Comprehensive study of optical tweezers

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Abstract. This article introduces the development of optical tweezers through some examples. There is not much difference between traditional and new type of optical tweezers, the principle is similar, only that other techniques and instruments are added on the basis to help carry out some deeper investigation, for example, the principle of optical microscope is to use the optical system to magnify the image of an object, so that we can observe the tiny structures and details that are invisible to the naked eye, the principle of this kind of microscope is based on the properties of refraction and reflection of light, by focusing the light Focus on the sample, and then magnify it to our eyes or camera to form a clear image, the light will be refracted when passing through a transparent medium, the speed of light propagates at different speeds in different media, the direction of propagation of light will change when it enters from one medium to another, the phenomenon is one of the principles of the optical microscope. Other examples will be specified in this paper to illustrate the role of optical tweezers.

Keywords: Optical tweezers, light, trap, beams, momentum.

1. Introduction

When Kepler first described the sun's rays being deflected by a comet's tail in 1619, he realised that light could impose a force on matter. The radiation pressure along the path of light transmission, however, was not anticipated until Maxwell's theory of electromagnetic around the turn of the nineteenth century, which included the phenomena of light [1]. With the use of a hot light source (such as an electric or arc lamp) and a torsion balance, the radiation pressure acting on macroscopic objects was identified by Nichols and Hull. Beth reported the first experimental discovery of torques created by macroscopic objects interacting with light a few decades later. He noticed quartz waveplates hung on thin quartz threads deflecting circularly polarised light as it went through them. The size of these impacts, though, was so negligible that any practical applicability was thought to be irrelevant [2]. It wasn't until 1970, in fact, that it was possible to focus enough optical power over a small enough region to appreciably impact the motion of miniscule particles or atoms, owing to the invention of lasers [3]. Arthur Ashkin created the optical tweezers [4-5], a laser beam that can control as well as immobilise small particles in an area of high intensity established at the focal point, as a result of this invention. The study of biomolecules, the measurement of forces at the nanoscale, and the investigation of the boundaries of quantum mechanics have all benefited from the new and more potent tools introduced by optical tweezers and other optical manipulation methods. From individual atoms to complete mammalian cells, optical manipulation is possible for a variety of objects, as shown in Figure 1. Arthur Ashkin was awarded the Nobel Prize in Physics in 2018 (together with half of the reward) for his work on optical tweezers.

Since the beginning of time, optical trapping and manipulation have been used in biological research, starting with their usage to catch individual Escherichia coli and tobacco mosaic viruses [6]. Early in the 1990s, methods for characterising the mechanical characteristics of biomolecules and motor proteins using optical force spectroscopy were established. These biomolecular motors are crucial for intracellular movement and mechanical operations in life. Biophysicists have been able to examine single-molecule nanoscale motor’s energies and kinetics utilizing optical traps, and optical force spectroscopy has shed light on the makeup of the following force-producing molecules [7]. From that time, optical tweezers have been used in a wide range of other fields, including physics, nanotechnology, chemistry, soft matter, and nano thermodynamics [8].

Ghislain and Webb created a novel scanning probe microscope employing light trap particles as probes to expand the capabilities of optical tweezers. This method, which later became known as photonic force microscopy [9], was capable of measuring forces ranging from femto- to pico-Newton, which is significantly less than methods relying on mechanical cantilevers that have been micro manufactured, like atomic force microscopy [10].

Applying cutting-edge beam shaping methods in which the structure of the beam is modified by diffractive optical elements (DOEs), such as by producing numerous optical traps at specified places, the spectrum of optical tweezers' applications has significantly grown. The DOE is typically positioned as a result, the multidimensional field dispersion on the trap plane is the Fourier transform of the complex field production on the plane of the diffractive optical component, which is a plane conjugate to the focal plane of the objective lens. The DOE is frequently a liquid-crystal spatial light modulator controlled by a computer [11], as it enables the dynamic alteration of the DOE's shape for real-time control of the optical traps' number, intensity, and location. This method may also be used to create more intricate trapping configurations, such as those that use a Laguerre-Gaussian beam, which produces torque by transferring angular momentum in orbit [12].

The design and manufacture of tweezers that are optical in nature is predicated on the development of force via optical momentum change, which is the cause of force generation (mechanical effect of light), similarly can be referred to the light pressure. The generation of laser light allows this force to be large enough to capture particles. We all know that light has wave-particle duality, and that under the interaction of light and matter, here we mainly consider the particle nature. If the direction of light changes when it crosses the critical surface of two media with different refractive indices, i.e., refraction, mie scattering also occurs. Here both refraction and mie scattering are elastic collisions. The light will be refracted, the direction will shift, and the momentum will change when a big transparent particle is exposed to a Gaussian beam. According to the momentum conservation rule, the difference between the photon's initial and final momentum is converted to a particle, and we may compute this force as a gradient force.

Some formulas as follows:

$$F = \Delta p / \Delta t$$

$$p = mc = E / c = h\nu / c = h / \lambda$$

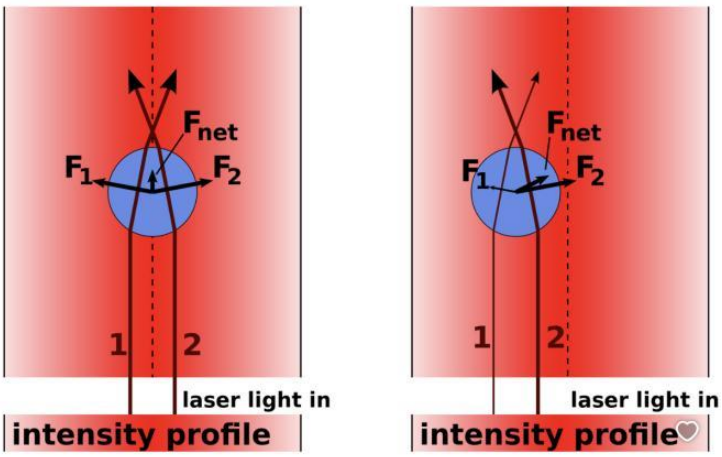


Figure 1. Schematic diagram of force analysis

When the particle is off the centre of the luminescent beam (right of Fig.1), the momentum transfer results in a combined force on the particle pointing in that position due to the higher light intensity in the centre of the beam. The particle experiences no transverse combined force when it is in the beam's centre (left of Fig.1). The particle is nonetheless a force was applied during light transmission by the unfocused laser light.

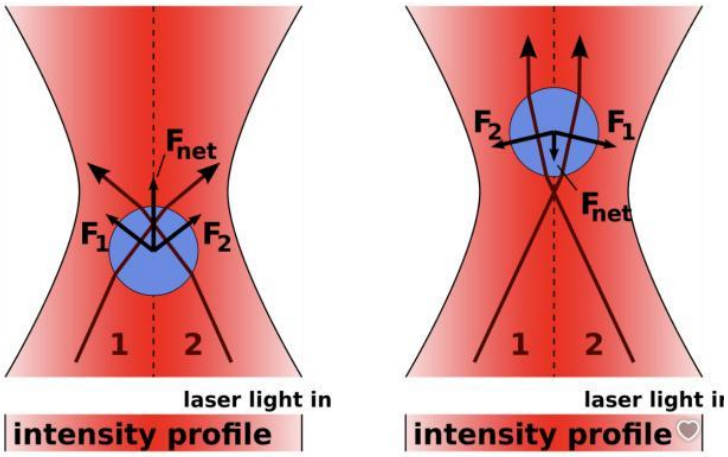


Figure 2. Schematic diagram of force analysis

Schematic diagram of force analysis was shown as Fig.2. Whether the particle is like left panel or right panel, the laser's focusing point, the transfer of momentum combines forces on the particulate that is directed towards the laser's focusing point. This lets the laser to isolate the particle into the laser's centre axis and in a specific position on the optical axis. The particles are thereby anchored in place only little behind the focussing point. (Slightly behind because of the force exerted on the particles by light scattering is towards light propagation) [13].

The mechanical action of momentum transfer between light and material particles is the foundation of optical tweezers. A common example of a mechanical action of light is the use of optical tweezers, which convincingly and completely shows that light has the fundamental feature of momentum.

Specifically, the optical tweezers technology's analysis is mainly to use a variety of computational methods to study the force of interaction among the targeted beam and the particles. Firstly, the interaction between single-beam gradient force traps and particles and their control on particles; secondly, the formation of new light traps after the focusing of new beams. In addition, there is also the problem of optical field distortion in the design and application of optical tweezers systems.

The single-beam gradient force trap theory underpins the optical tweezers theory. The single-beam gradient force trap concept clearly explains the mechanism of light capture and the elements influencing the light trap force. From the engineering aspects of the study, it can be inferred how to enhance the quality of these tweezers and how to optimise the optical tweezers instrument, leading to the invention of numerous types of tweezers which are optical.

The following analysis of particles in the optical trap is done by the optical trap force of the theoretical model of geometrical optics (RO) approximation model as well as electromagnetic (EM) model. In terms of the theory of optical tweezers optical domain, optical tweezers are developed via the strong convergence of the laser beam of optical potential well. As an estimate of the outcomes of the computation of the experimental reference value, the RO model theory is applicable to the geometry of particles bigger than the wavelength. In order to calculate the optical trap force size, explore the ophthalmic trap force of the eyepieces and the magnitude of the optical trap force, RO models are frequently employed. The RO model is widely used to determine the size of the optical capturing force and to study the effect of beam divergence on optical levitation. Combined with Gaussian beam scalar theory], the capture force of a strongly focused beam on particles is calculated. Without considering the volatility of light, we can study the force on microspheres in the light trap after lateral, axial and arbitrary displacements, and the tracing mode of incident light in different directions in space, etc. The theory of the RO model facilitates the analysis of the stresses on particles in three dimensions, and then we can analyse the stresses and dynamics of irregular particles (e.g., ellipsoids) subjected to light traps using the RO model to analyse the stresses on particles in light traps, and this can guide the experimental design and understanding of experimental phenomena well. The RO model can be used to analyse the force on particles in the optical trap, which can guide the experimental design and understanding of the experimental phenomena.

The interaction between light and matter is determined by the inherent qualities of optical fields, such as energy and momentum, as well as the spatial distribution of these physical variables, such as the optical field's intensity gradient, and so on. The study of optical fields in new types of optical tweezers. Therefore, it is crucial to regulate these optical fields. Therefore, regulating the nature of these light fields will directly change the results of light-matter interactions, which provides an important way to directly control light trapping. Changes in the nature of the light field can be achieved through light field modulation, such as amplitude, phase, and polarisation modulation. Therefore, a particularly important trend in optical tweezers is the combination of novel optical fields to achieve special or complex manipulation functions. The research of new optical tweezers optical field is supported by the rapid development of complex optical field modulation technology, such as spatial light modulation technology. New light field optical tweezers can not only achieve the different materials, different sizes of particles multi-degree of freedom manipulation, but also through the computer control, easy to achieve real-time intelligent manipulation, greatly expanding the scope of application of optical tweezers.

The new light field consists of vortex beams, self-accelerating beams, non-diffractive and self-repairing beams, and vector beams. Vortex beams transport orbital angular momentum, which are connected to phase singularities and may be transmitted to particles via contact with matter, causes particles to rotate in the light field. Common vortex beams include Laguerre-Gaussian beams and Bessel beams. Bessel beam belongs to the non-diffraction and self-healing beams, Bessel beams, unlike Gaussian beams, can be propagated across vast distances while keeping the size and dimensions of the central spot essentially unaltered, and in the process of transmission after encountering obstacles to block the original light field distribution can be restored very quickly. Because the Bessel beam has good stability in the propagation process, it is used to guide the particles along the axial transport distance of up to 3 mm, which is much larger than the axial capture depth of the optical tweezers with Gaussian beam. This distance is much larger than the axial capture depth of Gaussian beams, and multiple particles can be captured in multiple planes at 3 mm in the axial direction. Non-diffractive beams also include Mathieu beam, parabolic beam, Airy beam, etc. Among them, parabolic beam and Airy beam are the most popular. The parabolic beam and Airy beam are also self-accelerating beams. Self-accelerating beams appear to be accelerating in free space by bending at an angle during axial propagation instead of travelling in a straight line. Such beams can be used in light manipulation to transport particles along a set trajectory. Self-accelerating beams include Weber beams and spiral beams. In addition, inhomogeneous polarised light fields, such as radially polarised beams and angularly polarised beams, have superior convergence properties, which gives vector beams an obvious advantage in the manipulation of nanoparticles, especially metal nanoparticles [14].

2. Organization of the Text

2.1. Application Characteristics of Optical Tweezers Technology

Most of the objects that optical tweezers target are liquid-phase particles, and their operation in this phase is characterised by the medium and the Brownian force. Optical tweezers indirectly manipulate single molecules through the handle ball, so the handle ball is the bridge to study single molecules, to achieve sub-nanometre precision measurement, ultra-stable system becomes the guarantee of experimental research.

2.1.1. Medium and brownian force

Optic tweezers are the consequence of light and object interaction, with light and objects engaging via the medium. The commonly used medium is liquid, and the temperature, viscosity and refractive index of the liquid and other physical parameters determine the nature of the medium. Therefore, different liquid properties and parameters directly affect the interaction between light and the object, affecting the effect of light capture. The initial choice of medium should be optically transparent, and

its refractive index should be lower than that of the particles to be caught; the difference between the two values, n and n0, determines how well an item will be captured. Secondly, the chemical properties of the medium and its interaction with the particles should be considered.

Optical tweezers manipulation of particles equivalent to the colloidal system in the dispersed items, particles in the solution, that is, the medium for the dispersant. On the one hand, it is convenient to use the medium, by changing the parameters of the medium to design the experimental programme, the study of the pending scientific problems. On the other hand, the temperature of the medium with the environmental variability, the viscosity of the medium affects the light manipulation and the applied force's size, the refractive index of different media there are differences in these factors at the same time, these factors also for the design of experimental programmes and experiments to increase the difficulty of accurate measurements. As a result, the medium has a significant impact on how optical tweezers are used.

In the process of light capture particles, particles are subject to a variety of forces, including the viscous resistance of water and Brownian force in the light capture is very important, the measurement of the light trap force and its light trap parameters are mainly used in the two forces, and the viscous resistance and Brownian force is the study of soft matter colloidal system is an important parameter. The degree of intensity of the Brownian force is determined by the medium's qualities. The effect of the medium and Brownian force is always present during the manipulation and force measurement processes employing optical tweezers, and whether the Brownian force can be ignored depends on the scientific topic at hand and the experimental rigour.

2.1.2. Handle spheres and manipulation of biological single molecules

Far-field microscopy cannot observe nanoscale particles, optical tweezers manipulation of nanoparticles is indirectly manipulated by directly controllable microspheres as a handle nanoparticle, such as the manipulation of deoxyribonucleic acid (DNA), proteins, nucleic acids, and other biological macromolecules. Handled microspheres are classified as structural or functional. When using optical tweezers to stretch DNA or protein microfilaments, the ends of DNA or microfilaments need to be combined with handle microspheres in order to be manipulated by optical tweezers, and the microspheres only play the role of handles. In the study of antibody-antigen binding and molecular motor dynamics, protein molecules need to be modified on the surface of the microsphere, which is also a carrier for the research object.

2.1.3. Ultra-low noise and sub-nanometre precision measurements

Single-molecule research requires optical tweezers to achieve sub-nanometre precision, how to achieve high precision measurement, there are currently three main ways. Firstly, in the hardware configuration, try to avoid all kinds of mechanical noise, choose excellent devices, high time resolution and high precision spatial resolution. The laboratory is built in the basement, and the instrument is placed on the air cushion vibration isolation platform and fully enclosed. In the design of the instrument and environmental conditions, try to reduce air convection, sound vibration, magnetic field, and other external interference to ensure that the system in a good stable state operation. Feedback control enhance the detection accuracy of optical tweezers effectively, feedback control to take fixed-point experiments and fixed-force measurements to eliminate the fluctuation of the laser intensity and eliminate the drift of the objective lens, etc., to improve the resolution of the instrument measurement and the stability of the optical tweezers in three-dimensional space.

2.2. Application of Optical Tweezers

Optical tweezers were born at a time when nanotechnology was booming. Human understanding of the natural world and their own in-depth to the individual micro-mechanisms and functions of quantitative research, to independently grasp the objective laws and transformation of nature. As soon as optical tweezers were introduced, scientists foresaw that the technology of controlling micrometre-scale particles with optical force would have immeasurable development prospects and application potential. In the past 30 years, the applied research based on single-beam optical force controllable

particles has indeed proved the unique and indispensable value of this technology and its broad application areas. The uses of a pair of optical tweezers can be divided into four groups, thus, optical tweezers and cell biology, optical tweezers and single molecule biology, optical tweezers and colloid science, and optical tweezers and physics, in which optical tweezers have successfully solved many major scientific problems.

Optical tweezers in the field of physics applications, can confirm the previous cannot be experimentally verified physical laws, improve people's understanding of existing physical phenomena and laws, but also for other disciplines of physics to provide new research methods and experimental techniques, for example, in the verification of the mechanical effects of light and the precise measurement of force, acoustic microscopy, Brownian motion, nanotechnology, quantum mechanics, etc., showing that the employment of optical tweezers in the field of physics is growing their significance as a tool for advancing physics. Physics is increasingly becoming an important tool to promote progress.

2.2.1. New understanding of Brownian motion

In 1907, Einstein believed that the energy partition theorem applies to Brownian particles, but because the instantaneous speed of a single particle changes too quickly, so this prediction is difficult to prove directly from the experiment. 2010, Science Magazine reported that the usage of optical tweezers to detect the instantaneous speed of particles in a vacuum, the first experimental success in verifying the Brownian particles in line with the energy partition theorem.

The optical tweezers method to measure the instantaneous velocity of Brownian particles uses a trap formed by two orthogonally polarised light beams propagating in opposite directions to suspend a 3 μm sphere in the air. A fast position detector is used to obtain information about the position of the sphere by detecting the difference in light intensity signals between the two beams, which are strictly equally separated. The system calculates the x-direction displacement in relation to time. The Maxwell-Boltzmann velocity distribution curve is represented by the solid line, the noise is represented by the triangle signal, and the observed instantaneous Brownian motion velocity of one particle is about equal to 0.422 mm/s with an experimental error of 0.021 mm/s. This is a simple example of the Maxwell-Boltzmann distribution of velocities as well as the energy-mean-split theorem for Brownian motion, and it is extremely close to the theorem's expected value. (k BT/m = 0.429 mm/s). Brownian motion's distribution and energy equalisation theorem.

2.2.2. Optical tweezers manipulation of diamond nitrogen-vacancy colour centres

Diamond nitrogen-vacancy (NV) colour centres have received a great deal of publicity in the last couple of years, since they have very broad application prospects in quantum optics and biological fluorescent labelling. Particularly steady and useful as a single-photon source is the fluorescence of NV. For the measurement of physical properties including magnetic field, electric field, and temperature, NV may also be utilised as nanoscale sensors. The control of NV colour-centred nanoparticles in diamond is a technological bottleneck in its application, but optical tweezers with particle manipulation can be a suitable solution to this difficulty.

2.3. Further Applications

2.3.1. Design of a custom optical micromanipulation platform

Soft colloidal particles with adaptability have the potential to develop a wide range of industries, notably biotechnology, food and health, and oil recovery. However, it is difficult to characterise colloidal alterations in situ that result in functional responses. To examine the pH-driven structural alterations in emulsions, Manca as well as other inventors employed an integrated technique integrating an optical micromanipulation platform, polarised optical video microscopy, and microfluidics. This specially designed novel platform was used in conjunction along with synchrotron small-angle X-ray scattering to research water-based oleic acid systems that are connected to food and are pH-responsive. Individual aerosol droplets of oleic acid were examined using optical traps. Assembling and disassembling vesicle networks, monitoring phospholipase activity on individual

bilayer-encapsulated silica beads, capturing lipid droplets in live cells, directly measuring the charge of colloidal particles in nonpolar solutions, and monitoring vesicle networks have all been accomplished using optical tweezers [15].

Oleic acid/buffer mixtures at standard values of pH were analysed using a customised optical tweezer device in conjunction with a polarising microscope, which allows individual oleic acid particles to be manipulated and studied, and SAXS, which allows them to be statistically analysed individually. The optical tweezer device is shown in Fig.3.

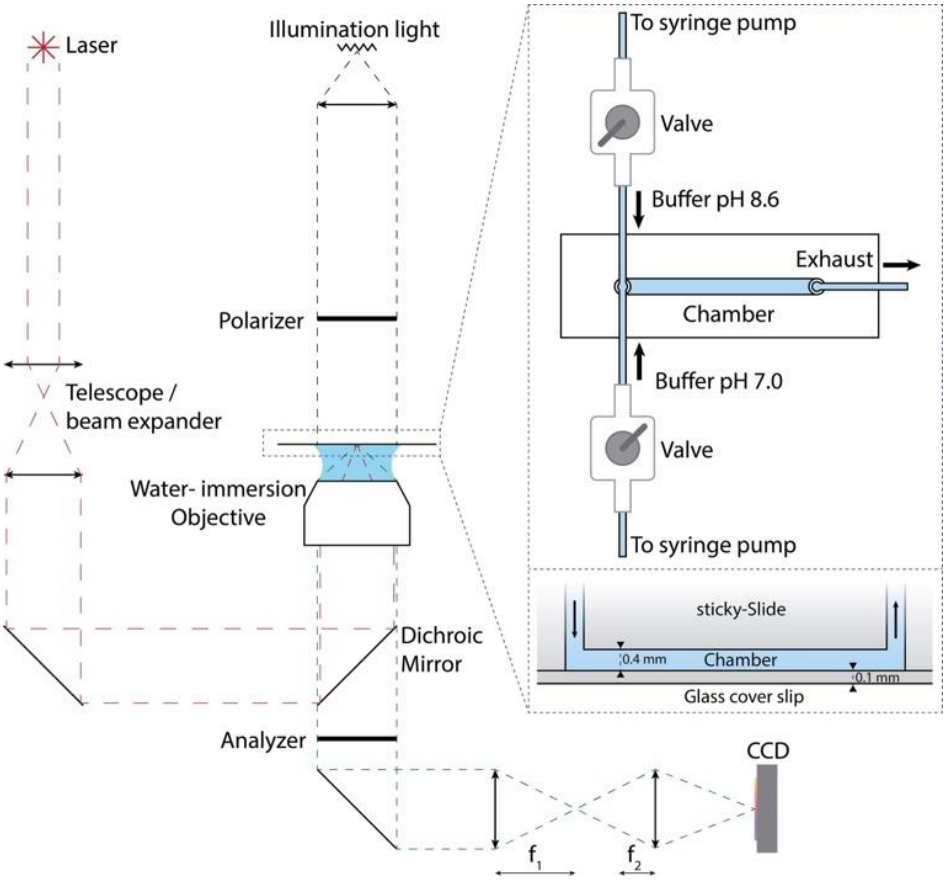


Figure 3. Schematic diagram of the optical tweezers system.

The device comprises of a microfluidic platform equipped with an image window made of m-sized glass and a hollow channel imprinted with that number. Two holes, one for injecting buffer and the other for draining buffer, provide access to the channel. A pipeline diverter that is in the injection hole enables the introduction of buffer solutions with various pH values changing the pH in the sample chamber with a syringe pump.

Three steps were used to complete the experiment: the multifibre layer oleic acid droplets with an approximate diameter of m were located and captured using a forceps device after the colloidal oleic acid/buffer system was injected inside the channel. The colloidal oleic acid/buffer system was then added to the sample chamber. Multi-micellar vesicles were chosen because the channel became red with the same pH buffer solution to reduce the number of particles in the optical volume and thus focus on the structure of a single captured particle, and they appear bright under a polarising microscope and thus can be readily distinguished from other non-birefringent droplets that are like normal emulsion droplets or mono-micellar vesicles. This enables the investigation of the impact of pH at the level of individual particles, and in particular the observation of structural changes in individual particles, utilizing a syringe pump (NE-1000, New Era Pump Systems Inc.). Multiple particles could be immobilised at once with the use of multi-capture optical tweezers, as well as the following tool was utilized in order to analyse the electrostatic interactions between oleic acid droplets that were brought on by changes in pH. These techniques enable the investigation of

interactions among colloidal particles, together with video microscopy [16] and rheological research [17].

Several time-shared traps can be made by including an acousto-optic modulator that bends the laser beam and causes the trap to move in the x-y plane. If the movement is faster than the time scale of Brownian motion, many objects can be immobilised simultaneously. Optically tweezing in split-time is the term for this method. A more complex tool for setting up many traps, called a holographic optical tweezers device, was also constructed, and employed in this work. Diffractive optical element (DOE) was used in place of the acousto-optic modulator to achieve this. This makes it possible to create many of optical traps that may be moved about and relocated in any direction. A computer-programmed liquid crystal spatial light modulator may generate any diffraction pattern. It effectively enhances the number of traps visible at any given time by splitting the laser light into many beams that are then focused by the objective lens at various places.

Individual oleic acid particles physically transition from micron-sized onion-type multicellular vesicles at pH 8.6 to nanostructured emulsions at pH less than 8.0, and lastly to oil droplets at pH less than 6.5, as demonstrated by this experiment. The smooth particle-water contact of onion-type vesicles changes to a rough particle surface at pH values below 7.5. The particles' self-propulsive motion is driven by pH-triggered changes in the interfacial tension of the water droplets, as well as bulk migration due to structural modification. The findings of the study contribute to our understanding of the structure-performance relationships in pH-responsive emulsions utilized in nutrition and drug delivery.[18]

2.3.2. The first optical tweezers based on light sheets.

Short-range colloidal contacts, cell-liposome interactions, rotation of tiny objects, and state transitions in liposomes have all been effectively observed using linear optical tweezers [19]. Prior until now, linear traps have been created using a variety of optical techniques, including scanning dot traps [20], holography, and beam shaping techniques [21]. While these methods have advanced the industry, they are slow and hard to use since they need exact alignment and scanning. Mondal and other experimenters created the first optical tweezers based on light sheets to overcome these constraints. LOT, as opposed to existing optical traps, captures things using a light sheet as a PSF. The results demonstrated that the approach could collect both medium beads and live HeLa cells without compromising cell viability. In fact, the technology aids in the shaping of living cells into diverse shapes, emulating in theory the tissue creation of the basic unit of life (the cell).

LOT can grab several items in a single line, in contrast to conventional point-capture tweezers. Even though the capture process is sped up, it's vital to realise that this capture is far less effective than traditional optical capture. The redistribution of intensity in lamellar objects as opposed to points is the main cause of this. On the other hand, LOT has the benefit of using modest pressures to concurrently grab several items. However, the method necessitates a laser with a much greater power level. According to their experimental findings, traditional traps often only require less than 5 mW, but LOT requires 52 mW of power (on the objective lens). In order to construct a diffraction-limited light sheet that generates a steady and strong light sheet PSF, the approach also requires cylindrical lenses and high NA objective lenses combined (shown as Figure 4).

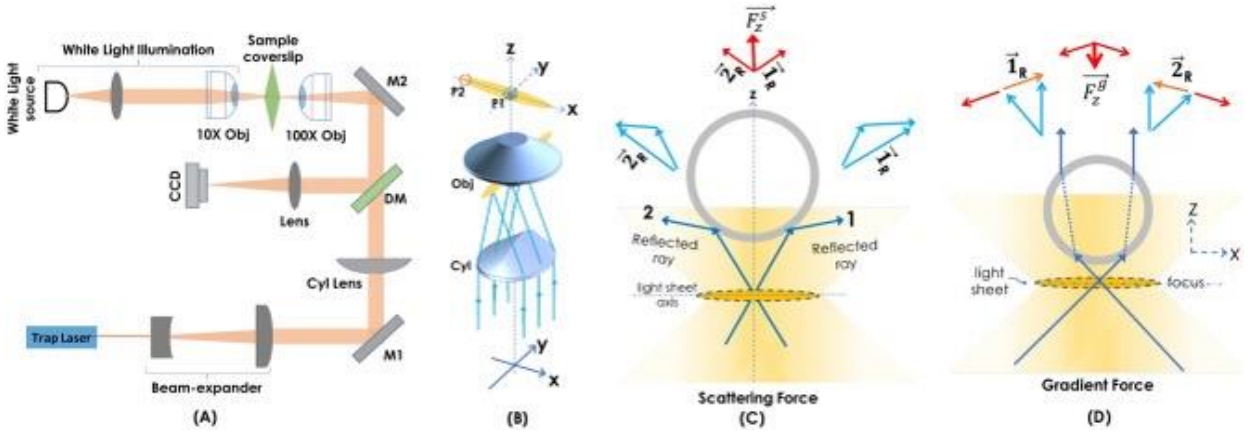


Figure 4. Schematic diagram of optical tweezers. (A) Schematic of the light sheet optical tweezer (LOT) system. (B) Combination of key optical elements (cylindrical lens and high NA objective) that produce the diffraction-limited light sheet. (C) The resulting scattering force (due to reflection of light) acting on the microparticles along the positive z-axis. (D) The gradient force acts on the particle along the negative z-axis due to refraction. The blue arrows show the elemental forces, and the red arrows show the resultant forces.

Overall, these light optical tweezers may be adjusted, are simple to align, and have unique features. For the approach to generate a sharply focused diffract limiting sheet, a cylindrical lens as well as high NA objective lens are needed. A focusing line (along the x-axis) perpendicular towards beam propagation (the z-axis) represents the resultant field.

Applications requiring planned and guided cell development may also benefit from the use of LOT. The method may be utilised to comprehend the ongoing disorderly growth of cancer cells. Normal cells react adequately to signals that regulate directional cell development, whereas cancer cells expand and divide uncontrollably in all directions. Studies on patterned cell development may be able to explain this conduct in this way. Patterned cell growth may also be used to neural networks and brain-on-a-chip models. The ability to recreate neural networks with certain topologies has shown to be crucial for understanding how neurons behave in hierarchical networks. Patterning may prove to be a crucial technique for understanding brain activity since it can be used to explain the behaviour of anything from some neurons to an entire complicated neural network. The method could also be helpful for applications like wound healing and controlled cell proliferation [22].

The field of optical manipulation is anticipated to improve thanks to LOT's capacity to concurrently collect many particles (both biological and nonbiological). Furthermore, LOT-PSF makes it appropriate for catching both cells as well as elongated objects, like cryptic nematodes. This broader the application of LOT to the study of free-living organisms without the need for fixation with glue or anaesthetics [23]. Scientists therefore anticipate that LOT will accelerate developments in the fields of optical manipulation, biophysics, and cell biology.

The LOT optical tweezers are an innovative design that relies heavily on light sheet geometry. When compared to standard optical tweezers, the approach is faster, more stable, and capable of collecting multiple particles in a single line or plane. To the best of our knowledge, this is the first optical sheet-based tweezer technology ever disclosed for optical capture applications. It is anticipated that this technique will enhance optical manipulation much more. It could open new possibilities in the fields of biological sciences (single-molecule biophysics and bioorganism biology) as well as atomic and colloidal physics. In the not-so-distant future, the approach could be optically modified to allow for planar trapping, in which particles are captured throughout the whole plane (produced by the light sheet) [24].

2.3.3. The first optical tweezers based on light sheets.

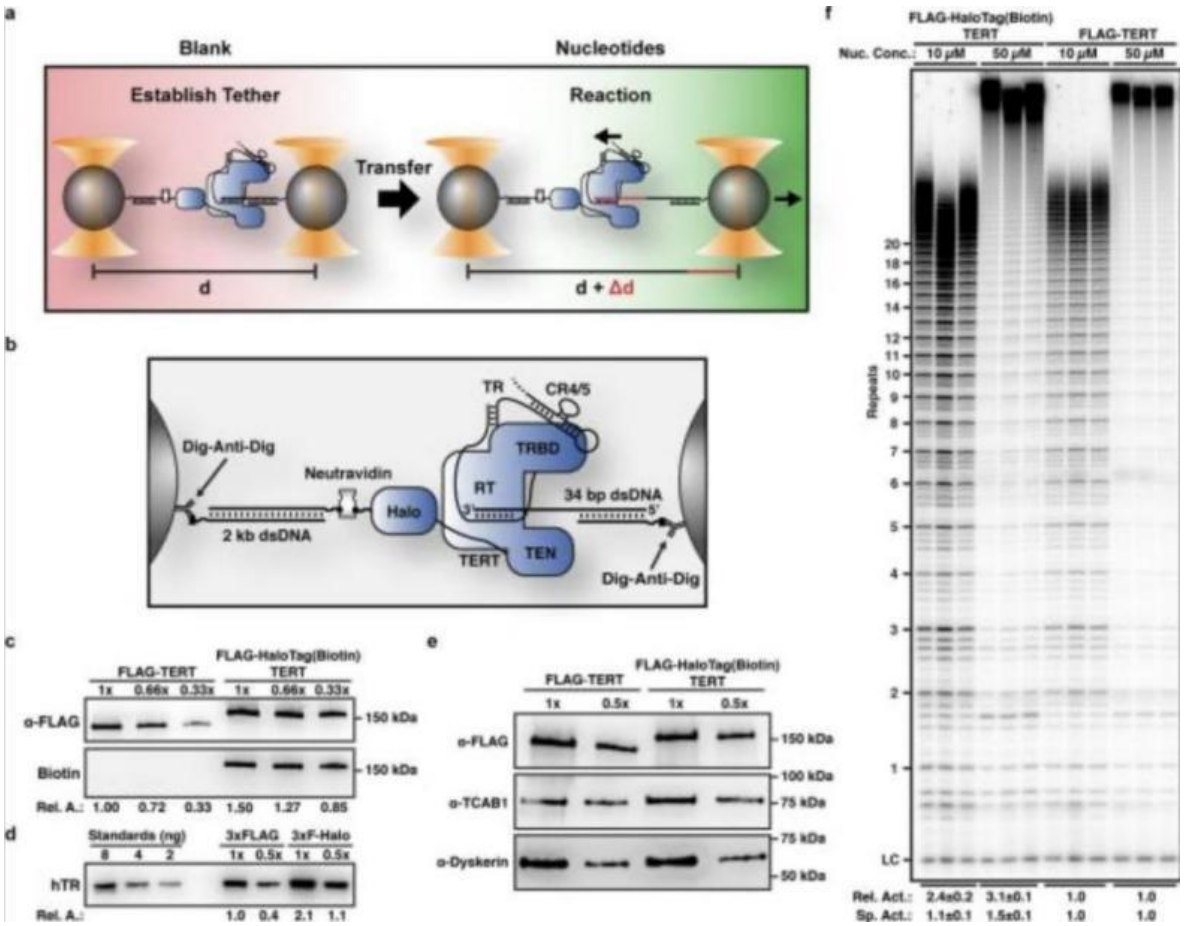


Figure 5. Schematic diagram of the single-molecule telomerase activity assay

Patrick et al. created a single-molecule telomerase activity experiment employing dual-well high-resolution optical tweezers in order to examine the substrate elongation of a single telomerase ribonucleoprotein (RNP) (Fig. 5a). Individual polystyrene beads had telomerase and its substrate bonded to them (Fig. 5b). A bond between the two beads is created by telomerase's attachment to its DNA substrate (Fig. 5a, b). The distance between the two beads increases when a tiny constant force (4.0–4.5 pN) is used on the tether to quantify the substrate elongation via telomerase (Fig. 5a). The magnitude of this force was chosen because it was sufficient for high-resolution measurements while causing only a small amount of system disruption. We utilised 3xFLAG-HaloTag on the biotin-modified TERT to bind telomerase to the head (Fig. 5b, c). Biotin-modified FLAG-TERT and 3xFLAG-HaloTag-TERT, which were co-purified with comparable relative concentrations of TR, TCAB1, and dyskerin, are present in telomerase. Western blots of purified telomerase-containing samples with 3xFLAG and 3xFLAG-Halotag-Tert are shown in Figure c. These samples serve as exemplary examples of 3 separate purifications. Anti-FLAG-M2-HRP (top) and poly-HRP-streptavidin (bottom) were used to identify the probes. Three phosphorylated DNA oligonucleotides complementary to TR were used as probes in Figure d's Northern blotting of RNA isolated from purified telomerase-containing 3xFLAG- and 3xFlag-Halotag-Tert samples (three exemplary instances of separate purification). The in vitro-transcribed full-length TR serves as the benchmark. Western blots of purified telomerase-containing 3xFLAG- and 3xflag-Halotag-TERT are displayed in Fig. E. The blot was probed with anti-FLAG-M2-HRP (top), TCAB1 (middle) as well as dyskerin (bottom) antibodies (three representative examples of independent purifications). These procedures demonstrate that labelling has no impact on telomerase RNP assembly. The reacting buffers contains 10 mM or 50 mM dNTPs and 50 mM KCl, Figure f depicts biotin-modified 3xFLAG-HaloTag-TERT

and 3xFLAG-TERT direct telomerase primer extension studies. Relative activities (n = 3, mean s.d.) were normalized to the total lane intensities of the LC and the corresponding 3xFLAG-TERT telomerase activities. This proved that neutral staphylin did not influence primer extension and that tagging had no impact on telomerase activity or POT1/TPP1 activation. Together, our findings imply that biotin modification of the 3xFLAG-HaloTag linked to the N-terminal of TERT has no impact on telomerase catalytic activity or assembly [25].

3. Optical tweezers technology development trend

Searching for the growing trend of optical tweezers research papers, the number of publications in important journals, patents on optical tweezers technology, these data fully demonstrate that the applied research results of optical tweezers technology is forward-looking and innovative, and that optical tweezers technology is moving towards a bright future and is widely used in various fields of research.

The prototype of optical tweezers instrumentation has been established since 1986, when the American scientist Ashkin invented optical tweezers. At the initial stage, only a few researchers from famous universities and research institutes in the world built different forms of optical tweezers experimental devices according to their own research needs. With the gradual maturation of optical tweezers technology and the demand for applications, the scope of application is also expanding. Optical tweezers technology can be easily connected with a variety of other optical technologies, such as laser microbeam, fluorescence excitation, confocal scanning microscope, Laaman spectrometer and other combinations of optical tweezer's technology itself from the micron precision manipulation and detection of the development of nanometre precision manipulation and detection. From single optical tweezers to multi-optical tweezers, linear optical tweezers to rotary optical tweezers formed a large family of optical tweezers. From the depth and breadth of optical tweezers technology, it has entered a new technology field with independent connotation and extension. In particular, the close integration of optical tweezers micro-manipulation with high-resolution imaging and digital image analysis has formed a powerful technology platform for single-molecule, single-cell, and microscopic experiments. Optical tweezers have opened many possible applications and will provide opportunities for many new sciences in the 21st century. The potential development trend and market demand for optical tweezers is attracting attention from businesses, and the optical tweezers industry is gradually forming.

After 30 years of dedicated research, the field of optical tweezers is embracing the future of booming technological applications. In recent years, more and more research groups have been involved in the research of optical tweezers technology in China, but most of them focus on the theoretical research, and fewer of them involve experiments. However, most of them focus on theoretical research, and few of them involve experiments. A comprehensive and in-depth understanding of optical tweezers technology and the need for instrumentation have become the urgent needs for the development of this field.

4. Summary

The 2018 Nobel Prize in Physics was awarded to American scientist Arthur Ashkin and others for their contributions to the field of laser physics. Arthur Ashkin's main contribution was "the invention of optical tweezers and their application to biological systems".

Optical forces, which arise from the exchange of momentum when light interacts with an object, can be used to manipulate particles and biomaterials at the micro- and nanoscale without contact. The physical mechanisms include gradient forces and radiation pressure. Gradient force is the polarisation of an object in an inhomogeneous electric field, attracting the object to the position where the electric field is strongest. Radiation pressure is caused by scattering, where photons carry momentum and

push objects in their path in the direction of light propagation. Stable optical capture is achieved when the gradient force is balanced with radiation pressure.

The manipulation principle of optical tweezers technology is based on the formation of an optical potential well by laser convergence, which can generate an intensity gradient near the focal point. Repulsion and attraction of the object is achieved based on the difference in refractive index between the object and the surrounding medium.

For particle sizes much larger than the laser wavelength, the optical gradient force can be calculated based on a geometrical optics model, which also analyses the relationship between refractive index and momentum conservation. For particle sizes much smaller than the laser wavelength, the particles are considered as point dipoles in an inhomogeneous electromagnetic field and are analysed according to the Rayleigh scattering mechanism. When the particle size is in the range of 0.1-10λ, the intermediate mechanism is generally used. The particle will be subjected to both gradient force and radiation pressure in the light trap, and balancing the two enables the manipulation of the particle. If the particles are to be attracted, the gradient force needs to be greater than the radiation pressure. This can be achieved with a high numerical aperture objective lens, which highly focuses the laser beam to create a diffractive field and enhance the field gradient, which can generate a force of several hundred piconewtons because the gradient force is proportional to the field gradient. Light can similarly carry angular momentum.

It is possible for a birefringent object to convert circularly polarised light into linearly or elliptically polarised light, which, according to the law of conservation of total momentum of a system, also causes the object to generate torque. As a result, particles incident with circularly polarised light will rotate at a constant angular velocity, which is affected by the viscous drag between the laser and the surrounding medium. Using this technique, the viscous drag of biological fluids can be determined on a microscopic scale.

Regarding the analysis of the basic equipment for the optical tweezer's technique, generally the laser is linearly polarised and in order to give angular momentum to the captured object, a quarter slide is added to convert the linear polarisation to circular polarisation. A microscope objective with a high numerical aperture improves the focusing ability of the laser.

Through the continuous discovery of scientists, optical tweezers have been invented in a variety of ways, of which linear optical tweezers, light sheet optical tweezers are more specifically described in this paper.

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