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Optically-induced dielectrophoretic technology for cancer cells identification and concentration

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***Abstract*— The detection and concentration of cancer cells in peripheral blood is of great importance for cancer diagnosis and prognosis. Optically-induced dielectrophoresis (ODEP) can achieve high resolution and low optical intensities, and the electrodes pattern can be dynamically changed by varied light pattern. In this paper, a special lens is used to project the entire image to the ODEP chip to achieve 2.6×2 mm^2 manipulating area. By changing projected light pattern, it is demonstrated to separate 10, 20, and 40μm PS (polystyrene) beads; HT-29, 20μm PS beads. The MCF-7 cells concentrated experiments are also demo at 100 μm/sec velocity.**

I. INTRODUCTION

The early detection of CTCs (circulating tumor cells) is a significant indicator for cancer prognosis and therapy. As the few numbers of CTCs, these cells are not easily detected. The ability to detect and concentrate CTCs [1-6] in peripheral blood is of great importance for cancer diagnosis and prognosis. However, the conventional manipulating techniques cannot achieve high resolution and high-throughput at the same time, including optical tweezers [7], electrophoresis (EP) force [8-9], dielectrophoresis (DEP) force [10], traveling-wave dielectrophoresis, magnetic tweezers, acoustic traps, hydrodynamic flows, and other technologies. Among them, optical tweezers can achieve high resolution to capture single particle, but the manipulation area is only about 100 micronmeters, and the high optical intensities (~10^7 W/cm^2) could damage cells. In addition, the EP and DEP force can achieve high throughput, but lack spatial resolution and cannot manipulate single cell. The ODEP operating principle is by using light to induce non-uniform electrostatic field, and manipulate micron particles or cells. ODEP [11-12] can achieve high resolution and low optical intensities (~10^2 W/cm^2), and the electrodes pattern can be dynamically changed by varied light pattern.

However, the light efficiency and manipulating area for ODEP are limited. Here, we present a special designed lens to project the entire light image to the ODEP chip to achieve high light efficiency and large manipulating area (2.6×2 mm^2). The generated ODEP manipulation force can be expressed as [13]:

$$F_{DEP} = 2\pi r^3 \varepsilon_m \,\mathrm{Re}[K(\omega)]\nabla E^2$$

$$K(\omega) = \frac{\varepsilon_p^* - \varepsilon_m^*}{\varepsilon_p^* + 2\varepsilon_m^*}$$

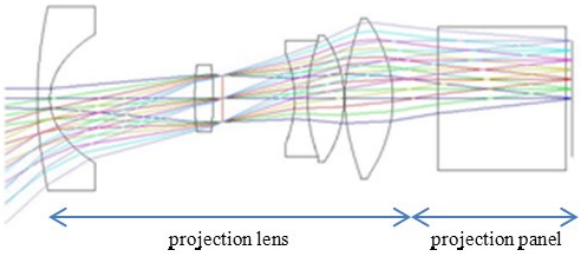
$$\varepsilon_p^* = \varepsilon_p - j\frac{\sigma_p}{\omega} \qquad \varepsilon_m^* = \varepsilon_m - j\frac{\sigma_m}{\omega}$$

where F_{DEP} represents the ODEP force, r is the particle radius, ε_m and ε_p are the permittivities of the surrounding medium and the particle, respectively, σm and σ_p are the conductivities of the medium and the particle, respectively, K(ω) is the Clausius-Mossotti (CM) factor, E is the magnitude of the imposed a.c. (alternating current) electric field, and ω is the angular frequency of the applied electric field.

II. ODEP lens design

In general, the ODEP system utilized a commercial projector through an objective lens to project the light pattern onto the ODEP chip. Due to the low iris, the controllable area is limited. Here, a special designed optical lens is proposed. Figure 1 shows the projection lens 2D layout and specification; the panel is 1.3 "SVGA; the lens focal length is 19.8mm; and the structure is 2P3G (2 plastics 3 glasses). The projector (EPSON EB-G5900) panel is 0.8 "TFT-LCD with 1024×768 resolution, and the pixel size is 15.8μm. Figure 2 shows the illuminance distribution and angular distribution for light projecting to the panel, and the light source will be used as the base value to calculate the light through the lens according to ODEP chip features. Figure 3 is the 2D-layout for light lens inversion, and the light tracking results for blue, green, red and grass green. Figure 4 is the irradiating distribution irradiated on the ODEP chip.

Figure 1 (top) 2D layout of projection lens and (down) the specification of projection lens

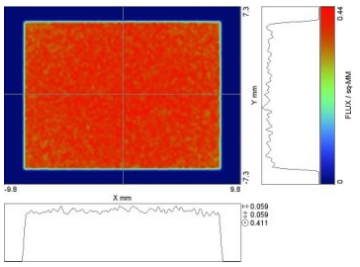


(top)

Specification of lens	
Focal length	19.8
Image circle	1.3" (diagonal= 33 mm)
F/#	3
Projection size	28"

(down)

Figure 2 (top) The irradiance on 0.8" panel and (down) angular distribution



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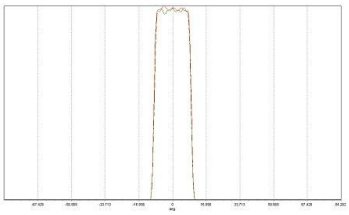

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Figure 3 2D layout of Reversing Projection lenses

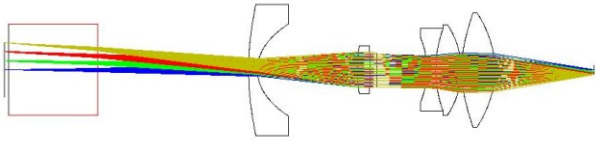
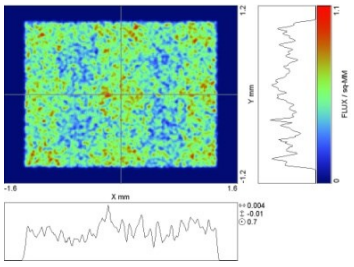


Figure 4 Irradiance on ODEP chip with (top) large emitting cone angle and (down) small emitting cone angle.



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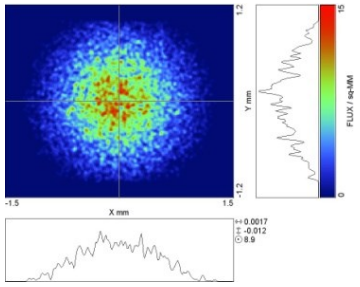


(down)

III EXPERIMENTAL SET-UP

The ODEP chip structure and system are shown in Figure 5 and Figure6, separately. The system is divided into three parts: virtual electrodes generation system, ODEP chip, and image acquisition system. The optical patterns of the virtual electrode are generated by the computer animation software, and through a special lens to project entire light pattern onto the ODEP chip, and the image is presented on a computer screen through the lens group and CCD-equipped microscope to achieve large manipulating area. By high efficiency of the classification algorithm, cells can be identified accurately and rapidly.

The ODEP chip structure consists of two indium-tin-oxide (ITO) glasses and spacer, and the liquid solution containing the cells is sandwiched between the two ITO glasses. In which, the bottom ITO glass is coated with a 50 nm n^+ a-Si:H layer and a 1 μm undoped a-Si:H layer by plasma-enhanced chemical vapor deposition (PECVD). An alternating current (AC) bias is applied between the two ITO glasses to generate an electrostatic field in the system. The AC bias is supplied by a function generator (GW instek GFG-8020H; 0~2 MHz, 0~20 V). The spacer is defined by a 3M double sided tape, and the gap size is from 30 μm to 100 μm according to the manipulated particles. In this paper, the spacer gap is fixed to 30 μm.

A commercial LCD projector (Epson EB-G5900) through a special designed lens projects the entire optical images onto the ODEP chip. In addition, a CCD-equipped microscope (ICX204, Sony) was used to observe the manipulation of micro particles in the system. The microscope can zoom from 0.52× to 6.5×.

The prepared polystyrene (PS) microbeads (diameter: 10 μm, 20 μm, and 40 μm; Duke Scientific Corporation, California, USA) were suspended in a 0.1 % bovine serum albumin (BSA, Sigma, Taiwan). The peripheral blood mononuclear cell (PBMC) is prepared in an 8.5% sucrose solution (Sigma,cat. No.S0389, Taiwan). Two kinds of CTCS are prepared for the ODEP experiment: HT-29 (human colon cancer cells) and MCF-7 (human breast cancer cells). The cells are suspended in a 8.5% sucrose solution (Sigma,cat. No.S0389, Taiwan).

Figure 5 ODEP chip: manipulating micro beads or cells

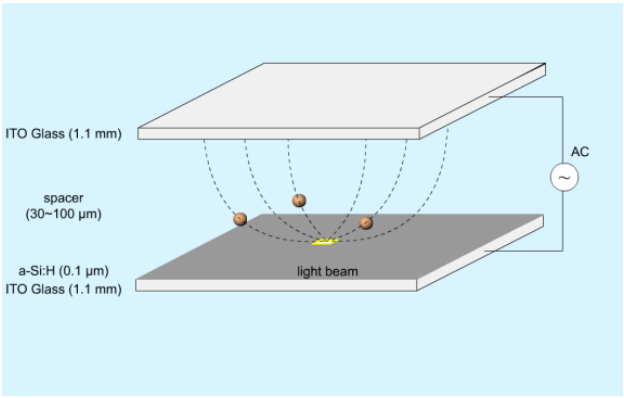
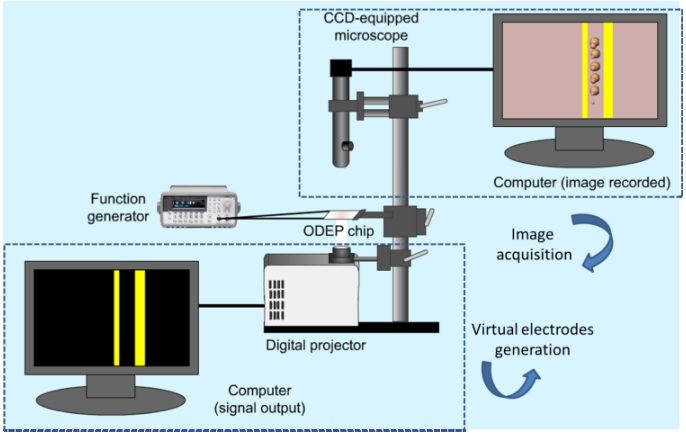


Figure 6 The ODEP system



III. RESULTS AND DISCUSSION

A non-uniform electrostatic field is created near the illuminated spots. The particles or cells interact with the local electrostatic and induce dipoles. When the permittivity of the particles is greater than surrounding medium, the particles experience positive ODEP force. Then, the particles will be attracted to the illuminated spots. On the contrary, when the permittivity of the particles is lower than surrounding medium, the particles experience negative ODEP force. Then, the particles will be pushed away from the illuminated spots.

Here, we have demonstrated to separate the 10μm, 20μm polystyrene beads and HT-29, 20μm PS beads by a 40μm light line width, as shown in Figure 7 and Figure 8. The operating condition is: light velocity =10~100μm/sec, fluidic is static, frequency= 100 kHz, voltage= 24 V.

By designing microfluidic channels with light pattern and optimizing operating parameters (e.g. frequency, voltage), the 40 μm PS beads can be confined in the central channel, while the 10 μm PS beads are randomly flowing through the channels, as shown in Figure 9. The operating condition is: light is static, fluidic velocity =50μm/sec, frequency= 50kHz, voltage= 24V.

Another microfluidic channels designed can transport the 20 μm PS beads to the desired channel, and the 10 μm PS beads are randomly flowing through the channels, as shown in Figure 10. The operating condition is: light is static, fluidic velocity =50μm/sec, frequency= 50kHz, voltage= 24V.

Cells concentrate experiments for MCF-7 are achieved at the speed about 100μm/sec, as shown in Figure 11. The operating condition is: light velocity =100 μm/sec, fluidic is static, frequency= 50kHz, voltage= 20V.

Figure 7 10 μm and 20 μm PS beads separating video.

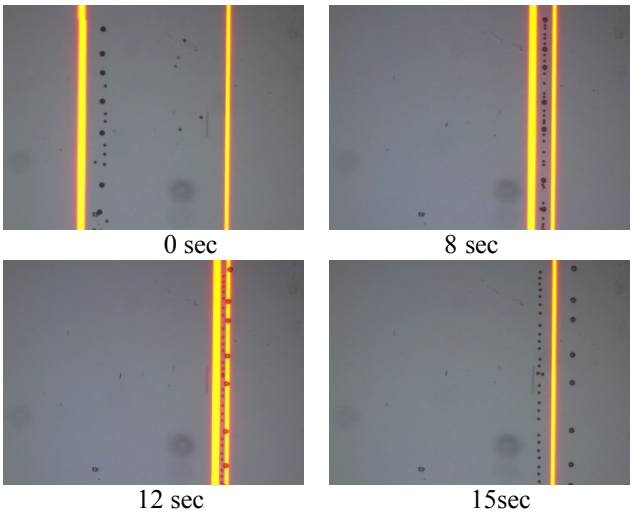


Figure 8 HT-29 and 20 PS beads separating video.

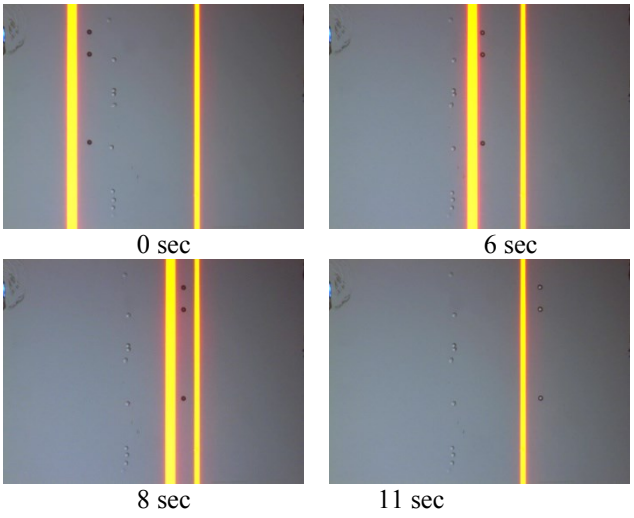


Figure 9 10μm and 40 μm PS beads separating video.

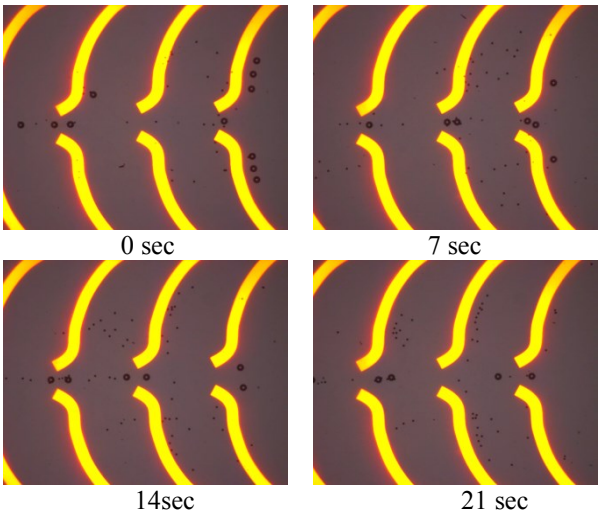


Figure 10 10 μm and 20 μm PS beads separating video.

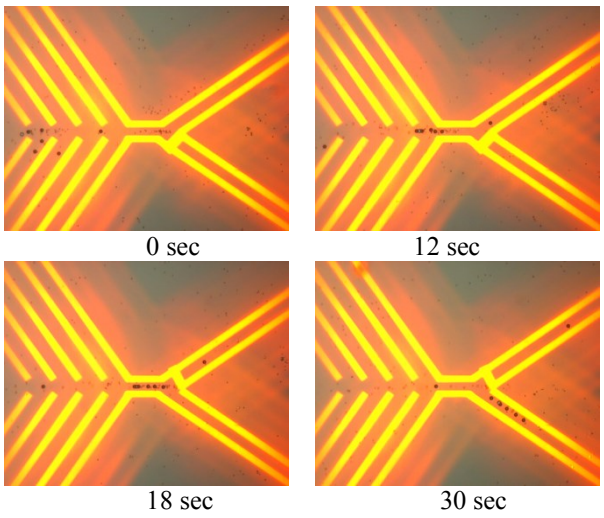
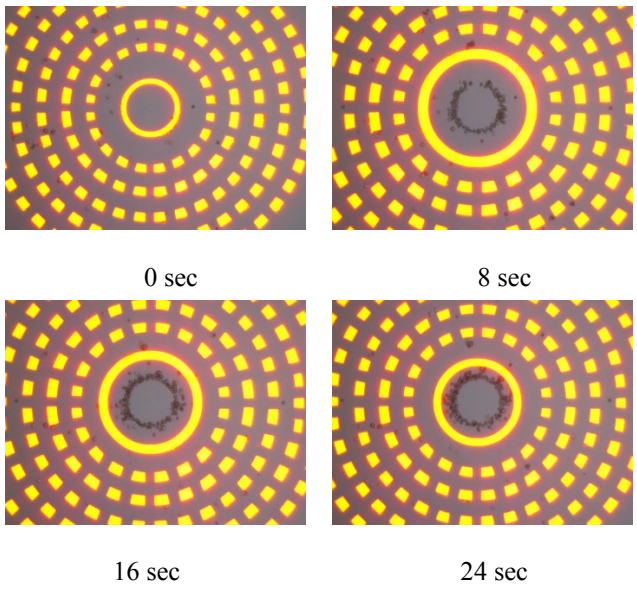


Figure 11 Cells concentrate experiments for MCF-7



IV. Conclusion

This paper combines the optical projection technology, the optical image-driven technology, and the microfluidic chip technology to separate and concentrate micro beads and cells. The ODEP technology can achieve high detection efficiency, disposable, low sample consumption, low power consumption, small size and low cost. Compared to traditional DEP chip, the ODEP can achieve high resolution and low optical intensities, and the electrodes pattern can be dynamically changed by varied light pattern.

In this paper, a special lens is used to project the entire image to the ODEP chip to achieve 2.6×2 mm^2 manipulating area. By changing projected light pattern, it is demonstrated to separate 10, 20, and 40μm PS beads; HT-29, 20 PS beads. The MCF-7 cells concentrated experiments are also demo at 100 μm/sec velocity.

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