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Development of a hybrid DEP-SAW device for trapping/sensing target cells

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ABSTRACT

For detecting cells by Surface Acoustic Wave sensors, a sacrificial layer with antigens is usually used to trap cells. This paper introduces a new idea where Dielectrophoresis force traps target cells instead of a sacrificial layer that reacts with target cells and sensed by the surface acoustic wave. Therefore, one can use the sensors more than once, and it is possible to trap different types of cells with different dielectric properties. The device is simulated, and the main parameters of a Dielectrophoresis trapping system and Surface Acoustic Wave sensor, have been introduced and optimized. The effects of focused and unfocused electrode are studied numerically on the displacement of the sensor. Eventually, the feasibility of using the hybrid sensor to trap and detect target cells is investigated experimentally. Experimental results show that the Dielectrophoresis-Surface Acoustic Wave sensor can trap and detect the White Blood Cells, RPMI and U87.

1. Introduction

Surface Acoustic Wave (SAW) in piezoelectric materials was introduced by Lord Rayleigh in 1885 [1]. White and Voltmer developed the use of an InterDigital Transducer (IDT) in 1965 [2]. SAW is one of the waves that propagate along the surface of a substance. In SAW sensors, comb-shaped electrodes are coated on a piezoelectric substrate. By applying a sine wave with a specific frequency to the IDTs, vibrations are created in the piezoelectric substrate. The acoustic wave propagates along the surface of the substrate while oscillating perpendicularly to the direction of oscillations. SAW's penetration through the thickness of substrates is almost as significant as its wavelength. Therefore, the substantial part of the wave energy is on the surface of the substrate. Sound wave velocity in piezoelectric materials is about 10–5 times less than that of electromagnetic waves. Thus, the sound wavelength in piezoelectric materials is 10–5 times less than electromagnetic waves, making it suitable to fabricate a compressed and integrated system [3]. Recently, SAW sensors have been widely used. Biological sensors that operate based on surface waves could be a very reasonable replacement for expensive biological sensors like Surface Plasmon Resonance (SPR), Fluoro Immunoassay (FIA) or Radio Immunoassay (RIA) [4,5]. In order to increase the sensitivity of SAW sensors, acoustic energy on the surface of the substrate should be maximum and wave scattering should be minimum [6]. To achieve this goal, Love wave devices have been developed.

In this device, Shear Horizontal-SAW (SH-SAW) propagates through a piezoelectric substrate coated by a waveguide layer [7]. The most critical component of a typical SAW sensor is a thin film sensitive layer to trap target cells. A wide variety of materials have been used as thin film sensitive layer including polymers, carbon nanotubes and Graphene oxide [8–15]. Sensitive or sacrificial layers have two disadvantages. First, they are costly; second, they are sensitive to specific cells or biological target cells. Finally, the reaction layer sacrifices and then it is not possible to use the sensor again.

Some trapping mechanisms have been developed which are not reactive such as sacrificial layers. For instance, using acoustic pressure, electric field or magnetic field are the bases of the methods to trap target cells. Acoustic tweezer is one of the most commonly used methods to manipulate particle using the standing pressure wave [16,17]. This method is used to trap particles which are larger than the wavelength. Also, Dielectrophoresis (DEP) is used to manipulate and separate cells in microfluidic systems [18,19]. The DEP force depends on the gradient of the electric field and dielectric properties of particles and its medium. Different electrode patterns have been proposed to achieve this gradient [20,21].

In this paper, a novel SAW sensor is developed to trap and detect cells using the DEP force. The DEP is used to trap target cells, and SAW sensor is used to detect the cells. There is no sacrificial layer in the DEP-SAW sensor. Therefore, one can use the sensors more than once. Besides, it is possible to trap different types of cells with different dielectric properties using the DEP force. Trapping cells using the DEP force and Love wave propagation in lithium niobate ($LiNbO_3$) with

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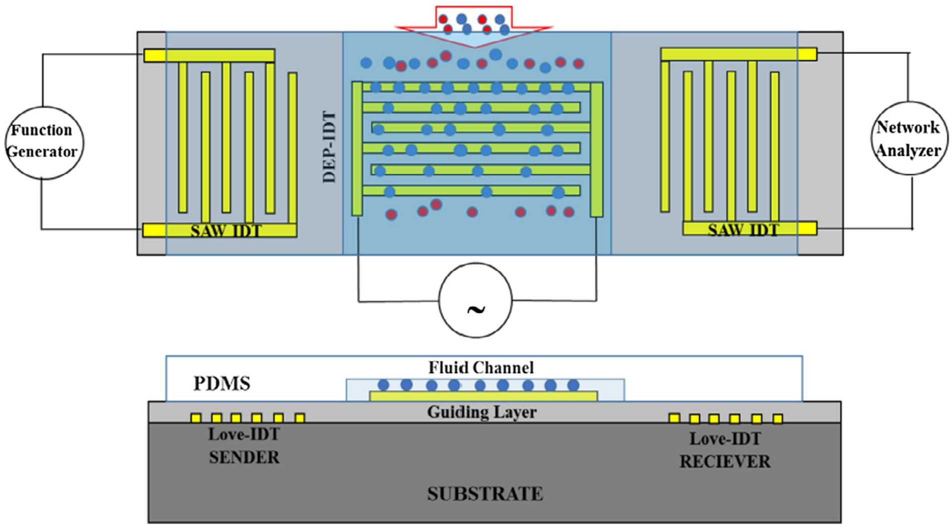

Fig. 1. DEP-SAW sensor components.

guiding layers of zinc oxide (ZnO) has been simulated numerically. The main parameters of a Dielectrophoresis trapping system and Surface Acoustic Wave sensor have been introduced and optimized. Eventually, the feasibility of using the proposed sensor to trap and detect White Blood Cells (WBC), RPMI and U87 cells have been shown experimentally.

2. Principles of the DEP-SAW sensor

Love wave is a type of shear waves which has shear oscillations tangent to the surface and perpendicular to the propagation direction. It is practically formed when a guiding layer is located on a piezoelectric surface. The main prerequisite for the propagation of Love wave is that the shear wave speed in the guiding layer should be lower than that of the substrate. Any changes on the substrate properties can change the wave speed and the wave attenuation. For instance, the reaction of the substrate with a thin layer on the surface can change the acoustic properties of the substrate. Hence, it is possible to detect a particular gas, chemical, molecular or biological material through measuring the sound speed or receiving wave amplitude in the substrate. Adding any mass on the surface of the sensor can change the wave amplitude of the receiving IDT, which in turn changes the S_{21} parameter of the sensor.

In a typical SAW sensor, there is a sacrificial layer on the delay line to make a reaction with the target cells. In this paper, the DEP force is used instead of the sacrificial layer to trap cells. In the DEP phenomenon, when a dielectric cell is put in a non-uniform electric field, if the electrical permittivity of the cell is less than the medium, the cells will move away from the point with the highest electric field gradient. On the other hand, if the electric permittivity of the cells is higher than that of the medium, the cell tends to move towards the point with the highest electric field gradient.

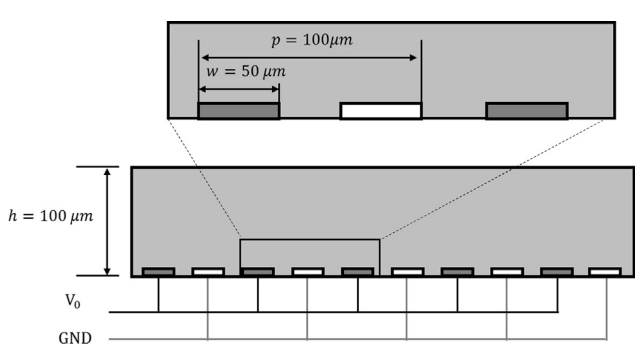

Fig. 2. DEP electrodes and boundary conditions of the simulation.

Fig. 1 indicates the components of the hybrid DEP-SAW sensor. Electrodes, substrate, wave guiding layer and fluid channel are made up of gold, $LiNbO_3$, ZnO and polydimethylsiloxane (PDMS), respectively. The task of DEP electrodes is to create a non-uniform electric field to trap target cells. The Mixture of cells enters the channel which is guided towards the DEP electrodes. The electric field frequency is chosen in a manner that the target cells are affected by the positive DEP force and attracted to the electrodes edges (blue dots), while other cells are affected by the negative DEP force and washed away by the fluid flow (red dots). Trapped cells on the delay line change the mechanical properties of the substrate.

Thus, by calibrating the sensor's output, it is possible to determine the number of the trapped cells by the DEP force without using any sacrificial layer. By interrupting the applied voltage of the DEP electrodes, the trapped cells can be easily washed away by the fluid flow, thereby will prepare the sensor for the next tests.

3. Theoretical equations

3.1. DEP force

When dielectric particles are located under an electric field, they will be polarized. If a non-uniform electric field is exerted, the net force will be determined in the following Eq. (1) [22]:

$$F_{DEP} = (p\cdot\nabla)E \tag{1}$$

In the above equation, p accounts for particle bipolar moment and E for electric field intensity. Particle bipolar moment in an alternating electric field is calculated by the Eq. (2):

$$p^* = v\alpha^* E \tag{2}$$

where p^* is complex conjugate of p, v is particle volume and α^* stands

Table 1
electrical property of WBC, Latex and medium.

Property	Unit	WBC	Latex	Medium
Relative permittivity – ε	–	104 [28]	–	78
Internal electrical Conductivity – σ	mS/m	650 [28]	2.55 [29]	800
Membrane electrical conductivity σ	S/m	237 [28]	0.93 [29]	–
Radius	µm	6.2 [28]	5 [29]	–
Mass	kg	1.01e−12 [30]	0.5e−12 [29]	–