Optoelectronic Tweezers – Optical Manipulation using LEDs and Spatial Light Modulators

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1. Introduction

Optical manipulation of biological cells in microfluidic devices is a powerful technique for high-throughput cell-based assays. It offers several advantages compared with other techniques: it is non-invasive, contamination-free, and needs no or minimum fabrication for the microfluidic devices. The most well-known optical manipulation tool is optical tweezers [1, 2]. To achieve array format manipulation for high-throughput assays, holographic optical tweezers [3] and vertical cavity surface-emitting laser (VCSEL) array traps [4] have been reported. However, these systems require very high optical power since the total amount of optical power is proportional to the number of traps. In addition, the manipulation area is limited by the tight focusing requirement.

Recently, we reported a massively parallel optical manipulation tool called optoelectronic tweezers (OET) [5]. It uses direct optical images to create high-resolution dielectrophoresis (DEP) virtual electrodes on a photoconductive surface. The optical images are generated by a spatial light modulator, which enables us to dynamically change the electrode pattern in real time. Each trapping site can be as small as a single pixel (~ 1.5 μm in our current system), sufficient to manipulate single cells or micrometer-sized particles. Thanks to high resolution optical projection, the OET is particularly suited for array-based cell manipulation. We have demonstrated 15,000 individually addressable traps.

Another important aspect of OET is the low power requirement. Since the light beam is only used to address the virtual electrodes, the optical power density requirement is 100,000 lower than that of optical tweezers. The OET can be powered by an incoherent light source such as light-emitting diodes (LED). We have successfully used OET to trap *E. coli* bacteria [6] and red and white blood cells [7], as well as the automated concentration of HeLa cells [8].

Similar devices have recently been reported by other research groups [9]. In this talk, we will review the current state of the art of optoelectronic manipulation in microfluidic devices, and describe the experimental results we have obtained with OET.

2. Device Structure

The OET creates optically-induced dielectrophoresis by creating virtual electrodes on a photosensitive surface. The optical setup and device structure of OET is shown in Fig. 1. The OET device uses two electrodes: an upper transparent electrode consisting of a 100-nm-thick indium-tin-oxide (ITO) layer on a glass substrate, and a lower photosensitive electrode. The photosensitive electrode consists of a glass substrate, a 100-nm-thick ITO layer for electrical bias, a thin (50 nm) highly-doped hydrogenated amorphous silicon (a-Si:H) layer, and an intrinsic, 1-μm-thick photoconductive layer of a-Si:H. Spacers are placed between the electrodes to form a chamber that is 100 μm in height. The height is adjustable by spacer thickness. Aqueous solutions containing cells or microparticles are introduced into this chamber. An ac voltage is placed across the two OET electrodes to provide the electric field necessary for operation.

Optical patterns are focused onto the photosensitive OET electrode, typically by a 10x microscope objective (N.A. = 0.3). The optical patterns can be created by intensity modulators, such as the digital micromirror device (DMD, Texas Instruments). The optical source OET actuation is flexible, as low light intensities are sufficient, and coherent light is not required. The types of light sources used in our experiments described include a 0.8-mW HeNe laser, a 100-W halogen lamp, a 625-nm LED, and a 10-mW, 635-nm diode laser.

3. Experimental Results

The OET has been shown to trap and transport a wide variety of microparticles and biological cells. Polystyrene particles with sizes from 4.5 μm to over 40 μm have been successfully trapped by OET. The polystyrene particles experience both negative and positive dielectrophoresis forces, depending on the frequency of the AC bias. At high frequency (~ 1.5 MHz), the OET force is positive and the particles are concentrated to the illuminated spots. At low frequencies (~ 100 kHz), the OET force is negative, which enables us to form a "light cage" around the particle [10]. Using a digital light projector to create dynamic optical patterns, many microfluidic functions have been demonstrated [11, 12], including individually addressable light cage arrays, and separation of heterogeneous polystyrene particles using comb-shaped OET patterns. An "optical conveyor" has been realized by a train of moving light cages [5]. Sorting of particles with size difference as small as ~ 1 μm has been demonstrated using a virtual optical

machine with a tilted optical conveyor patterns [5]. An alternative sorting technique based on image analysis has also been demonstrated to separate a mixed sample of 15- and 20-μm-diameter polystyrene beads in real time [13].

A large number of traps can be generated by the DMD spatial light modulator. We have successfully demonstrated 15,000 individually addressable OET traps for 4.5-μm polystyrene particles [5].

OET has also been used to manipulate live cells, including the trapping and manipulation of red and white blood cells, and the automated collection of HeLa cells. We also perform the selective concentration of live human B cells from a mixture of live and dead cells. Recently, spatial separation of live Jurkat and HeLa has been achieved using dynamic OET consisting of moving light line patterns [14]. Another group has used a similar device and setup to trap yeast cells [15].

4. Conclusions

We have demonstrated optical particle manipulation using incoherent light. By integrating a spatial light modulator and direct-imaging with optoelectronic tweezers, many dynamic, reconfigurable manipulation patterns can be employed. Using a variety of patterns, we have realized live cell and microparticle collectors, single-particle traps, and individually addressable single-particle arrays. Such particle manipulation techniques have many applications to experiments with biological cells and microparticles.

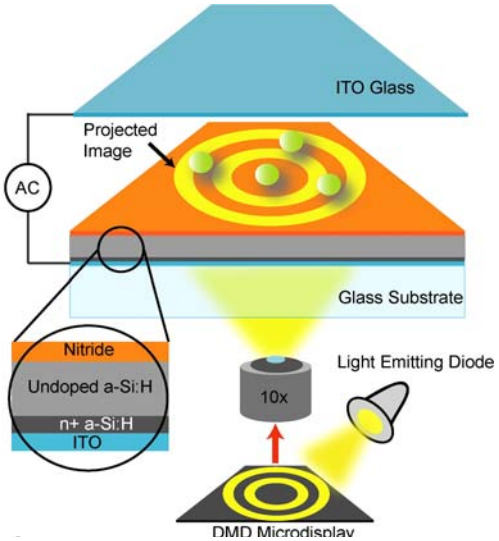

Figure 1 Schematic of optoelectronic tweezers (OET)

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