Simultaneous transport of multiple biological cells by VCSEL array optical traps

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Abstract: We demonstrate the use of vertical cavity surface emitting laser arrays (VCSEL arrays) for simultaneous optical trapping, transport and active manipulation of live biological cells and microspheres, with impact on biochip array and assay technologies.

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1. Introduction

All-optical micromanipulation of micro- and nano-sized objects and biological samples through the use of optical tweezers, also known as optical traps, has become a common and useful scientific tool [1-5]. Experiments using optical tweezers have demonstrated the precise manipulation of living cells and organelles within cells [6], as well as exploration of the function and forces applied by molecular motors on such biological molecules as DNA and RNA [7-8]. In the swiftly emerging field of microfluidic lab-on-a-chip devices where the capability of transporting large arrays of biological samples in parallel can aid, for instance, the processing of cellular assays, the controlling devices must be small and be replicated in large arrays to accommodate the need in biological experiments of performing multiple, simultaneous experiments in parallel.

Previously we have reported on a technique whereby a standard packaged Hermite-Gaussian spatial mode VCSEL may be converted to a Laguerre-Gaussian mode laser through a simple post-fabrication current annealing process [9]. These higher order Laguerre-Gaussian modes resemble a toroidal shape with most of the optical power located in the outer ring of the mode. Theoretical and experimental demonstrations have shown that Laguerre-Gaussian mode laser can offer advantages over fundamental Gaussian mode lasers for three-dimensional optical trapping [10-12]. In the tightly focused beam of a three-dimensional optical trap, the greatest axial restoring force comes from photons at the largest incident angle. Photons in the center of the beam, on the other hand, produce an axial scattering force, which has a destabilizing effect on the optical trap. Removing power from the central portion of the beam by changing from fundamental Gaussian to Laguerre-Gaussian mode increases the optical trap strength along the beam axis.

In this presentation we present the novel use of vertical cavity surface emitting laser arrays (VCSEL arrays) for the parallel optical capture and transport of multiple biological cells. For a single VCSEL beam optical tweezers, we have found that the types of cells that can be manipulated will vary according to the ratio of the maximum output power of the VCSEL to the radius of the cell and its index of refraction relative to the surrounding media.

Conventionally an optical communications device, VCSEL arrays provide the advantages of being compact, individually addressable, potentially very inexpensive, and compatible with other functions desirable in biological lab-on-a-chip devices. For flexibility in various applications, VCSELs can be designed to operate at different wavelengths ranging from the blue, using wide bandgap materials [13], to the infrared using GaAs-AlGaAs. Furthermore, tunable VCSELs have been demonstrated [14] which can find use in various bio-photonics applications such as fluorescence excitation or spectroscopic analysis.

2. Experimental Setup and Results

An array of 15µm aperture proton-implant VCSELs at 850nm wavelength (Honeywell, Inc.) is coupled into a 100x, 1.25 NA oil-immersion microscope objective to create the optical tweezers array, as seen in Fig. 1. Heating within the sample is reduced by the use of 850nm light, which has low absorption in both the biological cells and the surrounding solution [15]. Several lenses serve to properly couple the VCSEL illumination into the back-aperture of the microscope objective. Coupling is also aided by a microlens array, which decreases the effective divergence angle of the VCSELs. Imaging of the sample plane with a CCD camera is performed through a dichroic beamsplitter. A two-axis motorized stage with a speed controller is used to perform drag force measurements. The sample is mounted on the motorized stage along with an additional three-axis alignment stage. The side-firing design we employ demonstrates trapping of biological cells without relying on gravity for trap stability, as is the
case with traditional inverted-microscope designs. A separate AlGaAs diode laser source (Melles Griot) is used to create a fundamental Gaussian mode optical tweezers, allowing comparison between the fundamental Gaussian and Laguerre-Gaussian mode tweezers.

We demonstrate trapping of 2x2 arrays of biological cells and measure the maximum trapping force of individual VCSEL traps. Measurements of the trapping force of the optical tweezers are performed on both biological and inert particles, including roughly 10^6/mL concentrations of live yeast cells (Fleischmann’s) and human red blood cells (San Diego Blood Bank) in Alsever’s solution, and 5µm and 10µm polystyrene microspheres (Bangs Laboratories, Inc.) in deionized water. To measure the optical trapping force, the trapped particle is dragged with increasing velocity through the surrounding medium until the fluidic drag force overcomes the maximum optical trapping force at some critical velocity. Assuming a spherical particle in laminar flow, the fluidic drag force at the critical velocity is determined from the Navier-Stokes’ equation

\[ F_{\text{drag}} = 6\pi\eta r \dot{\nu} \]  

that equates drag force with drag velocity, where the viscosity \( \eta \) for water is (10^{-3} N s/m²) and \( r \) is the particle radius [16-17].

Fig. 1. Experimental setup for VCSEL optical tweezers array

Four red blood cells in a 2x2 array were simultaneously captured and transported by the 2x2 array of VCSEL optical traps. This transport is illustrated in Fig. 2 as a sequence of CCD images showing four red blood cells in motion relative to a reference cell stuck to the sample surface. Notice the separation between cells remains constant as the group moves, held in position by optical force alone. Each cell is then individually placed at a desired location within the sample by turning off its corresponding VCSEL once in position. The pitch between optical traps of roughly 15µm is high enough to hold separate cells without overlapping. Alternatively a lower pitch array of VCSEL traps can be built that hands off particles larger than the pitch from trap to trap by sequentially turning neighboring VCSELs on and off [4].
Maximum force in the VCSEL optical trap varies depending on the size and relative index of refraction of the trapped particle, and scales with optical power as seen in Fig. 3. The maximum transverse drag force and hence the maximum optical trapping force achieved in our system is 5.7 pN for the 10 µm diameter beads, 1.8 pN for the 5 µm diameter beads, 0.79 pN for the 5 µm diameter human red blood cells, and 2.7 pN for the 4 µm yeast cell, for the maximum achievable tweezers power at the sample of 3.0 mW. Eq.1 overestimates the force on the yeast cell however, since the cell’s shape is ellipsoidal rather than spherical. Curiously, smaller particles achieve a higher maximum velocity although larger particles actually experience a higher optical trapping force. This effect can be explained by noting that the fluid drag force increases more rapidly with particle size than the VCSEL tweezers force. Lateral force comparisons between the roughly Laguerre-Gaussian mode VCSEL trap and a fundamental Gaussian mode trap showed similar lateral force levels, demonstrating that a VCSEL trap can perform as well as a fundamental Gaussian mode trap at the same power level. Theoretical reports indicate that a Laguerre-Gaussian mode should have a higher axial force than an equivalent fundamental Gaussian mode [10-12]. Our experimental apparatus is not suitable to accurate measurements of the axial force due to the increase in spherical aberration at increasing depths within the fluid sample, which decreases trap strength. Since optical power is so important to trap strength, choice of VCSEL design influences the performance of a VCSEL optical trap. Our use of VCSELs that are multimode, due to their 15 µm aperture, provides more power than a single mode VCSEL. Proton implant VCSELs employed here likewise provide more power than the oxide aperture alternative.
3. Conclusions

As a result of our experiments, we know that a Laguerre-Gaussian VCSEL optical trap has comparable transverse trapping force when compared with a fundamental Gaussian mode trap for both biological and inert particles. Armed with this knowledge we incorporated a VCSEL array into an optical trap system to show that 850nm VCSELs are capable of optically trapping and manipulating biological cells and polystyrene microspheres in an individually controllable and parallel fashion. The high device density and compactness achievable with VCSEL arrays makes them favorably suited for optical micromanipulation applications where individual manipulation of cells and high throughput are necessary, such as multiple cell parallel transport in biochip array technologies.

4. References


Fig. 3. Optical force achieved by VCSEL trap on biological cells and microspheres. Compares force of VCSEL trap (Laguerre Mode) to a fundamental Gaussian mode trap generated by a diode laser.