges with smaller radius. Electric field arrows starts from the positive then goes through the channel to the negative electrodes.

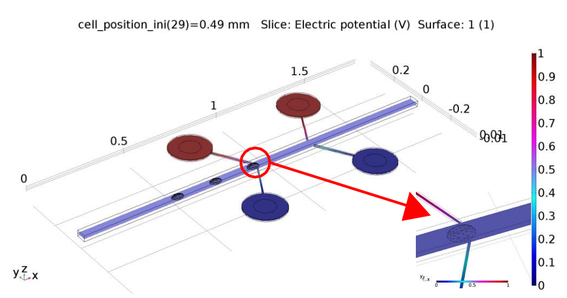

Fig. 4. Electric Potential field, V when leukocyte cross the electrodes

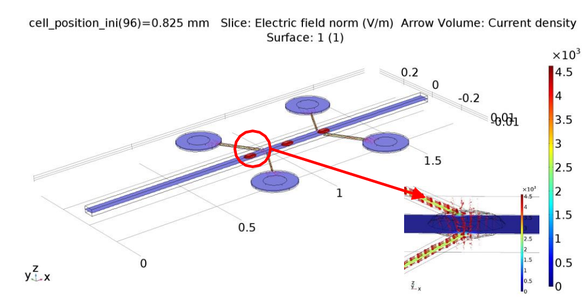

Fig. 5. Electric field, E when leukocyte cross the electrodes

- Current and impedance calculation results are shown in Figue.7. Each inset figure in Figure.7 corresponds to 3 stages, namely, Far away, arriving and departing.
- We see from Fig.6 that current trends to concentrate in cells during passing through the electrodes regions, consequently, results in larger terminal current and lower terminal impedance.
- The differenced structure lead to immune the common mode noise and results in higher signal to noise ratio. At the same time, it can be functioned as double checking the cell numbers.

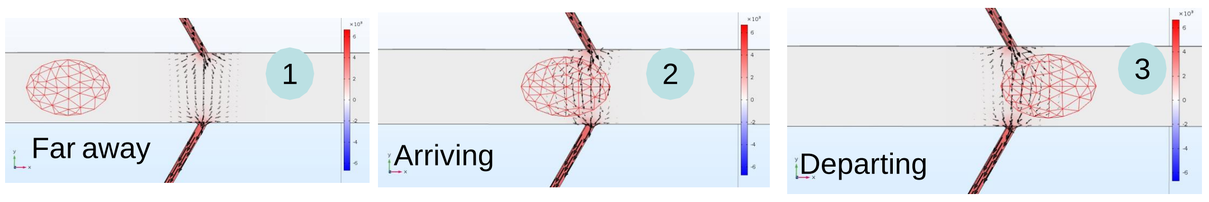

Fig. 6. Current density and directions at different transporting stages.

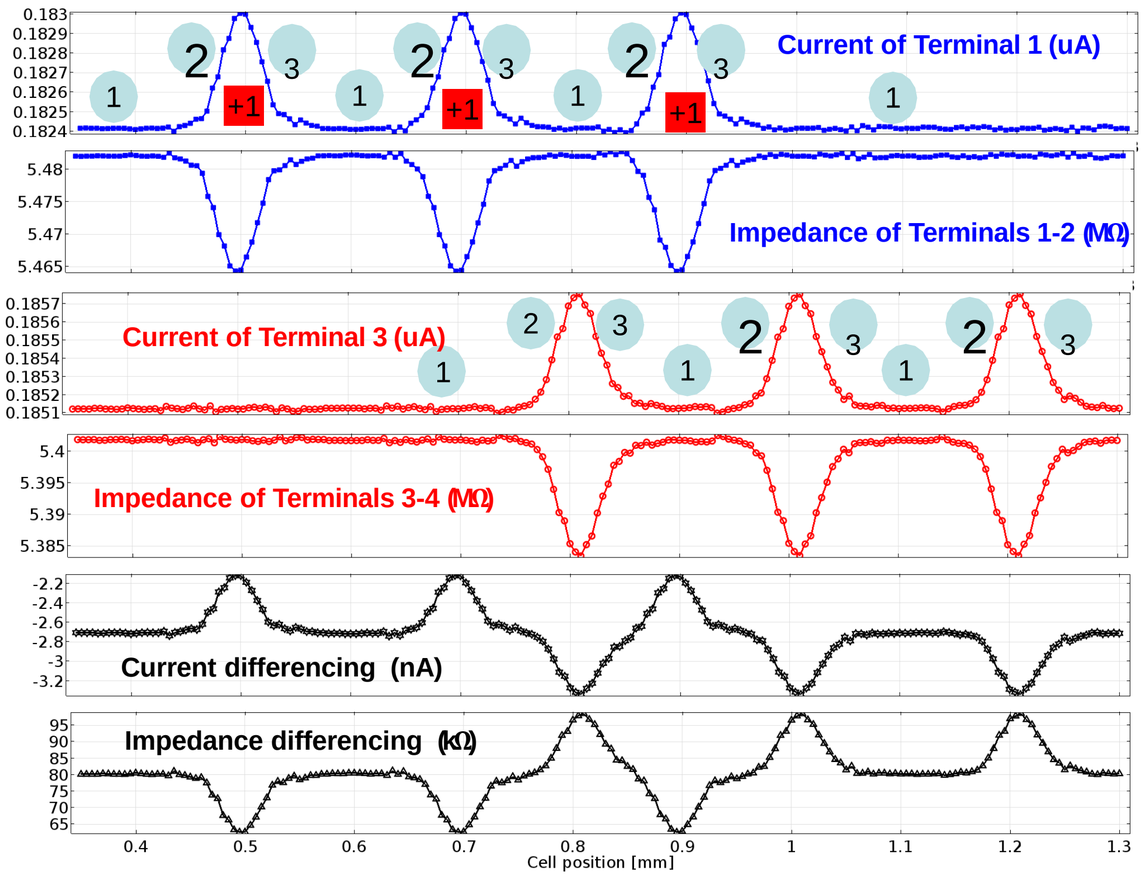

Fig. 7. Simulated Sensing Signals of currents in Terminal 1 and 3, impedance between terminals 1-2 and 3-4, and current differencing results at different stage.

Future Work

Adding the separation stage and separating cells from blood. Through parallelism counters, calculating data of different kinds of cells.

References

[1] MEI, Zhe; LIU, Zhiwen; ZHOU, Zhiguo. A compact and low cost microfluidic cell impedance detection system. 2016.