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Manipulation of microspheres and biological cells with multiple agile VCSEL traps

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Abstract

A microscope-integrated vertical cavity surface emitting laser (VCSEL) array trapping system capable of independent control, rotation, and batch processing of biological cells is developed and demonstrated. The trapping system is applied for manipulation of yeast cells and PC-12 cells. In our trapping system, a single VCSEL trap serves as a collector and distributor, while an array of VCSEL traps functions like a chip, enabling parallel processing of multiple objects. The trapping system here differs from earlier VCSEL tweezers set-ups in several ways, including (1) the optical traps are mobile with the addition of a static sample holder; and (2) both a single and an array of optical traps can be controlled independently by tilting mirrors at the conjugate planes of the objective back aperture, and their relative depth can be adjusted without losing trapping power. These enhancements provide an advantage for lab-on-a-chip devices that contain microfluidics, since the background flow resulting from moving the sample plane introduces complexity and uncertainty in the velocity and force analysis on microparticles or cells. In addition, independent control of traps can offer more flexibility in multi-target manipulation. Here, we address optical design considerations for keeping stable trapping performance while multiplexing. Potential improvements based on two independently controlled VCSEL arrays are discussed and related applications are investigated.

Keywords: Optical tweezers; Microfluidic system; Vertical cavity surface emitting lasers; Micromanipulator; Lab-on-a-chip; Biological cells

1. Introduction

Optical trapping was first introduced in 1970 by Ashkin as a purely physical phenomenon of radiation pressure on micron-sized particles [1]. With the discovery of optical trapping with a single laser beam in 1986 [2], optical tweezers have been widely investigated as a non-invasive manipulation technique for microparticles, such as biological cells and microspheres for biomedical research. Experimentally, the use of laser traps has not been limited to the precise manipulating living cells and organelles within cells [3–5], but also has been recently expanded to exploring the functions and forces applied by molecular motors on biomolecules such as DNA and RNA [6]. Integration of optical tweezers as a scientific tool for biochip technologies, however, has met with considerable delay due to the prohibitive cost of conventional lasers and the large system volume they occupy. Vertical cavity surface emitting lasers (VCSELs) provide a solution to this problem in that they are semiconductor microlaser diodes that emit light vertically from the surface and can be fabricated in 2-D array efficiently on a 3 in. wafer using standard microelectronic fabrication methods. Substituting VCSELs and VCSEL arrays for standard diode and gas lasers provides the ability to meet the demands of current biochip and lab-on-a-chip technologies, which require that the controlling devices be small and have the ability of being replicated in large arrays, so that multiple, simultaneous experiments can be performed in parallel and at a low cost.

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Optical trapping of live biological cells and microspheres based on a VCSEL array has been demonstrated in earlier research by fixing the laser trap and moving the sample container with a translation stage [7,8]. Nevertheless, when microfluidic channel systems (lab-on-a-chip devices) come into play, the background flow introduces some complexity and uncertainty in the analysis of velocities and forces of microparticles. Therefore, the capability of transporting microparticles without moving the sample container becomes a necessity, while at the same time, independent control of multiple optical traps is highly desirable to obtain more flexibility in object manipulation.

To utilize optical tweezers in biological applications, lasers with wavelength ranges from 800 to 1100 nm are preferred because of the low absorption by living specimens and the surrounding buffer solution. To extrapolate further on optical wavelength absorption, research on cell viability shows that cellular stress and photodamage are minimal in the range of 800–850 nm, which includes the wavelength of the VCSELs to be used in our system (850 nm) [9–12]. Since the maximal optical output power of a present VCSEL is fairly low (∼5 mW), and the relative refractive index of biological cells in the buffer medium is small (∼1.05), the available optical force is relatively weak (<5 pN). Fortunately, the Laguerre–Gaussian mode output from the VCSEL helps to form a stronger optical trap since the highest intensity is located at the outer ring of the optical aperture, resulting in a stronger 3-D optical confinement at a lower power level [13].

As a precision optical instrument, a microscope has stable and well-aligned internal optics and multiple I/O ports for simultaneous access. Integrating optical tweezers into a microscope takes advantage of all those features, and provides a compact and robust laser-manipulating system with space for functional upgrade, such as fluorescence study. According to the mounting direction of the objective lens, various configurations are available for optical tweezers. For the inverted structure used in our system, the laser beam enters the objective vertically from the downside, therefore the scattering force generated by photon momentum transfer is upwards. This counteraction of gravity and scattering force releases the requirement on numerical aperture (NA) of objective lens for 3-D trapping and alleviates the adhesion between samples and the slide, thus makes particle manipulation easier.

In this article, an optical system of independently controlled 3-D agile laser tweezers (consisting of a single laser tweezers and an array of laser tweezers) is designed according to the effect of beam symmetry and incident power on the performance of optical trapping. The microscope-integrated, VCSEL-based micromanipulator has been demonstrated and the measurement of power versus angle distribution at the microscope objective back-aperture shows good uniformity. Experimental results of batch processing and rotation of yeast cells and PC-12 cells are presented and followed with a discussion on possible improvements in the optical system. Finally, potential applications of the micromanipulator in biomedical research are explored.

2. Design of the optical system

To build an independently controlled multiple laser tweezers system, one needs to first create a single agile (movable) laser trap, then combine two or more such laser traps and make their operation uncorrelated. Generally, agile laser tweezers can be realized in three ways: (1) intensity adjustment between adjacent VCSELs in an array [14]; (2) dynamic holography [15]; and (3) beam deflection [16,17]. Intra-VCSEL array movement is not suitable for long distance continuous transportation due to the limitations in resolution and pitch of current VCSEL arrays. Dynamic holography has advantages in complex trapping patterns, especially for large, real time trapping arrays, but needs high computation volume and suffers from low efficiency and speed. Among beam deflectors, electro-optical deflectors (EOD) and acousto-optical deflectors (AOD) are cumbersome to be extended to 2-D applications and have relatively small tilting ranges (±0.6°). Based on factors such as speed, moving range, accuracy, stability, complexity, cost and system arrangement flexibility, tilting mirrors are chosen to realize agile laser tweezers in our system [18].

A good agile laser trap should maintain a relatively constant trapping power throughout its whole displacement range to allow effective object manipulation. Best trapping performance exists with the largest NA, a symmetrical trapping beam, and high enough optical power. The tilting mirror scheme realizes the displacement of a laser trap by varying the orientation of the incident beam. However, since the effective back focal plane and the back aperture of a microscope objective do not coincide with each other, the optimal trapping conditions described above cannot be maintained when the incident angle changes (Fig. 1). In previous experiments, we performed an evaluation of the influence of beam symmetry and power clipping on trapping performance [18]. From the results of the experiments we concluded that to have constantly strong laser tweezers while multiplexing (moving the trapping spot on the sample plane), complete power filling of the objective back aperture is more essential than beam symmetry. Therefore, all the optics in our system are designed to guarantee that the back aperture rather than the effective back focal plane of the microscope objective is completely filled in the whole moving span of the laser trap.

2.1. Optical realization of a two-dimensional agile laser tweezers array

To integrate the micromanipulator into a Nikon Eclipse TE200 inverted microscope, an infinity-corrected objective requiring collimated incident light is used. Accordingly, telescope optics is used in the system to serve four functions: keeping the incident light collimated, imaging the multiplex-