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Measurement of viscosity of liquids using optical tweezers

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ABSTRACT

We propose a method for measuring viscosities of unknown liquids by using optical tweezers combined with optical microscopy. We trapped 1-μm particles in water–glycerin mixtures and analyzed the dependence of the motion on viscosity. Based on our calibration with various water–glycerin mixtures, we propose a method for determination of viscosities of unknown liquids with high accuracy. We discuss how the method can be applied to measure the viscosity of liquids that are available only in small quantities. This non-invasive method of studying viscosities could be especially applicable in investigations of biological samples.

1. Introduction

Optical trapping is a widely used technique in many applications such as Raman spectroscopy of singly trapped beads or biological cells [1,2], photonic force microscopy with functional nanostructures [3], and the manipulation and assembly of nanotubes and nanoparticles. Various particles (e.g., atoms [4], gold and silver nanospheres [5], nanoparticles and quantum dots [6,7], microscopic bubbles [8], and aerosol droplets [9]) can be trapped, manipulated, and assembled with optical tweezers while using laser microscopy to study the physical or biological processes. Optical tweezers are effective tools in mechanical and single molecule measurements [10], single cell and single molecule sorting [11], trapping and rotation of bacteria [12], the study of bacterial adhesion [13], and study of red blood cell aggregation [14]. Laser trapping can be combined with a variety of other optical techniques. For instance, the combination of optical tweezers with simulated emission depletion nanoscopy [15] has been reported. In that study, polymer particles were attached to both sides of a strand of DNA to trap and stretch the DNA. Six-fold resolution over confocal imaging was demonstrated. Another example of combination is 3D holographic optical tweezers with a spinning-disk confocal microscope for the study of the kinetics of cell division in yeast [16].

The objective of the present work is to develop an optical system combined with optical tweezers to be used for measuring and analyzing viscosity inside biological cells, cell elasticity, and the transportation of particles by the cell. For the viscosity case, Marina Kuimova and others have developed a unique approach to measuring the microviscosity of the environment of a molecular rotor which is applicable to biological systems [17]. They are able to determine the viscosity by measuring its fluorescence lifetime. In our case, we are able to measure viscosity by analyzing the micro displacements of the trapped bead in different directions. Analyzing biological cell viscosity can be applied for the cell diagnosis and will provide a better understanding of the drugs delivery to the cell.

2. Experimental setup

In this paper, we present an experimental technique for analyzing the viscosity inside a small volume of liquid. This technique utilizes optical tweezers and is principally compatible with live cell imaging. To describe our technique, we briefly explain the fundamental theory of optical tweezers. An optical trap is formed by tightly focusing a laser beam with an objective lens of high numerical aperture (NA). The optical trapping force can be described as the sum of two forces, the gradient and scattering forces. The gradient force pulls the particle towards the focal region while the scattering force pushes the bead in the direction of light propagation.

The system combining an optical microscope with optical tweezers was constructed, as shown in Fig. 1. The epifluorescence imaging path with the microscope allows us to visualize short distances of movement of the particles that are as small as 300 nm. The NIR laser ($Nd:YVO_4$) with a wavelength of 1064 nm was used to reduce damage from the optical trap because the optical absorbance of biological tissues and cells is lower at wavelengths higher than the visible wavelengths [18,19].

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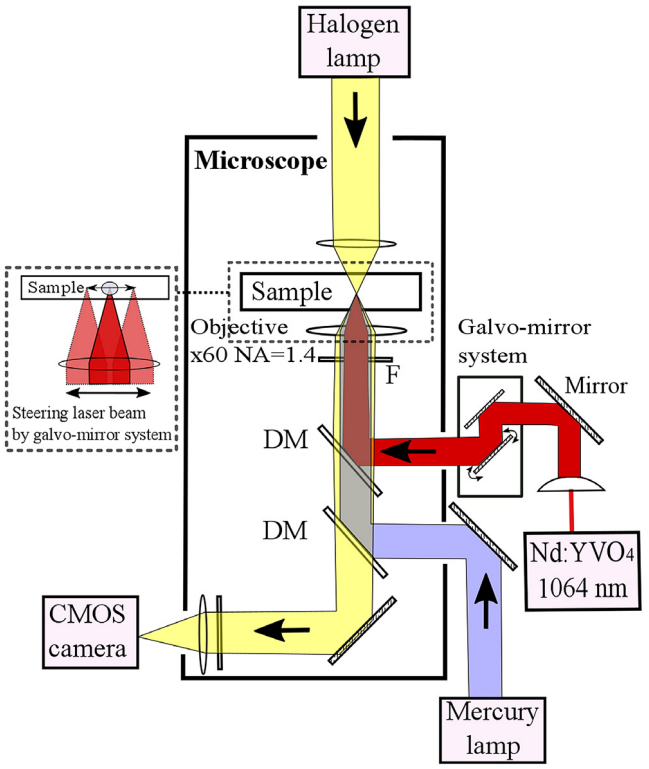

Fig. 1. Optical setup based on combination of an optical microscope and optical tweezers. A Nd:YVO_4 laser was used for laser trapping. A mercury lamp was used for fluorescence imaging. DM, dichroic mirror.

This plays an important role in the case of biological samples, as the absorption of laser radiation can damage the sample.

In our experimental setup, the trap was formed by tightly focusing the NIR laser beam with the objective lens of 1.4 NA and 60× magnification. The trapped particles were observed by imaging fluorescence or transmitted light on the CMOS camera. The trapped particle was manipulated by steering the laser beam with a galvo-mirror system (mounted XY Galvo set from GSI Lumonics, 010-3030015). For the observation of particles with sizes of a few hundred nanometers, the fluorescence was excited by a mercury lamp and dichroic mirrors and filters were used to block the excitation light. 35 mm petri dishes with 12 mm cover glass affixed to their bottom were used as a trapping chamber. This type of chamber enables high magnification and fluorescence observation under a microscope. The chamber for trapping was filled by the sample liquid.

The trajectory, amplitude, and the frequency of the movement of the trapped bead can be controlled by a galvo mirror system, as shown in the inset of Fig. 1. As a preliminary test, we trapped and manipulated 1-μm diameter polymer spheres. The trapped particles were moved along short distances of 5 μm. A major advantage of this technique is that, depending on the application, the distance and the direction can be changed. This provides the ability of measuring the dense and inhomogeneous space inside a cell.

3. Results

3.1. Trapping and resolving 300 nm fluorescent particles

Different types of cells can uptake different sizes of particles. Depending on the size, shape, and variation in the surfaces of nanoparticles, a particular cellular internalization route may be preferred over others [20]. There are cells that can uptake 1 μm particles [21], for example human umbilical vein endothelial cells (HUVEC), human urinary bladder carcinoma ECV 304, head and neck tumor HNX 14C. For calibration of the presented technique 1-μm diameter particles were used, however we demonstrate that the trapping and visualization of 300 nm is possible for the case if the cell uptakes smaller than 1-μm diameter particles. For possible future applications, we demonstrate that particles as small as 300 nm can also be trapped in three dimensions. Polymer spheres 300 nm in diameter were trapped in water. To test whether the particle can be trapped in three dimensions (3D), we slightly changed the z-position of the focal plane. Fig. 2 shows two different focal positions. At both positions, the trapped particle was seen to stay in focus while the particles that were not trapped changed focus.

3.2. Dependence of particle displacement on the frequency of trap motion

Various concentrations of water and glycerin were used in our experiment. In presented experiment 10%–40% water/glycerin mixtures were used. Glycerin is well studied and soluble in water, good for varying viscosities.

The amplitude and trajectory of the trap movement were fixed, but the frequency was variable. The range of applied frequencies was 1–20 Hz. Fig. 3 represents an example of manipulation of a trapped particle in our experiment. We investigated the relationship between sample viscosity and the displacement of the trapped particle. With increasing frequency, the displacement of the trapped particle decreases because of the drag force caused by the viscosity of the liquid. By

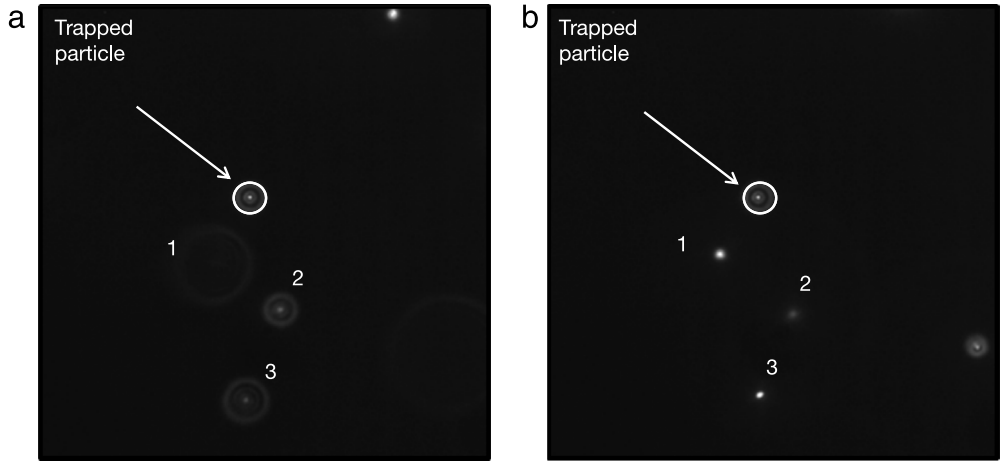

Fig. 2. Trapping 300-nm fluorescent polymer spheres in 3D. The trapped particle is marked by a white circle and arrow. Several un-trapped particles are marked: 1, 2, and 3. Images (a) and (b) were captured at two different z positions.