Major Accomplishments in 2009 on Femtosecond Laser Fabrication: Fabrication of Bio-Microchips

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Abstract: Femtosecond (fs) lasers have become common tools for microfabrication and nanofabrication, and a large amount of research has been carried out in this field in 2009. This paper reviews the major areas of achievement in 2009 relating to bio-microchips such as the so-called lab-on-a-chip (LOC) and optofluidics.

Index Terms: Femtosecond laser, microfabrication, bio-microchip, lab-on-a-chip, optofludics.

Over the past few decades, the rapid development of femtosecond (fs) lasers has opened up new avenues for materials processing, and they have already become common tools for microfabrication and nanofabrication. Fabrication using fs lasers is still a highly active research field in material science from the standpoint of both fundamental physics and the development of practical applications. One important recent advancement is the development of both spatial and temporal beam-shaping techniques that allow higher efficiency, quality, and resolution during fabrication [1]. Using the ISI Web of Knowledge, a search for scientific papers published in 2009 with the keywords "femtosecond laser" and "fabrication" produced 157 hits in subjects including micromachining [2], surface modification [3], surface nanostructuring [4], waveguide writing [5], photonic device fabrication [6], 3-D microfabrication and nanofabrication [7], two-photon polymerization [8], nanomaterial synthesis [9], and bio-tissue treatment [10]. Among these research areas, the number of papers describing fabrication of bio-microchips, such as the so-called lab-on-a-chip (LOC), optofluidics, and micro total analysis systems (μ-TAS), is significantly increasing. In this review, some relevant accomplishments related to the fabrication of bio-microchips using fs lasers in 2009 are introduced.

Optofludic devices have been fabricated by integrating optical waveguides into commercial fused-silica LOCs for photonic biosensing [11]. High-quality waveguides intersecting the microfluidic channel in the LOC were written by internal modification of the refractive index using a focused scanned fs laser beam. The fabricated devices had the capability to excite fluorescent molecules flowing in the microfluidic channels with high spatial selectivity. Further, the optofluidic devices were fabricated using only an fs laser [12], [13]. 3-D microfluidic channels were first formed in fused silica by fs laser direct writing followed by selective wet etching in a hydrofluoric (HF) acid solution [14]. The optical waveguides intersecting the microchannel were subsequently integrated into the microchannels by refractive-index modification using the fs laser beam. A single red blood cell (RBC) in diluted human blood introduced into the microchannel was detected by two different

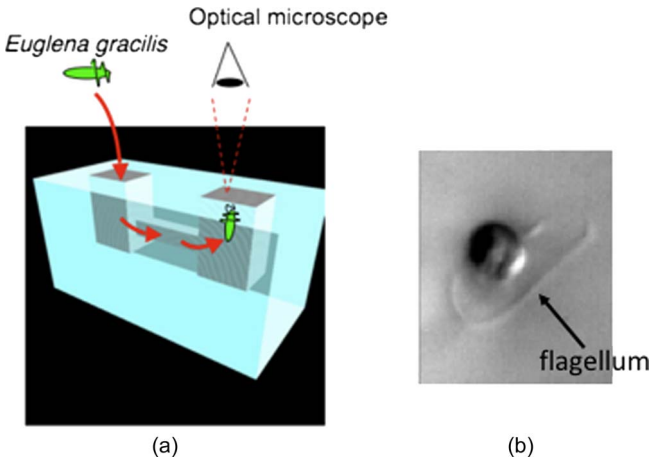

Fig. 1. (a) Schematic illustration of the concept of a nanoaquarium and (b) microscopic image of the front view of *Euglena gracilis* swimming upward in the microchannel in the nanoaquarium.

optical methods. In the first, the transmitted light intensity of an He-Ne laser beam coupled into the optical waveguides was measured. When the cell arrived at a specific region in the microchannel where the waveguides crossed, a decrease occurred in the intensity of the transmitted light due to scattering by the cell, resulting in detection of the cell. The second method involved detection of fluorescence emission from a dyed RBC excited by an Ar laser beam delivered through the optical waveguide.

A more sophisticated demonstration of the capabilities of fs lasers in the fabrication of optofluidics was the integration of a Mach–Zehnder interferometer into a microfluidic channel for label-free sensing of liquid samples [15]. The simple 3-D microfluidic channel was fabricated in fused silica by fs laser direct writing followed by HF etching. A Mach–Zehnder unbalanced interferometer was then integrated with the fabricated microchannel. The interferometer had two optical-waveguide arms of slightly different length, one of which intersected the microchannel, while the other passed above it. The interferometer can produce fringes when a sufficiently large spectral region is scanned with a tunable laser. When the light propagating through one of arms travels through a different medium, the fringe pattern becomes shifted due to the slight change in refractive index. Thus, variations in the refractive index of the content of the microchannel can be detected by measuring the shift in wavelength of the fringes. The sensitivity of the integrated interferometer was tested by filling the microchannel with glucose-D solutions of different concentrations. The fabricated optofluidic devices succeeded in clearly distinguishing solutions with concentration differences of just 50 mM, which was equivalent to a sensitivity of 1×10^{-3} in refractive index.

Another interesting application of bio-microchips is dynamic observation of aquatic microorganisms [16], [17]. Some species of microorganisms have survived almost unchanged for more than 500 million years. Some of them undergo extremely rapid motion, which is unusual in the macroworld in which we live, and display unique 3-D patterns of movement defying gravity. Most of these microorganisms are single-celled, and thereby, it is very important to explore the dynamics of their movement and their physiological energy-generation mechanisms in order to fully understand the functioning and potential abilities of the individual cells that make up multicellular organisms, including human beings. Therefore, observation of microorganisms is currently a challenging subject for cell biologists. However, using the conventional observation method, in which the microorganisms are placed in a Petri dish with water and are observed using an optical microscope with a high-numerical-aperture objective lens, it is often difficult to capture clear images due to their rapid movement and their small size. The use of a microchip with a 3-D microfluidic structure, which is referred to as a nanoaquarium, scales down the observation site, that is, the microorganisms become three-dimensionally encapsulated within a limited volume, which still provides sufficient space for movement. This makes it much easier to capture images of their movements, as shown in Fig. 1(a). The nanoaquarium was fabricated in a photosensitive glass microchip by fs laser direct

writing followed by thermal treatment, HF etching, and additional thermal treatment. It enabled us, for the first time, to obtain an image of the front view of *Euglena gracilis* swimming upward in the microchannel, as shown in Fig. 1(b). The rapid motion of the flagellum, whose diameter was several hundred nanometers, was also clearly observed. To date, several kinds of nanoaquariums with different structures and functionalities have been successfully fabricated for specific purposes, including the analysis of flagellum motion of *Euglena gracilis*, determining the information-transmission process used by *Pleurosira laevis*, observations of high-speed motion of Cryptomonas, and Phormidium assemblage to seedling roots for the promotion of vegetable growth.

Fabrication using fs lasers allows the 3-D integration of various functions in a single glass microchip with easy assembly of each microcomponent and without the need for cumbersome processes for stacking and joining substrates. Such direct fabrication of truly 3-D microstructures can be realized only by fs laser fabrication. Finally, we emphasize that such 3-D microfabrication techniques will have a significant impact on the manufacture of integrated microchips that are highly efficient for on-chip biosensing and analysis.

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