Optoelectronic Tweezers for Manipulation of Cells and Nanowires

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Abstract

Optoelectronic tweezers (OET) is a new optical manipulation technique to trap individual particles with sizes ranging from tens of nanometers to hundreds of micrometers [1]. Using optically-controlled dielectrophoretic force, OET enables complex, dynamic manipulation functions using light intensities up to 100,000 times lower than that of conventional laser tweezers. This paper will review the principle of the OET, and highlight recent advances in manipulating semiconductor nanowires and biological cells in culture media.

Introduction

The ability to trap and move objects at the micro/nanoscale in a non-contact manner is highly sought after in many fields of science and engineering, including colloidal science and cell and molecular biology. Many trapping mechanisms have been studied over the years, including optical tweezers, electrophoresis, dielectrophoresis (DEP), magnetic tweezers, acoustic and hydrodynamic forces. Among them, the optical tweezers [2] and the DEP [3] are most widely used to manipulate non-charged particles. Both use the interaction between a dipole and a non-uniform electromagnetic field, the former at optical frequency while the latter at ac frequencies between kHz and MHz. In optical tweezers, the non-uniform field is created by an objective lens with high numerical aperture. In DEP, it is generated by hardwired microelectrodes patterned on a substrate. Both forces are proportional to the gradient of the intensity (square of the field). The force is usually positive (attractive) in optical tweezers but it can be either positive (attractive) or negative (repulsive) for DEP, depending on the relative polarizability of the object and the media. Simultaneous trapping of multiple objects are made possible by holographic optical tweezers [4] and matrix electrode arrays with integrated CMOS decoders [5].

The optical tweezers have revolutionized our understanding of molecular motors [6] and had a major impact in colloidal science [4]. However, they also have some drawbacks. The high optical power requirement (~ 1 mW/trap), especially in the visible wavelength, can result in optical and/or thermal damage to live biological specimens [7]. Nanoparticles are often destroyed thermally before they can be trapped stably. DEP can trap particles with sizes ranging from approximately 1 mm down to 14 nm [8]. Unlike optical tweezers, dielectrophoresis is capable of a large effective particle manipulation area, limited only by the size of the device. However, DEP needs microfabricated electrodes with hardwired electrical connection for particle manipulation, limiting the flexibility of this technology.

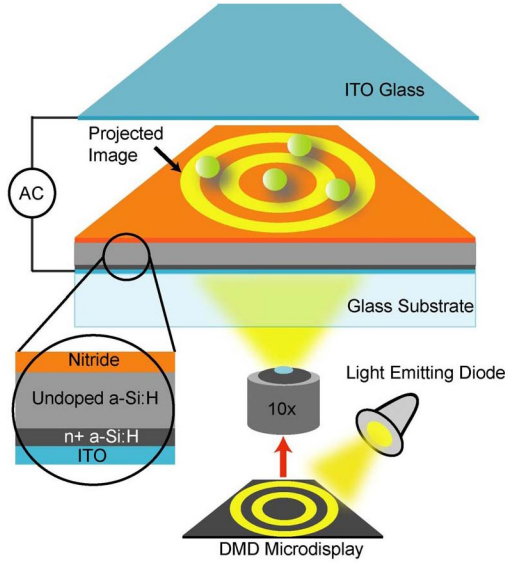

Figure 1. Schematic of the optoelectronic tweezers (OET) setup [1]. Light patterns generated by a digital-micromirror-device (DMD) are imaged onto the OET device through an objective, turning the photoconductive surface into a programmable virtual electrode for dielectrophoresis (DEP).

We have proposed a new optical manipulation technique that combines the flexibility of optical tweezers with the power of DEP without their drawbacks. This technique, called optoelectronic tweezers (OET), is shown schematically in Figure 1 [1]. Instead of hardwired electrodes, OET uses a projected light pattern on a photoconductive surface to generate "virtual electrodes". Together with an ac voltage bias across the sample chamber, the DEP forces are initiated optically. Thanks to the photoconductive gain, the optical power requirement is reduced by about 100,000 times compared with optical tweezers. This enables the formation of large trap arrays. It also permits the use of low-cost light source such as lamps or light-emitting diodes (LED) as optical coherence is not required. Indeed we have demonstrated an individually addressable array with 15,000 particle traps over an area of 1.3 mm^2 using a single LED source and a digital micromirror device (DMD) spatial light modulator [1]. The trapped particles include polystyrene beads [9], *E. coli* bacteria [10], and red and white blood cells [1]. Using dynamic optical patterns, OET can also be used to separate particles or cells by

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sizes or other visual attributes [11-14]. Since its introduction in 2003 [9], several other research groups have reported related works on OET [15-21].

Recently, we have extended the capabilities of OET to trapping of semiconducting and metallic nanowires [22] and biological cells in highly conductive physiological buffer solutions [23]. This paper will provide an overview of the principle and design trade-offs of OET, and highlight the recent advances in trapping nanowires and biological cells.

Device Structure and Setup

The schematic of the OET device is shown in Figure 2(a). It consists of a bottom photosensitive electrode and a top transparent indium-tin-oxide (ITO) electrode. The liquid containing the particles is sandwiched between these two electrodes. Our initial experiments used a 1-µm-thick amorphous Si as the photosensitive electrode. An ac voltage bias is applied across the electrodes. Light patterns generate virtual electrodes on the photoconductive surface and interact with particles through DEP, as illustrated in Figure 2(b). A typical setup for optoelectronic trapping is shown in Figure 1. The DMD turns the featureless OET device into a million-pixel optical manipulator. The optical power density on OET is typically around 0.1 to 10 W/cm^2.

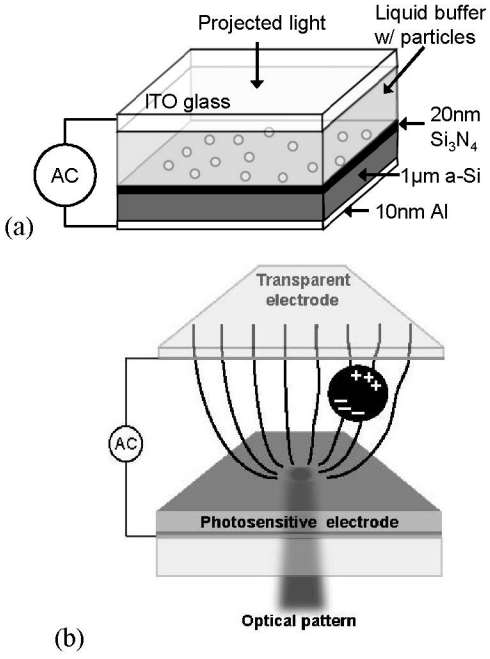

Figure 2. Schematics illustrating (a) the structure and (b) the principle of optoelectronic tweezers (OET).

Optoelectronic Trap Array

Polystyrene beads experience negative OET force at 100 kHz bias. They can be confined by "light cages". Figure 3(a) shows a 4x5 array of individually addressable traps for 45-µm beads. The size of the cage can be tailored according to the particle size, as illustrated in Figure 3(b) for trapping a mixture of 20- and 45-µm beads. Once trapped, the beads can be transported by moving the light cage, at velocities up to 40 µm/sec. Since DMD can generate any arbitrary pattern in real time, we can program it to perform a wide variety of functions. For example, Figure 4 shows the operation of an "optical sorter". A scanning optical comb pattern separates 20-µm particles from 45-µm particles.

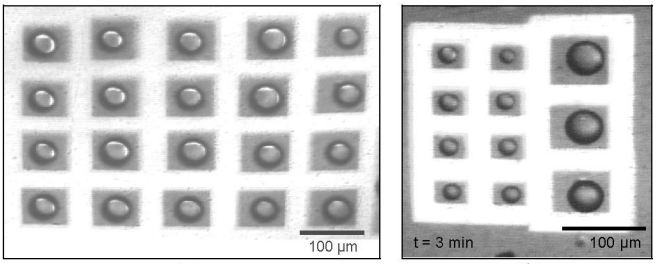

Figure 3. (a) 4x5 array of individually addressable OET trap array for 45-µm beads. (b) Trap array for a mixture of 20 and 40µm beads.

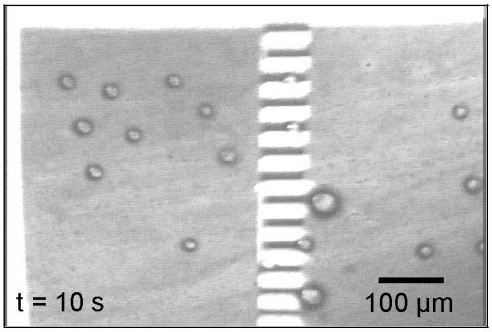

Figure 4. Scanning optical comb pattern for separating 20 and 45µm beads.

Trapping of Single Semiconductor Nanowires

The force exerted by optical tweezers is proportional to the volume of the particle. It reduces rapidly as particle size shrinks towards nanoscale. At the same time, the Brownian motion of the particle is stronger for smaller particles. Therefore, it requires a larger force to create a stable trap, and an even higher optical power to produce such traps. Trapping of semiconductor nanowires have been demonstrated using both holographic optical tweezers [24] and single-trap optical tweezers [25]. However, it requires a very high optical power density (~ 10^7 W/cm^2). It was noted that such high optical power could induce rapid heating and result in vaporization of the nanowire for wavelength shorter than that of the nanowire bandgap [24]. This is mitigated by spreading the traps along the nanowire using holographic optical tweezers, at the expense of more complicated operation.

OET (and DEP) relies on electrical gradient force. Like optical tweezers, it is also proportional to the volume of the particle. Fortunately, the real part of the Clausius-Mossotti (CM) factor that describes the relative polarizability of semiconductor nanowires is 100 to 1000 times larger than that of spherical nanoparticles with the same diameter, thanks the high aspect ratio of the nanowires. Therefore, the force exerted on

nanowires by OET is significantly larger than that by optical tweezers.

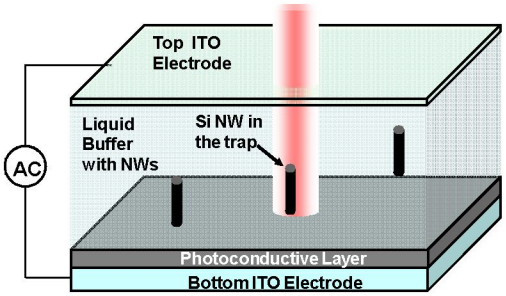

Figure 5. Schematic illustrating OET trapping of nanowires. When the ac voltage bias is applied, the nanowires are aligned vertically and trapped at the highest intensity spot.

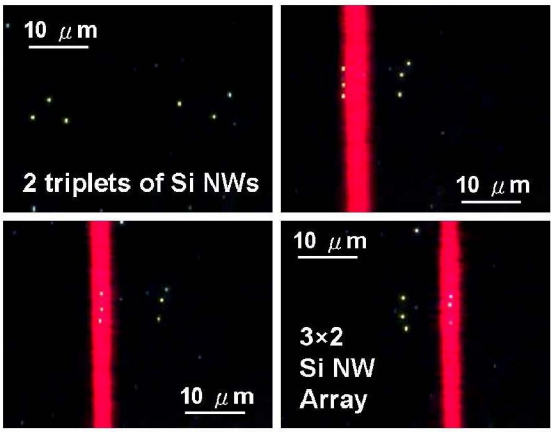

Figure 6. Snap shots of video clips illustrating OET trapping and assembly of a 3x2 array of Si nanowires with 100 nm diameter.

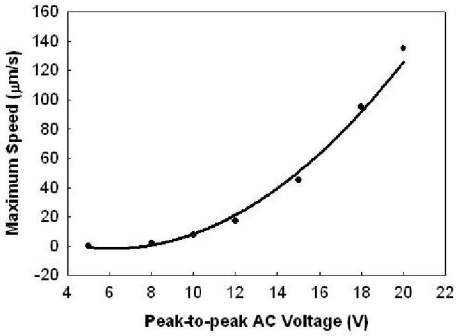

Figure 7. Maximum transport speed of trapped Si nanowires versus bias voltage.

We have successfully trapped individual semiconductor as well as metallic nanowires with diameters of 100 nm and length of several microns [22]. Doped semiconductor nanowires as well as metallic nanowires experience positive OET force. We have successfully trapped and transported single nanowires using a 100-μW HeNe laser source. It is interesting to note that even with an optical beam diameter of 10 μm, we are able to separate nanowires spaced by less than 1 μm by moving the light spot. Figure 6 shows the assembly of a 3x2 array of nanowires using a line-shaped light pattern in OET. Figure 7 shows the maximum transport speed of Si nanowire (100 nm diameter) versus the bias voltage. A maximum speed of 135 μm/sec is obtained at a voltage bias of 20 V_{pp}.

Manipulation of Biological Cells in Physiological Media

The OET manipulation of red and white blood cells and HeLa cells have been previously demonstrated [26], as well as the selective concentration of live human B cells from dead cells [1]. However, the amorphous-Si-based OET has been limited to operate only in low-conductivity solutions (less than 0.1 S/m). Typical culture media has a conductivity of 1.5 S/m. Thus, to manipulate cells in a conventional OET device, the salts that are usually present in cell culture media are replaced by osmotically-equivalent amounts of non-electrolytes to maintain the osmotic pressure on the cell membranes. These low-conductivity media are non-physiological, and eventually reduce cell viability [27]. The usage of non-physiological media also limits many biological applications, such as cell culturing and electroporation.

We have proposed a single crystalline Si phototransistor-based OET (Ph-OET) that enables the manipulation of cells in highly-conductive physiological buffers and cell culture media [23]. The schematic structure of Ph-OET is shown in Figure 8. With 100 times higher photoconductivity, we were able to trap HeLa and Jurkat cells with optical power density as low as 1 W/cm^2. A transport velocity of 35 μm/sec is achieved at 10 W/cm^2 (Figure 9).

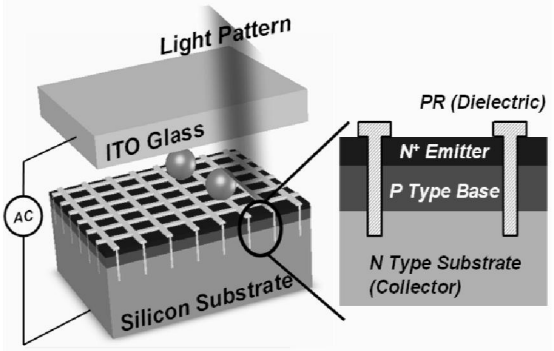

Figure 8. Schematic of phototransistor-OET for manipulating biological cells in physiological buffer solutions.

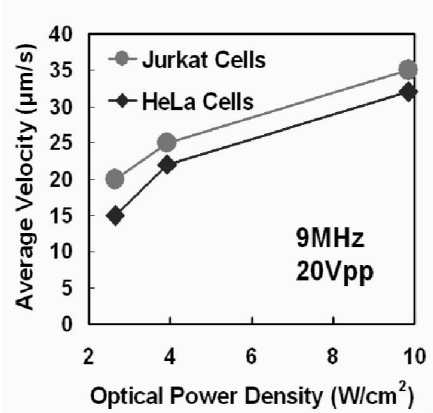

Figure 9. The maximum transport speed of trapped cells versus the optical power density illuminated on the phototransistor-OET. A maximum speed of 35μm/sec is achieved at a very low power density of 10 W/cm^2.

Conclusions

We have described a new optical manipulation technique called optoelectronic tweezers (OET). It combines the advantages of optical tweezers and dielectrophoresis, and is capable of trapping and transporting colloidal particles with diameters of tens of nanometers to hundreds of micrometers. Trapping of individual semiconductor nanowires with 100-nm diameter has been achieved. Novel phototransistor-OET capable of trapping live cells in physiological buffer solutions is also discussed.

Acknowledgment

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References

[1] P. Y. Chiou, A. T. Ohta, and M. C. Wu, "Massively parallel manipulation of single cells and microparticles using optical images," *Nature,* vol. 436, pp. 370-372, Jul 21 2005.

[2] A. Ashkin, J. M. Dziedzic, J. E. Bjorkholm, and S. Chu, "Observation of a single-beam gradient force optical trap for dielectric particles," *Optics Letters,* vol. 11, pp. 288-90, 1986.

[3] H. A. Pohl, *Dielectrophoresis: The Behavior of Neutral Matter in Nonuniform Electric Fields*: Cambridge University Press Cambridge, UK, 1978.

[4] D. G. Grier, "A revolution in optical manipulation," *Nature,* vol. 424, p. 810, 2003.

[5] N. Manaresi, A. Romani, G. Medoro, L. Altomare, A. Leonardi, M. Tartagni, and R. Guerrieri, "A CMOS chip for individual cell manipulation and detection," *Solid-State Circuits, IEEE Journal of,* vol. 38, pp. 2297-2305, 2003.

[6] K. C. Neuman and S. M. Block, "Optical trapping," *Review of Scientific Instruments,* vol. 75, pp. 2787-809, 2004.

[7] Y. Liu, G. J. Sonek, M. W. Berns, and B. J. Tromberg, "Physiological monitoring of optically trapped cells: Assessing the effects of confinement by 1064-nm laser tweezers using microfluorometry," *Biophysical Journal,* vol. 71, pp. 2158-2167, Oct 1996.

[8] T. Müller, A. Gerardino, T. Schnelle, S. G. Shirley, F. Bordoni, G. DeGasperis, R. Leoni, and G. Fuhr, "Trapping of micrometre and sub-micrometre particles by high-frequency electric fields and hydrodynamic forces," *Journal of Physics D: Applied Physics,* vol. 29, pp. 340-349, 1996.

[9] P. Y. Chiou, Z. Chang, and M. C. Wu, "A Novel Optoelectronic Tweezer Using Light Induced Dielectrophoresis," in *IEEE/LEOS International Conference on Optical MEMS*, Kona, Hawaii, USA, 2003, pp. 8-9.

[10] P. Y. Chiou, W. Wong, J. C. Liao, and M. C. Wu, "Cell Addressing and Trapping Using Novel Optoelectronic Tweezers," in *17th IEEE International Conference on Micro Electro Mechanical Systems (MEMS)*, Maastricht, Netherlands, 2004, pp. 21-24.

[11] P. Y. Chiou, A. T. Ohta, and M. C. Wu, "Continuous Optical Sorting of HeLa Cells and Microparticles Using Optoelectronic Tweezers," in *IEEE/LEOS International Conference on Optical MEMS and Their Applications*, Oulu, Finland, 2005, pp. 83-84.

[12] P. Y. Chiou, A. T. Ohta, and M. C. Wu, "Microvision-activated automatic optical manipulator for microscopic particles," in *18th IEEE International Conference on Micro Electro Mechanical Systems (MEMS)*, Miami, FL, USA, 2005.

[13] Y.-P. Huang, Y.-S. Lu, Y.-H. Chang, J. A. Yeh, and C. Lee, "Continuous cell sorting and interactive cell handling on channel-less chips using image dielectrophoresis," in *TRANSDUCERS '05. The 13th International Conference on Solid-State Sensors, Actuators and Microsystems. Digest of Technical Papers. Seoul, South Korea. Korean Sensors Soc. 5-9 June 2005*, 2005.

[14] A. T. Ohta, P.-Y. Chiou, H. L. Phan, S. W. Sherwood, J. M. Yang, A. N. K. Lau, H.-Y. Hsu, A. Jamshidi, and M. C. Wu, "Optically Controlled Cell Discrimination and Trapping Using Optoelectronic Tweezers," *Selected Topics in Quantum Electronics, IEEE Journal of,* vol. 13, pp. 235-243, 2007.

[15] Y.-S. Lu, Y.-H. Chang, S.-P. Tseng, and J. A. Yeh, "Virtual Particle Channels Based on Optical Dielectrophoresis Forces," in *IEEE/LEOS International Conference on Optical MEMS*, Takamatsu, Kagawa, Japan, 2004.

[16] Y.-S. Lu, Y.-P. Huang, J. A. Yeh, and C. Lee, "Image driven cell manipulation using optical dielectrophoresis (ODEP)," in *The Second Asian and Pacific Rim Symposium on Biophotonics (IEEE Cat. No.04EX927). IEEE. 2004, pp.238-9. Pisactaway, NJ, USA.*, Taipei, Taiwan, 2004.

[17] K. Dholakia, "Micromanipulation - Optoelectronic tweezers," *Nature Materials,* vol. 4, pp. 579-580, Aug 2005.

[18] Y.-S. Lu, Y.-P. Huang, J. A. Yeh, C. Lee, and Y.-H. Chang, "Controllability of non-contact cell manipulation by image dielectrophoresis (iDEP)," *Optical and Quantum Electronics,* vol. 37, pp. 1385-95, 2005.

[19] S. L. Neale, M. Mazilu, M. P. MacDonald, J. I. B. Wilson, K. Dholakia, and T. F. Krauss, "Size resolution with light-induced dielectrophoresis (LIDEP)," in *Optical Trapping and Optical Micromanipulation III*, San Diego, CA, USA, 2006, pp. 632618-10.

[20] G. J. Shah, P. Y. Chiou, J. Gong, A. T. Ohta, J. B. Chou, M. C. Wu, and C.-J. Kim, "Integrating Optoelectronic Tweezers for Individual Particle Manipulation with Digital Microfluidics Using Electrowetting-On-Dielectric (EWOD)," in *19th IEEE International Conference on Micro Electro Mechanical Systems (MEMS)*, Istanbul, Turkey, 2006, pp. 130-133.

[21] W. Choi, S. H. Kim, J. Jang, and J. K. Park, "Lab-on-a-display: a new microparticle manipulation platform using a liquid crystal display (LCD)," *Microfluidics and Nanofluidics,* vol. 3, pp. 217-225, Apr 2007.

[22] A. Jamshidi, P. J. Pauzauskie, A. T. Ohta, P. Y. Chiou, H.-Y. Hsu, P. Yang, and M. C. Wu, "Semiconductor Nanowire Manipulation Using Optoelectronic Tweezers," in *20th IEEE International Conference on Micro Electro Mechanical Systems (MEMS)*, Kobe, Japan, 2007.

[23] H. Y. Hsu, A. T. Ohta, P. Y. Chiou, A. Jamshidi, and M. C. Wu, "Phototransistor-Based Optoelectronic Tweezers For Cell Manipulation In Highly Conductive Solution," in *The 14th International Conference on Solid-State Sensors, Actuators and Microsystems (Transducers 2007)*, Lyon, France, 2007.

[24] R. Agarwal, K. Ladavac, Y. Roichman, G. Yu, C. Lieber, and D. Grier, "Manipulation and assembly of nanowires with holographic optical traps," *Optics Express,* vol. 13, pp. 8906-8912, 2005.

[25] P. J. Pauzauskie, A. Radenovic, E. Trepagnier, H. Shroff, P. Yang, and J. Liphardt, "Optical trapping and integration of semiconductor nanowire assemblies in water," *Nat. Mater,* vol. 5, pp. 97-101, 2006.

[26] A. T. Ohta, P.-Y. Chiou, and M. C. Wu, "Optically controlled manipulation of live cells using optoelectronic tweezers," in *Optical Trapping and Optical Micromanipulation III*, San Diego, CA, USA, 2006, pp. 632617-11.

[27] J. Voldman, "Electrical forces for microscale cell manipulation," *Annual Review Of Biomedical Engineering,* vol. 8, pp. 425-454, 2006.