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Living cell manipulation in a microfluidic device by femtosecond optical tweezers

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ABSTRACT

We have realized cell sorting and manipulation in a fabricated microfluidic device by a self-constructed femtosecond optical tweezer efficaciously. The used microfluidic device with two micro-pools inside silica glass is fabricated by water-assisted femtosecond laser ablation and subsequent heat treatment. After the heat treatment, the diameter of the fabricated microchannels could be reduced significantly and the internal surface of the device could also be made much smoother comparatively, which was crucial for the subsequent experiments of living cell manipulation and cell sorting by using femtosecond optical tweezers because of the optical beam quality required. Our experimental results show that we can manipulate cells very easily by our self-constructed femtosecond optical tweezer, which demonstrates that the incorporation of the microfluidic device and the femtosecond optical tweezer is accessible and practical for the micromanipulation experiments, such as cell sorting and manipulation.

1. Introduction

Since proposed firstly by Ashkin [1] almost 30 years ago, optical tweezers have attracted great deal of attention, because it could manipulate the microscopic objects very easily in physical and biological experiments [2,3]. Especially, in recent years, some novel optical tweezer systems have been proposed and constructed, such as surface plasmon optical tweezers [4], vortex optical tweezers [5], femtosecond optical tweezers [6,7], femtosecond vortex optical tweezers [8], and so on. Due to their potential use in quantitative analysis of tiny force experiments, the optical tweezers have been widely applied to the biological experiments, such as the biopolymers' behavior under stress [9], unraveling DNA molecules [10], the walking methods of the motor proteins along molecular tracks [11] and so on. Nowadays, manipulation of living cells is very important in medical testing and cell analysis. One of the most common tools for particle manipulation is optical tweezers. And the cell manipulation by optical tweezers is often in a plate [12], special micro-tank [13], or other microfluidic systems [14,15], for sorting particles or controlling and analyzing single-cells [13,16,17].

In this letter, we present a practical method to realize the manipulation of living cells in a self-fabricated microfluidic device by femtosecond optical tweezers. Firstly, we fabricated a microfluidic device in commercial silica glass for cell sorting and manipulation by using water-assisted femtosecond laser ablation and followed by heat treatment [18,19]. The microfluidic device had two micro-pools and four microchannels. After the heat treatment, the internal surfaces of the fabricated microchannels and the micro-pools would be smooth enough for transmitting the laser beam without distortion. Secondly, the femtosecond seed laser pulses could be focused in the device by a microscope, which could be used as the femtosecond optical tweezers. The experimental results show that *Bacillus subtilis* could be moved in the fabricated microchannels and could form certain patterns in the fabricated micro-pool very easily. The incorporation of microfluidic device and femtosecond optical tweezers is useful in the field of cell sorting and manipulation.

2. Experimental setup

The glass samples used in this work are commercially available silica glass ($70SiO_2 \cdot 20Na_2O \cdot 10CaO$) which are cut into 10 mm × 10 mm × 2 mm with the upper and lower surfaces polished. The side surfaces are polished into small angle slopes. The experiments are carried out with a Ti:sapphire regenerative amplified laser system (Coherent Inc.). The repetition rate, central wavelength and pulse width of the regenerative amplified femtosecond laser are 1–1000 Hz, 800 nm, and 120 fs, respectively. Fig. 1 shows a schematic drawing of the experimental setup. A mechanical shutter with 100 ms response time is used to control the appropriate ablation time, and a circular aperture is employed to

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improve the quality of the incident beam. The linearly polarized Gaussian laser beam is focused by an optical microscope (20 ×/0.45, Nikon). The silica is moved by a computer-controlled X–Y–Z translation stage with a resolution of 100 nm. A charge coupled device (CCD) connected to a personal computer is used for monitoring the whole direct-writing process in real time. The images could be captured by the CCD camera.

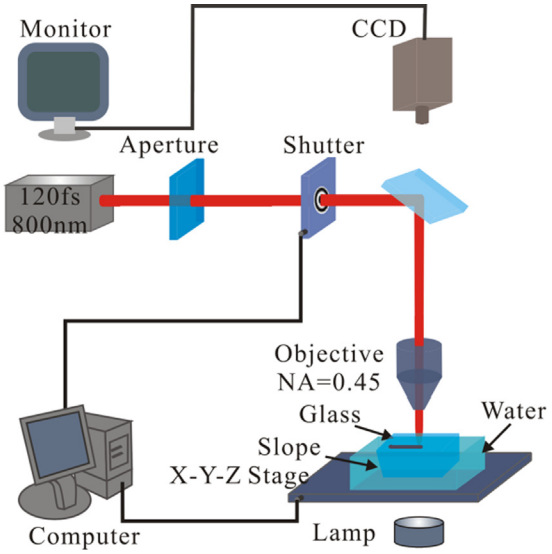

Fig. 1. The experimental setup for fabrication of microfluidic devices.

3. Results and discussion

For fabricating the microfluidic device, we first focused the laser beam on the slope surface of the used silica glass as shown in Fig. 1. Then, we dropped some distilled water around the silica glass. In our fabricating process, for obtaining excellent experimental results, we chose the pulses energy of 6 μJ. When the femtosecond laser ablated the silica glass on the surface of the slope, the distilled water was introduced into the microchannels and then the ablated debris could be ejected from the microchannels with high pressure caused by the focused pulses; therefore the blocking effect and redeposition of the ablated material could be reduced greatly. The microfluidic device is fabricated by moving the translation stage step by step controlled by a personal computer according to the designed structure. The fabricated microfluidic device has been shown in Fig. 2(a), which is fabricated at 500 μm below the surface of silica glass. The diameter of the fabricated microchannels is about 50 μm. The fabricated sample was put into a furnace, the temperature in the furnace was set at

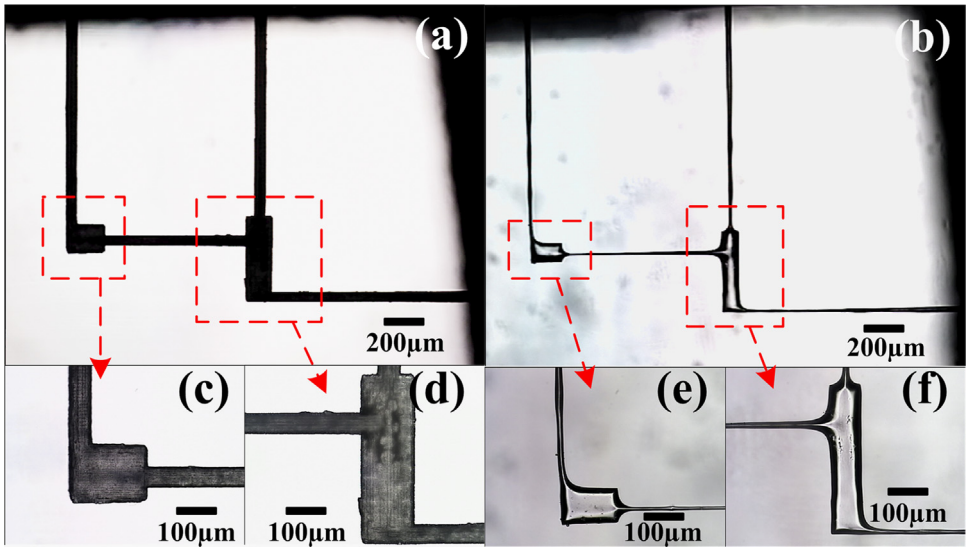

Fig. 2. (a) The fabricated microfluidic device at 500 μm below the surface of silica glass. (b) The microfluidic device after heat treatment. (c, d) The micro-pools before heat treatment. (e, f) The micro-pools after heat treatment.

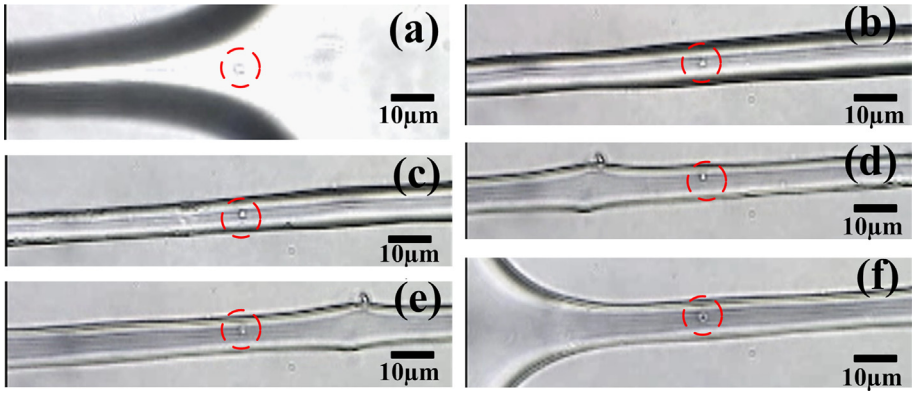

Fig. 3. (a) The *Bacillus subtilis* was captured at the head of microchannel. (b)–(e) The *Bacillus subtilis* was moved in the microchannel by the femtosecond optical tweezer. (f) The *Bacillus subtilis* was at the end of the microchannel controlled by the femtosecond optical tweezer.