A revolution in optical manipulation

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Optical tweezers use the forces exerted by a strongly focused beam of light to trap and move objects ranging in size from tens of nanometres to tens of micrometres. Since their introduction in 1986, the optical tweezer has become an important tool for research in the fields of biology, physical chemistry and soft condensed matter physics. Recent advances promise to take optical tweezers out of the laboratory and into the mainstream of manufacturing and diagnostics; they may even become consumer products. The next generation of single-beam optical traps offers revolutionary new opportunities for fundamental and applied research.

new generation of techniques that use the forces exerted by carefully sculpted wavefronts of light offers precisely the level of access and control needed for rapid progress at the frontiers of several branches of science and engineering. In particular, optical forces are ideally suited to manipulating mesoscopic systems, which are characterized by length scales ranging from tens of nanometres to hundreds of micrometres, forces ranging from femtonewtons to nanonewtons and time scales ranging upward from a microsecond. In biology, this range covers many of the inter- and intracellular processes responsible for respiration, reproduction and signalling. In physics and chemistry, it corresponds to the stillpuzzling interface between classical and quantum mechanical behaviour, which is made all the more perplexing by the general inapplicability of statistical many-body theory in this realm. Fulfilment of the promise of mesoscopic engineering has been held back by the need for tiny motors to drive micromachines and for robust human-scale interfaces with atomic-scale nanotechnology. Until quite recently, the options for manipulating, analysing and organizing mesoscopically textured matter have been limited. The advent of flexible multifunctional optical traps meets this need.

Many of the most powerful optical manipulation techniques are derived from single-beam optical traps known as optical tweezers (see Fig. 1), which were introduced by Arthur Ashkin, Steven Chu and their coworkers at AT&T Bell Laboratories^{1,2}. An optical tweezer uses forces exerted by a strongly focused beam of light to trap small objects. Although the theory behind optical tweezers is still being developed, the basic principles are straightforward for objects either much smaller than the wavelength of light or much larger. Small objects develop an electric dipole moment in response to the light's electric field, which, generally speaking, is drawn up intensity gradients in the electric field toward the focus. Larger objects act as lenses, refracting the rays of light and redirecting the momentum of their photons. The resulting recoil draws them toward the higher flux of photons near the focus³. This recoil is all but imperceptible for a macroscopic lens but can have a substantial influence on mesoscopic objects.

Optical gradient forces compete with radiation pressure resulting from the momentum absorbed or otherwise transferred from the photons in the beam, which acts like a fire hose to blow particles down the optical axis. Stable trapping requires the axial gradient force to dominate, and is achieved when the beam diverges rapidly enough away from the focal point. For this reason, optical tweezers are

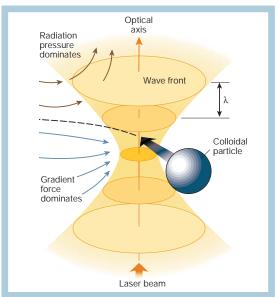


Figure 1 Optical tweezers use a strongly focused beam of light to trap objects. Intensity gradients in the converging beam draw small objects, such as a colloidal particle, toward the focus, whereas the radiation pressure of the beam tends to blow them down the optical axis. Under conditions where the gradient force dominates, a particle can be trapped, in three dimensions, near the focal point.

usually constructed around microscope objective lenses, whose high numerical apertures and well corrected aberrations focus light as tightly as possible.

Optical tweezers can trap objects as small as 5 nm (refs 4,5) and can exert forces exceeding 100 pN (refs 6-8) with resolutions as fine as 100 aN (refs 9-11). This is the ideal range for exerting forces on biological and macromolecular systems and for measuring their responses. Biological and medical applications of optical tweezers have been reviewed extensively^{2,12,13}, and so just a few examples of their uses will be outlined. Optical tweezers have been used to probe the viscoelastic properties of single biopolymers (such as DNA), cell membranes, aggregated protein fibres (such as actin), gels of such fibres in the cytoskeleton, and composite structures (such as chromatin and chromosomes). They have also been used to characterize the forces exerted by molecular motors such as myosin, kinesin, processive enzymes and ribosomes. These measurements have revealed that cells use mechanical forces not only for mobility, motility and chromosome sorting during

reproduction but also for regulating gene transcription, inter- and intracellular signalling and respiration. As a natural extension of these studies, optical tweezers offer great promise for intracellular surgery, for instance, in modifying the chromosomes of living cells¹⁴. On a larger scale, optical tweezers are useful for selecting individual microbes from heterogeneous populations. In addition, their ability to transport and modify cells precisely has led to clinical applications in such areas as *in vitro* fertilization¹⁵.

In the physical sciences, the unique ability of optical tweezers to organize matter non-invasively has led to a burst of activity in the field of classical statistical mechanics, including the first direct measurements of macromolecular interactions in solution¹⁶. Each new round of measurements has led to surprises, including the discovery of anomalous attractions between like-charged colloidal particles¹⁷, oscillatory colloidal interactions mediated by the entropy of smaller entities in solution^{18–21} and hydrodynamic fluctuations that may be interpreted as transient violations of the second law of thermodynamics²².

In all of these cases, and a great many more, fundamental insights emerged from manipulating specially chosen systems at just one or two discrete points. New frontiers of science and engineering would present themselves if optical traps could interrogate more general and more complex systems at many points at once, if they could induce chemical as well as physical transformations and if they could exert torques as well as forces. Recent advances in physical optics reveal that such multifunctional optical traps can be crafted from single beams of light by subtly modifying their wavefronts. The resulting optical micromanipulators provide unprecedented access to the microscopic world.

Manipulating the microscopic world

Figure 2 schematically depicts an optical tweezer system in which a strongly converging objective lens focuses beams of laser light into optical traps. A collimated TEM_{00} beam passing straight into the input pupil of the lens comes to a focus in the middle of the focal plane of the objective lens, where it forms a trap. Sweeping the angle of incidence translates the trap across the field of view. If the beam diverges, it focuses downstream of the focal plane, whereas if it converges, it focuses upstream.

Translating an optical trap, creating multiple optical traps and converting these into multifunctional optical traps are greatly facilitated by first forming an image of the input pupil of the lens using the telescope in Fig. 2. Any beam passing through the pupil's image, which is centred at point A in Fig. 2, also passes through the actual pupil and forms a trap. Tilting the beam as it passes through the image scans the optical trap. A single rapidly scanned optical tweezer can trap multiple particles by dwelling briefly on each one before moving on to the next^{23,24}. The extent and complexity of such multiparticle patterns are limited by the time required to reposition each of the multiple wandering objects. Scanned optical tweezers, furthermore, are restricted to the focal plane of the lens. Even so, scanned optical tweezers are extremely useful for organizing planar assemblies of colloidal particles²⁵, for testing new ideas in statistical mechanics²⁶ and for measuring macromolecular interactions²⁷.

Placing a diffractive beamsplitter at the pupil's image converts a single input beam into several beams, each of which forms a separate optical trap. Such a beamsplitter can be a computer-generated hologram, and the resulting trapping patterns are known as holographic optical tweezers (HOTs) ^{28,29}. To see how this works, consider multiple beams all passing simultaneously through point A on their way to being focused into optical traps. Their superposition creates a distinctive interference pattern centred at point A. Imprinting this pattern onto the wavefronts of a single input laser beam transforms the one beam into the desired fan-out of beams and thus forms the same pattern of optical traps.

The input beam's electric field, $E(\rho) \exp(i\varphi(\rho)) \epsilon$, around point A is characterized by a real-valued amplitude $E(\rho)$ and phase $\varphi(\rho)$, both of which are functions of position transverse to the optical axis

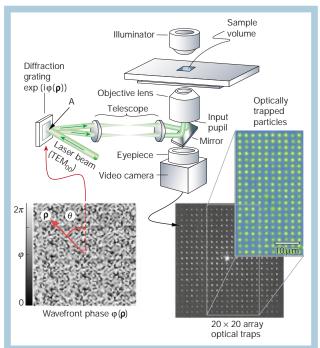


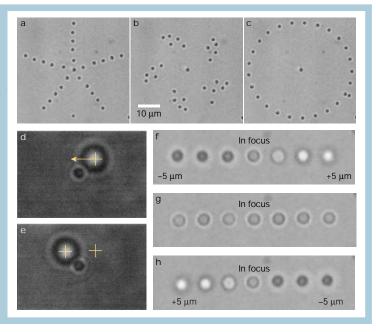
Figure 2 Creation of a large number of optical tweezers by using a computergenerated holograms. Projecting a collimated TEM_{00} laser beam through the input pupil of a strongly converging lens such as a microscope objective creates a single optical tweezer. The telescope in this implementation creates an image of the objective's input pupil, centred at point A. Multiple beams passing through point A therefore pass into the objective lens to create multiple optical traps. A single TEM_{00} laser beam can be spilt into an arbitrary fan-out of beams all emanating from point A by an appropriate computer-designed diffraction grating centred there. The example phase grating $\phi(\rho)$ creates the 20 \times 20 array of traps shown in the video micrograph. These are shown trapping 800 nm diameter polystyrene spheres dispersed in water. This figure was adapted with permission from ref. 31 $^{\circ}$ Elsevier Science Ltd. Bar, 10 μ m.

and a polarization vector ε describing the field's orientation. A multibeam interference hologram generally would modify both the amplitude and the phase of the input beam, with the amplitude modifications diverting power away from the optical traps. Fortunately, a variety of iterative optimization algorithms have been developed $^{29-31}$ to create equivalent holographic beamsplitters that modify only the phase of the input beam. Such a phase-only diffractive optical element (DOE), also known as a kinoform, was used to create the 20×20 optical traps shown in Fig. 2.

Holographic optical tweezers really hit their stride when a computer-addressed spatial light modulator (SLM) was used to project sequences of trap-forming kinoforms in real time^{30–32}. An SLM imposes a prescribed amount of phase shift at each pixel in an array by varying the local optical path length. Typically, this is accomplished by controlling the local orientation of molecules in a layer of liquid crystal, although arrays of microelectromechanical (MEMS) mirrors are also becoming available for SLM applications. Slightly displacing the traps from one pattern to the next transfers particles along arbitrary three-dimensional (3D) trajectories^{30–32}, animating matter with light in much the same way that cartoons animate light with matter. Figure 3 shows this principle in action.

In a variation on this theme, the generalized phase contrast (GPC) technique converts a pattern of phase modulation across an SLM's face directly into the corresponding intensity modulation in the focal plane of the objective lens³³ and thus creates arbitrary planar trapping patterns. The conversion involves an annular phase plate similar to that used in phase contrast microscopy. This approach avoids the need to calculate holograms and thus is extremely efficient.

Figure 3 Polysterene and silica spheres in two- and three-dimensional configurations of holographic optical tweezers created from a single laser beam with a computer-designed hologram of a single beam's wavefront. **a–c**, Thirty-six water-borne polystyrene spheres, 800 nm in diameter, are trapped in a plane and reconfigured with dynamic trapping patterns. Reproduced with permission from ref. 31 © Elsevier Science Ltd. Bar, 10 μ m. **d,e**, Two 1 μ m diameter silica spheres being moved past each other in two different planes. Reproduced with permission from ref. 30 © Elsevier Science Ltd. The different appearance of the spheres results from their different heights relative to the microscope's focal plane. **f–h**, Seven 1 μ m diameter silica spheres being moved up and down through seven different planes. Reproduced with permission from ref. 31 © Elsevier Science Ltd.



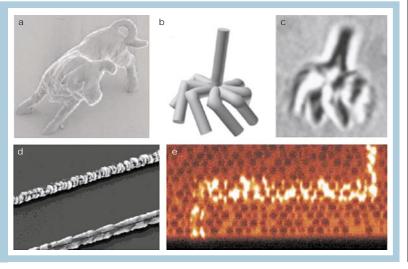
The spatial resolution of existing SLMs currently limits the GPC technique to creating lateral traps rather than 3D optical tweezers, but GPC has still proved useful for rapidly organizing small objects in thin samples³⁴.

Even static arrays of optical traps have exciting and surprising applications. For example, an array of traps can continuously sort fluid-borne particles, acting much like a sieve. The array sorts particles on the basis of their different affinities for optical traps and for their affinity for the externally applied driving force. Inclining a regular array with respect to the driving force deflects the selected fraction so that it can be collected separately from the other, undeflected fraction³⁵. Unlike most sorting techniques that operate on discrete batches of sample, optical fractionation works continuously and can be dynamically optimized by adjusting the wavelength, intensity and geometry of the trap array. Moreover, because optical fractionation relies on the object's ability to hop from potential well to potential well, it is exponentially sensitive to particle size and so promises unparalleled size resolution³⁶.

An array of traps may also be viewed as a tailor-made potential energy landscape for interacting colloidal particles. Determining how strongly interacting systems evolve on modulated substrate potentials is a classic problem in statistical physics, and colloids in modulated optical fields constitute a rare model system where microscopic interactions can be measured and controlled while macroscopic thermodynamic properties unfold^{37,38}. Insights obtained from studying optically modulated colloids are relevant to analogous systems such as atoms adsorbed on crystal surfaces, electrons passing through charge density waves and 2D electron gases, magnetic flux quanta passing through defects in type II superconductors and motor proteins translating along filaments in living cells. Early studies demonstrated that modulation along even one direction can freeze a 2D colloidal fluid^{39,40}. Deeper modulation actually melts the substrate-induced crystal⁴¹ by suppressing inter-row coupling⁴². More recent studies have demonstrated other intriguing behaviours. such as rotational melting in an array of multiply occupied traps^{38,43}, and have shed new light on the mechanisms by which magnetic flux lines invade superconductors 37,38.

Time-varying potential energy landscapes created with dynamic optical traps promise new insights into the operation of molecular motors by providing a powerful experimental system within which to study thermal ratchets²⁶ and related models in non-equilibrium statistical mechanics⁴⁴. Once perfected, such ratchet potentials will also

Figure 4 The diffraction-limited focus of an optical tweezer is ideal for spatially localized photochemistry. Examples include: $\bf a$, the fabrication of a photopolymerized sculpture whose finest features are roughly 100 nm across (reproduced from ref. 84 © Macmillan Magazines Ltd); the fabrication of a light-driven turbine, shown as a solid model of a photopolymerized turbine with submicrometre features in $\bf b$ and as an actual turbine suspended in water in $\bf c$ (reproduced with permission from ref. 50 © American Institute of Physics); $\bf d$, fine lines of MoS_2 deposited on a glass substrate by photoreduction of an aqueous salt solution (reproduced with permission from ref. 51 © Wiley-VCH); and $\bf e$, a three-dimensional fluorescent polymer structure embedded in a colloidal crystal (reproduced from ref. 54 with permission from P. Braun).



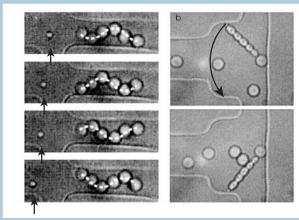


Figure 5 Optical pump and valve constructed of colloidal particles in microfluidic channels activated with optical tweezers. **a**, The flow of water created by the colloidal peristaltic pump is shown by the position of the tracer particle, which is indicated with an arrow (reproduced with permission from ref. 85 © American Association for the Advancement of Science). **b**, The colloidal valve flap is flipped with an optical tweezer and directs particles either downward (top) or upward (bottom). Reproduced with permission from ref. 55 © American Institute of Physics.

be useful for dynamically sorting mesoscopic objects and transporting them through tiny integrated laboratories for processing and testing⁴⁵.

All such studies provide valuable insights into how nature creates and exploits hierarchically organized structures. Once these principles are understood, they will be extraordinarily useful for creating new materials and devices to order. Until then, many of the most interesting three-dimensionally structured functional systems can be assembled using many optical tweezers operating in concert. Indeed, optical tweezers have an essentially unique ability to construct 3D heterostructures with features ranging in size from a few nanometres to a few millimetres. The real power of this approach only becomes apparent when optical trapping is combined with other techniques to create permanent structures with embedded functionality.

Nanofabrication with optical tweezers

Once assembled, tweezer-organized structures can be fixed in place, for instance, by sintering or gelling. The tweezers themselves can be used in this process. In particular, the intense illumination at an optical tweezer's focus is ideal for driving photochemical reactions in restricted volumes. If the reaction rate depends strongly on intensity, the resulting spatially resolved photochemistry can yield features smaller than the wavelength of light.

The first such application of optical tweezers involved the spatially resolved photo-oxidation of biological materials such as chromosomes 46.47. Essentially, a scalpel was created from light. Optical scalpels and scissors have been used for surgery on living cells 15,48 as well as for ablating subwavelength structures into microscopic substrates 49.

Spatially resolved photochemistry using optical tweezers has been used to fabricate small complex 3D structures such as the examples shown in Fig. 4. Figure 4a–c shows 3D plastic structures created by multiphoton photopolymerization in scanned optical tweezers. The smallest features in Fig. 4a are about 100 nm across. The tiny turbine in Fig. 4b, c not only was created in this way but also was trapped and spun on its axis with an optical tweezer ⁵⁰. Arrays of interlocking turbines and gears assembled and driven by light have already been demonstrated ⁵⁰. Other photochemical transformations provide opportunities for optical tweezers to create 3D electronic and photonic structures. The fine lines of MoS₂ in Fig. 4d were patterned on glass by photoreduction of aqueous salts, and similar results have been obtained in silver, gold and oxidized copper ⁵¹.

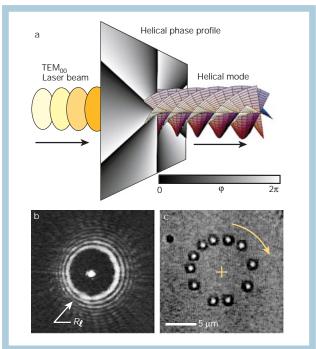


Figure 6 Optical vortices and optical spanners created from helical modes of light. **a**, The helical phase profile $\varphi(\rho) = \ell \theta$ converts a TEM $_{00}$ laser beam into a helical mode whose wavefronts resemble an ℓ -fold corkscrew. **b**, Rather than focusing to a point, a helical mode focuses to an optical vortex whose radius R_{ℓ} is proportional to its pitch, ℓ . **c**, A single colloidal particle trapped in the optical vortex travels around its circumference, driven by the orbital angular momentum of the helical beam. This multiple exposure shows 11 stages, at 1/6 s intervals, in one 800 nm particle's transit. Reproduced with permission from ref. 67 © American Physical Society.

Beyond creating structures *de novo*, spatially resolved photochemistry can be used to modify pre-existing structures. The 3D optical waveguide structure in Fig. 4e demonstrates this principle. Here, a self-assembled crystal of colloidal silica spheres was perfused with a photosensitive precursor and selectively patterned with an optical tweezer to create the embedded polymer structure shown in Fig. 4e (ref. 52). Filling the gaps with a high-index material and then dissolving away the spheres and polymer would leave a tweezer-drawn waveguide pattern embedded in the otherwise self-assembled photonic crystal⁵³. This hybrid approach to creating hierarchically structured materials could sweep away many of the practical hurdles that have prevented self-assembled systems from making bigger inroads in photonics and electro-optical systems⁵⁴.

Using many optical tweezers to simultaneously organize prefabricated nanometre-scale parts and to stitch them together with spatially resolved photochemistry would yield a whole new category of hierarchically structured materials and devices. Such scale-spanning heterostructures would provide the building blocks for sensors, photonic devices and a host of other technologies. Hierarchically structured micromechanical systems hold similar promise for optomechanical and microfluidic applications. In this case, optical trapping also solves the outstanding problem of actuating such small devices. Some aspects of this solution involve the unusual and counterintuitive properties of traps created with newly discovered modes of light.

Optical actuators

Using conventional optical tweezers as actuators for micromachines is likely to speed up the adoption of lab-on-a-chip and related technologies for medical diagnostics, environmental testing and point-of-use microfabrication. Dynamic optical tweezers can both

organize and drive devices, such as the micrometre-scale hydraulic pump shown in Fig. 5a. The microscopic valve flap in Fig. 5b is an example of a photopolymerized colloidal heterostructure that is assembled and actuated with optical tweezers⁵⁵.

Modifying the wavefronts of the optical tweezers transforms them into whole new classes of optical traps, some of which have already found applications as actuators for unconventional micromachines. Some of the most useful of these are based on exotic modes of light whose properties have only recently been elucidated.

Figure 6a shows how the deceptively simple phase profile $\varphi(\rho) = \ell \, \theta$ transforms the parallel wavefronts of a TEM₀₀ laser mode into the corkscrew topology of a helical mode⁵⁶. Here, θ is the azimuthal angle around the optical axis and ℓ is an integer winding number (also known as the topological charge). The modified beam no longer focuses to a point, because the helical topology fosters destructive interference along the optical axis. Instead, it converges to a ring of light, as shown in Fig. 6b. The dark focus is suitable for trapping reflecting⁵⁷, absorbing⁵⁸ or low-dielectric-constant^{59,60} objects that would be damaged or repelled by conventional optical tweezers. Because such traps lack the radiation pressure from axial rays, they make more efficient traps for large dielectric objects than conventional optical tweezers do⁶¹⁻⁶³. Smaller dielectric particles are drawn to the ring's circumference, as shown in Fig. 6c.

What really distinguishes these ring-like optical traps is their ability to exert torques as well as forces 57,58,64 . Just a decade ago, Allen demonstrated that each photon in a helical mode carries an orbital angular momentum $\ell\hbar$, where \hbar is the quantum unit of angular momentum, in addition to its intrinsic spin angular momentum 56 . This orbital angular momentum takes the form of a tangential component to the beam's linear momentum density that can be transferred to illuminated objects $^{65-67}$. A single colloidal microsphere is shown circulating around such a topological ring-trap under the influence of the optical angular momentum flux in the time-lapse photograph of Fig. 6c. Such toroidal torque-exerting traps have come to be known as optical vortices 68 or optical spanners 69 , and they have potentially widespread technological applications. Studying the motion of objects in optical vortices has also provided valuable insights into the interplay of photon spin and orbital angular momentum $^{57,64-67,70}$, which have been useful in elucidating the quantum mechanical nature of helical beams.

An optical vortex's radius, R_ℓ , increases with topological charge 67,71 ; therefore, the intensity pattern can be tailored to different applications. For example, a properly scaled ring of light can be projected onto the teeth of a microfabricated gear, thereby creating a reliable micrometre-scale motor. The distributed drive made possible by projecting multiple optical vortices should also help to alleviate problems associated with friction in micromechanical systems. The spin angular momentum carried by circularly polarized optical tweezers similarly has been used to apply torques to birefringent components $^{72-74}$. Using an SLM to control the polarization of multiple optical tweezers opens up even more possibilities for developing extensive micromachines assembled and driven by light.

Some micromechanical applications may require no microfabrication at all. Rapidly circulating particles entrain flows that can mix and pump extremely small volumes of fluid. This solves a problem in microfluidic systems, whose laminar flows are ideal for transporting minuscule quantities of reagents but do not promote mixing when needed. Furthermore, the holographic optical tweezer technique can project multiple optical vortices, such as the 3×3 array in Fig. 7a, each with an individually specified intensity and topological charge 31 . Cooperative flows in such arrays can be reconfigured dynamically by modifying the trap-forming hologram, opening up the possibility of developing adaptive microfluidics on length scales ranging all the way down to tens of nanometres.

Other variations on this theme yield a family of distinct optical micromanipulators, each with its own applications. For example, superposing a helical beam on a conventional beam not only shows the helical wavefronts' structure, as in Fig. 7b, but also creates an

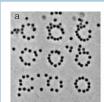






Figure 7 Generalizations of the optical vortex principle. **a**, The holographic optical tweezer technique can create arrays of optical vortices, each with individually specified intensity and topological charge. This 3×3 array of $\ell=30$ optical matrices is shown trapping 800 nm diameter polystyrene spheres. Reproduced with permission from ref. 31 © Elsevier Science Ltd. **b**, Trapped objects can be rotated within the interference pattern of an optical vortex and a plane wave. Such an optical rotator was created by interference of an $\ell=3$ helical mode with a plane wave. Reproduced with permission from ref. 75 © American Association for the Advancement of Science. **c**, An optical rotator created with a five-fold modulation of the helicity of an $\ell=60$ optical vortex. Reproduced with permission from ref. 67 © American Physical Society.

orientated intensity pattern that is useful for orientating asymmetric objects⁷⁵. Superposing instead a helical mode on its mirror-image counterpart creates 3D arrays of discrete traps that can be rotated arbitrarily in three dimensions by varying the beams' relative phase⁷⁶. Modulating the helical pitch of an optical vortex results in another class of optical rotators⁷⁷, an example of which appears in Fig. 7c. Further generalizations create intensity patterns related to the caustics seen at the bottom of swimming pools and which can move objects along complex trajectories transverse to the optical axis, all with static holograms and no moving parts. Other superpositions can focus on micrometre-scale dark regions surrounded by light on all sides known as optical bottles⁷⁸. These are useful for trapping very small dark-seeking objects, including clouds of ultracold atoms⁷⁸. Holographic arrays of optical bottles therefore should be useful for manipulating atoms⁷⁹, perhaps for quantum computing applications, and will help to extend pioneering efforts to apply optical tweezers to atomic physics80,81

Whereas azimuthal phase modulations extend optical tweezers into micromanipulators that are transverse to the optical axis, radial modulations create axial devices with an intriguing twist. The simplest non-trivial radial phase profile modification, $\varphi(\rho) = \gamma \rho$, transforms a TEM₀₀ beam into an approximation of a Bessel mode, a beam that propagates without diffracting even when focused to a wavelength-scale cross-section. The associated optical trap can extend for millimetres along the optical axis, as demonstrated in Fig. 8, and can precisely push particles over very large distances⁸³. The extended range of Bessel-beam arrays should increase the throughput of optical fractionation by orders of magnitude. Still more remarkably, Bessel beams are impervious to distortions by intervening particles and surfaces⁸⁴—they can reconstruct their wavefronts as they propagate away from disturbances. Combining the robustness of Bessel beams with the orbital angular momentum of helical modes yields optical devices that can reach deeply into complex systems to apply forces and torques where needed.

Future prospects

The ability to reach into the microscopic world dextrously and non-invasively at many points at once, to cut, assemble and transform with nanometre precision and submicrometre resolution and to do all these things with a single instrument promises revolutionary advances in many disciplines. The sections above highlight just a few of these advances. In particular, wavefront engineering provides a straightforward means to create large many optical traps in arbitrary 3D configurations, to move them freely and independently in three dimensions and to transform them into optical vortices, optical bottles, Bessel traps and a host of other all-optical tools.

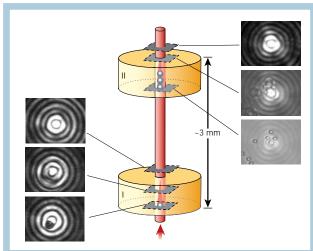


Figure 8 The radial phase profile $\varphi(\rho) = \gamma \rho$ creates a diffractionless Bessel beam that focuses to a long axial trap that can extend for millimetres. Here, the same beam is shown trapping multiple colloidal particles in two separate sample chambers separated by a distance of 3 mm. Bessel beams are impervious to distortions by intervening particles because wavefronts are reconstructed as they propagate away from disturbances. Left, a sphere is trapped between the central spot and the first ring of the Bessel beam in cell 1. A little way above, the beam is distorted, but further above, the beam is no longer distorted. The process is repeated for the same beam in cell II in the planes on the right. Reproduced from ref. 83 © Macmillan Magazines Ltd.

As tools for biology, multifunctional optical traps will facilitate new approaches to cell sorting, macromolecular purification, intracellular surgery, embryonic testing and highly parallel drug screening as well as great many other possibilities. The same tools have immediate applications for organizing mesoscopic matter into heterogeneous, hierarchically structured 3D functional systems, such as photonic circuit elements, integrated sensor arrays and high-density data storage devices. Combining this organizational capability with optical-tweezer-based spatially resolved photochemistry suggests bright prospects for optically assembling new materials and devices with features ranging in size from nanometres to millimetres and beyond.

In micromechanics and microfluidics, appropriately sculpted wavefronts of light can easily control motions and flows on a length scale that has challenged other technologies. In so doing, optical micromachines should hasten the adoption of lab-on-a-chip devices for diagnostics, sensing, testing, pathology and drug discovery. The same wavefront-shaping techniques can sort and purify materials in these tiny flows and direct them towards further stages of purification and analysis. Optical testing and manufacturing, thus, could be highly integrated, with a single instrument providing flow, sorting, organization, synthesis and assembly. In all of these areas, the emerging generation of optical manipulation tools should help to bridge the chasm between our macroscopic world and applications based on the physics, chemistry and biology of microscopic systems.

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- Ashkin, A., Dziedzic, J. M., Bjorkholm, J. E. & Chu, S. Observation of a single-beam gradient force optical trap for dielectric particles. Opt. Lett. 11, 288–290 (1986).
- Ashkin, A. History of optical trapping and manipulation of small-neutral particle, atoms, and molecules. IEEE J. Sel. Top. Quantum Elec. 6, 841–856 (2000).
- Ashkin, A. Forces of a single-beam gradient laser trap on a dielectric sphere in the ray optics regime. Methods Cell Biol. 55, 1–27 (1998).
- 4. Svoboda, K. & Block, S. M. Optical trapping of metallic Rayleigh particles. *Opt. Lett.* **19**, 930–932
- Ke, P. C. & Gu, M. Characterization of trapping force on metallic Mie particles. Appl. Opt. 38, 160–167 (1999).
- Ghislain, L. P., Switz, N. A. & Webb, W. W. Measurement of small forces using an optical trap. Rev. Sci. Instr. 65, 2762–2768 (1994).
- Rohrbach, A. & Stelzer, E. H. K. Trapping forces, force constants, and potential depths for dielectric spheres in the presence of spherical aberrations. Appl. Opt. 41, 2494–2507 (2002).

- Litvinov, R. I., Shuman, H., Bennett, J. S. & Weisel, J. W. Binding strength and activation state of single fibrinogen-integrin pairs on living cells. *Proc. Natl Acad. Sci.* 99, 7426–7431 (2002).
- Gittes, F. & Schmidt, C. F. Signals and noise in micromechanical measurements. Methods Cell Biol. 55, 129–156 (1998).
- Gittes, F. & Schmidt, C. F. Interference model for back-focal-plane displacement detection in optical tweezers. Opt. Lett. 23, 7–9 (1998).
- Pralle, A., Prummer, M., Florin, E. L., Stelzer, E. H. K. & Horber, J. K. H. Three-dimensional highresolution particle tracking for optical tweezers by forward scattered light. *Microsc. Res. Tech.* 44, 378, 386 (1990)
- Svoboda, K., Mitra, P. P. & Block, S. M. Fluctuation analysis of motor protein movement and single enzyme-kinetics. *Proc. Natl Acad. Sci.* 91, 11782–11786 (1994).
- Bustamante, C., Smith, S. B., Liphardt, J. & Smith, D. Single-molecule studies of DNA mechanics. Curr. Opin. Struct. Biol. 10, 279–285 (2000).
- 14. Berns, M. W., Tadir, Y., Liang, H. & Tromberg, B. Laser scissors and tweezers. Methods Cell Biol. 55,
- Wright, G., Tucker, M. J., Morton, P. C., Sweitzer-Yoder, C. L. & Smith, S. E. Micromanipulation in assisted reproduction: A review of current technology. Curr. Opin. Obstet. Gyn. 10, 221–226 (1998).
- Crocker, J. C. & Grier, D. G. Microscopic measurement of the pair interaction potential of chargestabilized colloid. *Phys. Rev. Lett.* 73, 352–355 (1994).
- Crocker, J. C. & Grier, D. G. When like charges attract: The effects of geometrical confinement on long-range colloidal interactions. *Phys. Rev. Lett.* 77, 1897–1900 (1996).
- long-range colloidal interactions. *Phys. Rev. Lett.* **77**, 1897–1900 (1996).

 18. Ohshima, Y. N. Direct measurement of infinitesimal depletion force in a colloid-polymer mixture by
- laser radiation pressure. *Phys. Rev. Lett.* **78**, 3963–3966 (1997).

 19. Crocker, J. C., Matteo, J. A., Dinsmore, A. D. & Yodh, A. G. Entropic attraction and repulsion in
- binary colloids probed with a line optical tweezer. *Phys. Rev. Lett.* **82**, 4352–4355 (1999). 20. Verma, R., Crocker, J. C., Lubensky, T. C. & Yodh, A. G. Attractions between hard colloidal spheres in
- semiflexible polymer solutions. *Macromolecules* **33**, 177–186 (2000).

 21. Yodh, A. G. *et al.* Entropically driven self-assembly and interaction in suspension. *Phil. Trans. R. Soc.*
- A 359, 921–937 (2001).

 22. Wang, G. M., Sevick, E. M., Mittag, E., Searles, D. J. & Evans, D. J. Experimental demonstration of violations of the second law of thermodynamics for small systems and short time scales. *Phys. Rev.*
- Sasaki, K., Koshio, M., Misawa, H., Kitamura, N. & Masuhara, H. Pattern formation and flow control
 of fine particles by laser-scanning micromanipulation. Opt. Lett. 16, 1463–1465 (1991).
- Sasaki, K., Fujiwara, H. & Masuhara, H. Optical manipulation of a lasing microparticle and its application to near-field microspectroscopy. J. Vacuum Sci. Tech. B 15, 2786–2790 (1997).
- Mio, C., Gong, T., Terray, A. & Marr, D. W. M. Morphological control of mesoscale colloidal models. Fluid Phase Equilibria 185, 157–163 (2001).
- Faucheux, L. P., Bourdieu, L. S., Kaplan, P. D. & Libchaber, A. J. Optical thermal ratchet. Phys. Rev. Lett. 74, 1504–1507 (1995).
- Verma, R., Crocker, J. C., Lubensky, T. C. & Yodh, A. G. Entropic colloidal interactions in concentrated DNA solutions. *Phys. Rev. Lett.* 81, 4004–4007 (1998).
- Dufresne, E. R. & Grier, D. G. Optical tweezer arrays and optical substrates created with diffractive optics. Rev. Sci. Instr. 69, 1974–1977 (1998).
- Dufresne, E. R., Spalding, G. C., Dearing, M. T., Sheets, S. A. & Grier, D. G. Computer-generated holographic optical tweezer arrays. Rev. Sci. Instr. 72, 1810–1816 (2001).
- Liesener, J., Reicherter, M., Haist, T. & Tiziani, H. J. Multi-functional optical tweezers using computer-generated holograms. Opt. Commun. 185, 77–82 (2000).
- Curtis, J. E., Koss, B. A. & Grier, D. G. Dynamic holographic optical tweezers. Opt. Commun. 207, 169–175 (2002)
- Reicherter, M., Haist, T., Wagemann, E. U. & Tiziani, H. J. Optical particle trapping with computergenerated holograms written on a liquid-crystal display. Opt. Lett. 24, 608–610 (1999).
- Mogensen, P. C. & Glückstad, J. Dynamic array generation and pattern formation for optical tweezers. Opt. Comm. 175, 75–81 (2000).
- Rodrigo, P. J., Eriksen, R. L., Daria, V. R. & Glückstad, J. Interactive light-driven and parallel manipulation of inhomogeneous particles. Opt. Exp. 10, 1550–1556 (2002).
- Korda, P. T., Taylor, M. B. & Grier, D. G. Kinetically locked-in colloidal transport in an array of optical tweezers. *Phys. Rev. Lett.* 89, 128301 (2002).
- 36. Ladavac, K., Kasza, K. & Grier, D. G. Optical fractionation. Phys. Rev. Lett. (in the press)
- 37. Korda, P. T., Spalding, G. C. & Grier, D. G. Evolution of a colloidal critical state in an optical pinning potential. *Phys. Rev. B* **66**, 024504 (2002).
- Mangold, K., Leiderer, P. & Bechinger, C. Phase transitions of colloidal monolayers in periodic pinning arrays. Phys. Rev. Lett. 90, 158302 (2003).
- Chowdhury, A., Ackerson, B. J. & Clark, N. A. Laser-induced freezing. Phys. Rev. Lett. 55, 833–836 (1985).
- Loudiyi, K. & Ackerson, B. J. Direct observation of laser-induced freezing. *Physica A* 184, 1–25 (1992)
- $41.\,Wei,\,X.\,\textit{et al.}\,T\,cell\,activation\,studied\,by\,optical\,trap.\,\textit{Biophys.}\,\textit{J.}\,\textbf{74}, A378\,(1998).$
- Bechinger, C., Brunner, M. & Leiderer, P. Phase behavior of two-dimensional colloidal systems in the presence of periodic light fields. *Phys. Rev. Lett.* 86, 930–933 (2001).
- Brunner, M. & Bechinger, C. Phase behavior of colloidal molecular crystals on triangular light lattices. *Phys. Rev. Lett.* 88, 248302 (2002).
- 44. Reimann, P. Brownian motors: Noisy transport far from equilibrium. Phys. Rep. 361, 57–265 (2002).
- 45. Koss, B. A. & Grier, D. G. Optical peristalsis. Appl. Phys. Lett. 82, 3985–3987 (2003).
- Ashkin, A., Dziedzic, J. M. & Yamane, T. Optical trapping and manipulation of single cells using infrared-laser beams. Nature 330, 608–609 (1987).
- 47. Liang, H., Wright, W. H., Cheng, S., He, W. & Berns, M. W. Micromanipulation of chromosomes in PtK2 cells using laser microsurgery (optical scalpel) in combination with laser-induced optical force (optical tweezers). Exp. Cell Res. 204, 110–120 (1992).
- 48. Bayles, C. J., Aist, J. R. & Berns, M. W. The mechanics of anaphase-B in A *basidomycete* as revealed by laser microbeam microsurgery. *Exp. Mycology* 17, 191–199 (1993).
- Fuhr, G. et al. Processing of micro-particles by UV laser irradiation in a field cage. Appl. Phys. A 69, 611–616 (1999).
- Galajda, P. & Ormos, P. Complex micromachines produced and driven by light. Appl. Phys. Lett. 78, 249–251 (2001).

- Lachish-Zalait, A., Zbaida, D., Klein, E. & Elbaum, M. Direct surface patterning from solutions: Localized microchemistry using a focused laser. Adv. Funct. Mat. 11, 218–223 (2001).
- Lee, W. M., Pruzinsky, S. A. & Braun, P. V. Multi-photon polymerization of waveguide structures within three-dimensional photonic crystals. Adv. Mat. 14, 271–274 (2002).
- within three-dimensional photonic crystals. Adv. Mat. 14, 271–274 (2002).
 53. Joannopoulos, J. D., Meade, R. D. & Winn, J. N. Photonic Crystals (Princeton Univ., Princeton, 1995).
- Taton, T. A. & Norris, D. J. Device physics: Defective promise in photonics. *Nature* 416, 685–686 (2002).
- Terray, A., Oakey, J. & Marr, D. W. M. Fabrication of linear colloidal structures for microfluidic applications. Appl. Phys. Lett. 81, 1555–1557 (2002).
- Allen, L., Beijersbergen, M. W., Spreeuw, R. J. C. & Woerdman, J. P. Orbital angular-momentum of light and the transformation of Laguerre-Gaussian laser modes. *Phys. Rev. A* 45, 8185–8189 (1992).
- O'Neil, A. T. & Padgett, M. J. Three-dimensional optical confinement of micron-sized metal particles and the decoupling of the spin and orbital angular momentum within an optical spanner. *Opt. Commun.* 185, 139–143 (2000).
- Rubinsztein-Dunlop, H., Nieminen, T. A., Friese, M. E. J. & Heckenberg, N. R. Optical trapping of absorbing particles. Adv. Quantum Chem. 30, 469–492 (1998).
- Gahagan, K. T. & Swartzlander, G. A. Trapping of low-index microparticles in an optical vortex. J. Opt. Soc. Am. B 15, 524–534 (1998).
- Gahagan, K. T. & Swartzlander, G. A. Simultaneous trapping of low-index and high-index microparticles observed with an optical-vortex trap. J. Opt. Soc. Am. B 16, 533–537 (1999).
- Ashkin, A. Forces of a single-beam gradient laser trap on a dielectric sphere in the ray optics regime. Biophys. J. 61, 569–582 (1992).
- 62. Simpson, N. B., McGloin, D., Dholakia, K., Allen, L. & Padgett, M. J. Optical tweezers with increased axial trapping efficiency. *J. Mod. Opt.* **45**, 1943–1949 (1998).
- O'Neil, A. T. & Padgett, M. J. Axial and lateral trapping efficiency of Laguerre-Gaussian modes in inverted optical tweezers. Opt. Commun. 193, 45–50 (2001).
- 64. He, H., Friese, M. E. J., Heckenberg, N. R. & Rubinsztein-Dunlop, H. Direct observation of transfer of angular momentum to absorptive particles from a laser beam with a phase singularity. *Phys. Rev. Lett.* 75, 826.820 (1995)
- Allen, L., Padgett, M. J. & Babiker, M. The orbital angular momentum of light. Prog. Opt. 39, 291–372 (1999).
- O'Neil, A. T., MacVicar, I., Allen, L. & Padgett, M. J. Intrinsic and extrinsic nature of the orbital angular momentum of a light beam. *Phys. Rev. Lett.* 88, 053601 (2002).
- 67. Curtis, J. E. & Grier, D. G. Structure of optical vortices. Phys. Rev. Lett. 90, 133901 (2003).
- $68.\ Gahagan,\ K.\ T.\ \&\ Swartzlander,\ G.\ A.\ Optical\ vortex\ trapping\ of\ particles.\ \textit{Opt.\ Lett.}\ \textbf{21},827-829\ (1996).$

- Simpson, N. B., Allen, L. & Padgett, M. J. Optical tweezers and optical spanners with Laguerre-Gaussian modes. J. Mod. Opt. 43, 2485–2491 (1996).
- Simpson, N. B., Dholakia, K., Allen, L. & Padgett, M. J. Mechanical equivalence of spin and orbital angular momentum of light: An optical spanner. Opt. Lett. 22, 52–54 (1997).
- Padgett, M. J. & Allen, L. The Poynting vector in Laguerre-Gaussian modes. Opt. Commun. 121, 36–40 (1995).
- Higurashi, E., Sawada, R. & Ito, T. Optically induced angular alignment of trapped birefringent micro-objects by linearly polarized light. *Phys. Rev. E59*, 3676–3681 (1999).
- Higurashi, E., Sawada, R. & Ito, T. Optically driven angular alignment of microcomponents made of in-plane birefringent polyimide film based on optical angular momentum transfer. J. Micromech. Microeng. 11, 140–145 (2001).
- Friese, M. E. J., Rubinsztein-Dunlop, H., Gold, J., Hagberg, P. & Hanstorp, D. Optically driven micromachine elements. Appl. Phys. Lett. 78, 547–549 (2001).
- Paterson, L. et al. Controlled rotation of optically trapped microscopic particles. Science 292, 912–914 (2001)
- MacDonald, M. P. et al. Creation and manipulation of three-dimensional optically trapped structures. Science 296, 1101–1103 (2002).
- 77. Curtis, J. E. & Grier, D. G. Modulated optical vortices. Opt. Lett. 28, 872-874 (2003).
- Arlt, J. & Padgett, M. J. Generation of a beam with a dark focus surrounded by regions of higher intensity: The optical bottle beam. Opt. Lett. 25, 191–193 (2000).
- McGloin, D., Spalding, G. C., Melville, H., Sibbet, W. & Dholakia, K. Applications of spatial light modulators in atom optics. Opt. Exp. 11, 158–166 (2003).
- 80. Gustavson, T. L. *et al.* Transport of Bose-Einstein condensates with optical tweezers. *Phys. Rev. Lett.* **88**, 020401 (2002).
- Chikkatur, A. P. et al. A continuous source of Bose-Einstein condensed atoms. Science 296, 2193–2195 (2002).
- 82. Arlt, J., Garces-Chavez, V., Sibbett, W. & Dholakia, K. Optical micromanipulation using a Bessel light beam. *Opt. Commun.* **197**, 239–245 (2001).
- Garces-Chavez, V., McGloin, D., Melville, H., Sibbett, W. & Dholakia, K. Simultaneous micromanipulation in multiple planes using a self-reconstructing light beam. *Nature* 419, 145–147 (2002)
- 84. Kawata, S., Sun, H.-B., Tanaka, T. & Takada, K. Finer features for functional microdevicecs. *Nature* **412**, 697–698 (2001).
- Terray, A., Oakey, J. & Marr, D. W. M. Microfluidic control using colloidal devices. Science 296, 1841–1844 (2002).