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Optical trapping and manipulation of neutral particles using lasers

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ABSTRACT **The techniques of optical trapping and manipulation of neutral particles by lasers provide unique means to control the dynamics of small particles. These new experimental methods have played a revolutionary role in areas of the physical and biological sciences. This paper reviews the early developments in the field leading to the demonstration of cooling and trapping of neutral atoms in atomic physics and to the first use of optical tweezers traps in biology. Some further major achievements of these rapidly developing methods also are considered.**

The technique of optical trapping and manipulation of small neutral particles by lasers is based on the forces of radiation pressure. These are forces arising from the momentum of the light itself. Nothing in the early history of light pressure forces using incoherent sources suggested useful terrestrial application. Only in astronomy, in which light intensities and distances are huge, did radiation pressure play a significant role in moving matter. With lasers, however, one can make these forces large enough to accelerate, decelerate, deflect, guide, and even stably trap small particles. This is a direct consequence of the high intensities and high intensity gradients achievable with continuous wave coherent light beams. Laser manipulation techniques apply to particles as diverse as atoms, large molecules, small dielectric spheres in the size range of tens of nanometers to tens of micrometers, and even to biological particles such as viruses, single living cells, and organelles within cells. Use of laser trapping and manipulation techniques gives a remarkable degree of control over the dynamics of small particles, which is having a major impact in many of the fields in which small particles play a role.

In atomic physics, for example, it is now possible to optically cool atoms to record low temperatures (a fraction of a microkelvin) and optically trap them at high densities. The availability of large numbers of cold atoms moving with velocities as low as 1 cm/s and deBroglie wavelengths comparable to the light wavelength has opened a wide range of new possibilities. Atomic fountains of cooled atoms have been devised that are capable of greatly improving the accuracy of atomic clocks. New types of atom interferometers have been developed using cold atoms with the potential for sensitive measurements, such as the measurement of the acceleration of gravity with large increases in sensitivity. A new field of atom optics is developing based on new types of atom lenses, beam splitters, and atomic mirrors. Applications to high definition lithography are being investigated. Recently, sufficiently low temperatures and high enough densities of trapped atoms have been achieved to observe the Bose–Einstein condensation of an atomic vapor to form a new coherent quantum state of matter having largely unexplored properties. This new condensate, however, has just been used to generate a coherent beam of atoms in what is essentially the first atomic laser.

In biological applications of optical trapping and manipulation, it is possible to remotely apply controlled forces on living cells, internal parts of cells, and large biological molecules without inflicting detectable optical damage. This has resulted in many unique applications. One of the most important of these is in the study of single motor molecules and mechano-enzymes. With so-called "optical tweezers traps," one can measure the forces generated by single motor molecules of kinesin and myosin in the piconewton range and, for the first time, resolve their detailed stepping motion of $\approx$10 nm per step as they move along the submicron microtubule and actin strands of the cytoskeleton. In a recent breakthrough experiment, the force generated by RNA polymerase was directly measured as it moved along a DNA molecule and transcribed an RNA strand. Another large area is the measurement of the mechanical (elastic) properties of parts of the cell cytoplasm, such as flagella of bacteria, the actin cytoskeleton of red blood cells, single microtubules, single actin filaments, nerve cell membranes, and long strands of single DNA molecules. The ability to separate living cells has been developed into a technique for the search and cloning of new high temperature anaerobic archaea bacteria. This is important for science and as a means of discovering new high temperature enzymes. Techniques of optically assisted *in vitro* fertilization are being studied as well as problems in cell recognition, cell fusion, chromosome motion during cell division, and the effects of gravity on plant roots.

This review gives a somewhat personal view of the early important developments in the field, from the early days of 1969 up to the time of the first observation of optical cooling and trapping of atoms in 1986, and to the time of the early discoveries with tweezers of the application of optical manipulation to biology in 1989. The subsequent exciting developments since those dates are treated somewhat more concisely, but most key events are mentioned.

Basic Forces and First Optical Trap. My interest in the subject was aroused in 1969 by the following order of magnitude calculation of the radiation pressure force of laser light on a small particle. Using a focused beam with a power of 1 W striking a particle of radius of $\approx$1 wavelength we get, by conservation of momentum, a force F of $\approx 10^{-3}$ dynes, assuming the particle acts as a perfect mirror reflecting all of the incident light momentum back on itself. In absolute terms, this is small. However, the particle acceleration F/m, because of the small mass m, is $\approx 10^5$ *g*, where *g* is the acceleration of gravity. This is quite large and should give rise to significant dynamical effects. This prompted a simple experiment (1) designed to look for particle motion from such a force. A sample of transparent latex spheres suspended in water was used to avoid any heating or radiometric forces. With

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just milliwatts of power, particle motion was observed in the direction of a mildly focused Gaussian beam. The particle velocity was in approximate agreement with our crude force estimates, suggesting that this was indeed a radiation pressure effect. However, an additional unanticipated force component was soon discovered that strongly pulled particles located in the fringes of the beam into the high intensity region on the beam axis. Once on axis, particles stayed there and moved forward, even if the entire beam was slued back and forth within the chamber. Particles were being guided by the light! They finally collected in a clump at the output face of the chamber. When the light was turned off, they wandered toward the fringes of the beam. If the light was turned on again, they were quickly pulled to the beam axis. Was this transverse force component light pressure, too?

Fig. 1 shows that both of these force components do indeed originate from radiation pressure. Imagine a high index of refraction sphere, many wavelengths in diameter, placed off-axis in a mildly focused Gaussian beam. Consider a typical pair of rays "a" and "b" striking the sphere symmetrically about its center O. Neglecting relatively minor surface reflections, most of the rays refract through the particle, giving rise to forces F_a and F_b in the direction of the momentum change. Because the intensity of ray "a" is higher than that of ray "b," the force F_a is greater than F_b. Adding all such symmetrical pairs of rays striking the sphere, one sees that the net force can be resolved into two components, F_{scat}, called the scattering force component pointing in the direction of the incident light, and F_{grad}, a gradient component arising from the gradient in light intensity and pointing transversely toward the high intensity region of the beam. For a particle on axis or in a plane wave, $F_a = F_b$, and there is no net gradient force component. A more detailed calculation of the sum of the forces of all the rays striking the sphere gave a net force in excellent agreement with the observed velocity. For a low index particle placed off-axis, the refraction through the particle reverses, $F_a < F_b$, and such a particle should be pushed out of the beam. This behavior was seen using micron-sized air bubbles in glycerol. One also observes, by mixing large and small diameter spheres in the same sample, that the large spheres move faster and pass right by the smaller spheres as they proceed along the beam. This is a form of particle separation and is expected from the simple ray-optic calculations.

The understanding of the magnitude and properties of these two basic force components made it possible to devise the first stable three-dimensional optical trap for single neutral particles. The trap consists of two opposing moderately diverging Gaussian beams focused at points A and B as shown in Fig. 1*b*. The predominant effect in any axial displacement of a particle from the equilibrium point E is a net-opposing scattering force. Any radial displacement is opposed by the gradient force of both beams. The trap was filled by capture of randomly diffusing small particles that wandered into the trap. The viscous damping of the liquid serves to dissipate all of the kinetic energy gained from the trapping potential and particles come to rest at the trap center. If one blocks one beam, the particle is driven forward and guided by the second beam. If one restores the first beam, the particle is pushed back to the equilibrium point E. It is surprising that this simple first experiment (1), intended only to show simple forward motion due to laser radiation pressure, ended up demonstrating not only this force but the existence of the transverse force component, particle guiding, particle separation, and stable three-dimensional particle trapping.

The success of these experiments on macroscopic particles prompted the hypothesis that "similar acceleration and trapping are possible with atoms and molecules using laser light tuned to specific optical transitions" (1). It was shown that a scattering force should exist for atoms in the direction of the incident light due to the process of absorption and subsequent isotropic spontaneous emission of resonant photons. The low intensity absorption cross-section of an atom is huge, approximately λ^2, but absorption saturation greatly reduces it, even at very modest light intensities (hundreds of watts per square centimeter). The problem of saturation of the scattering force was treated phenomenologically using the so-called "Einstein A & B coefficients" to calculate the fraction of time f an atom spends in the excited state. The scattering force is given by the rate of scattering momentum $F_{scat} = hf/\lambda t$, where t is the spontaneous emission lifetime. At high saturating intensities, the population of a 2-level atom equalizes and $f = \frac{1}{2}$. The magnitude of this saturated force is sufficient, however, to turn an atomic beam of sodium of average thermal velocity through a radius of curvature $\rho \cong 40$ cm, if applied continuously at right angles to the velocity to avoid any Doppler shifts (2). If one applies the saturated force in opposition to the atomic motion, one can stop atoms at the average velocity in a distance of $\rho/2 \approx 20$ cm, assuming one compensates for the large Doppler shift of the atomic resonance. It was suggested that one could use the scattering force to make an atomic beam velocity selector or an isotope separator (2). A scheme for exerting significant optical pressure on a gas of atoms also was proposed (1).

No consideration was given in Ashkin (2) to the gradient component of the force on atoms inasmuch as I did not understand how to treat the saturation of this force. The classical formula for the gradient force of an electromagnetic wave on a neutral atom, considered as a simple dipole, is the dipole force formula $\frac{1}{2}\alpha\nabla E^2$, where α is the optically induced polarizability of the atom or particle. For atoms, the polarizability is dispersive and changes signs above and below resonance in analogy with the change in sign of the gradient force on high and low index particles. α can be calculated by modelling the atom as a simple harmonic oscillator. This gradient force formula was considered earlier by Askar'yan (3) using lasers in a two-dimensional geometry, in connection with self-focusing, the force on electrons, atoms, and two-dimensional confinement of plasmas. Letokhov (4) also considered very weak, off-resonant one-dimensional confinement of atoms in laser standing waves for spectroscopic purposes. Neither work discusses the possibility of stable three-dimensional trapping of atoms.

Optical Levitation and Applications. The next advance in optical trapping and manipulation was the demonstration of the optical levitation trap in air, under conditions in which gravity plays a significant role (5). In the levitation trap, as shown in Fig. 2, a single vertical beam confines a macroscopic particle at a point E where gravity and the upward scattering force balance. The

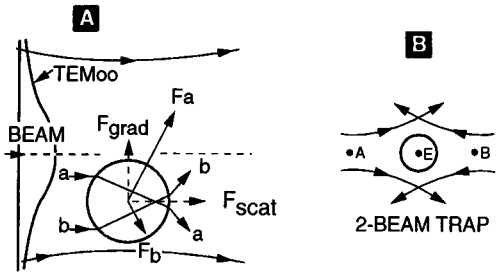

FIG. 1. (*A*) Origin of F_{scat} and F_{grad} for high index sphere displaced from TEM_{00} beam axis. (*B*) Geometry of 2-beam trap.

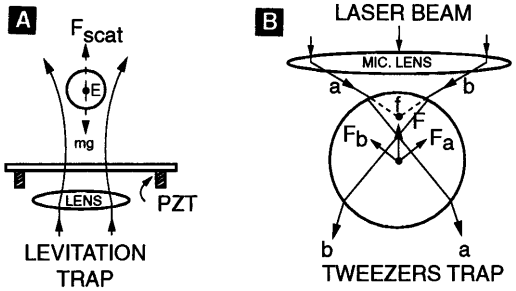

FIG. 2. (*A*) Geometry of levitation trap. (*B*) Origin of backward restoring force F for sphere located below tweezers focus *f*.

equilibrium is stable because of the increase in axial scattering force with decreasing height near E and the transverse confinement of the gradient force. Once aloft, levitated particles can be freely manipulated by simply moving the beam. With a pair of movable beams, one can assemble compound particles like spheroids, teardrops, spherical doublets, triplets, etc. (6). These complex particles align themselves in the beam and make ideal test particles for light scattering experiments. Levitation of hollow glass spheres, which are sometimes used as laser fusion targets, is also possible (7). One uses TEM_{01}* or do-nut mode laser beams having a hole in their center. Levitation in high vacuum is also possible using feedback to damp particle oscillations caused by beam fluctuations (8, 9). The feedback scheme both locks the particle at a fixed height and varies the levitating power in proportion to the negative of the velocity to give strong optical damping. Important to note, feedback locking provides a means of automatically measuring forces on particles because the change in power needed to hold the particle fixed is a direct measure of the applied force.

The feedback force measuring technique was used to measure the electric force on oil drops as they accumulated single electron charges in a modern version of the Millikan oil drop experiment (10) and to measure viscous drag forces on small particles (9), changes in radiometric forces with pressure (8, 9), and changes in the optical scattering force with axial position in the light beam (9). Use of feedback to measure the wavelength dependence of the levitating force with a tunable dye laser led to the discovery of the high Q optical resonances predicted by the Mie–Debye theory (11), which manifest themselves as peaks in the radiation pressure force and light scattering of a trapped spherical particle. Applications of these resonances, variously called surface–wave resonances, morphology-dependent resonances, or structure resonances, have had great impact on light scattering studies. High Q resonances offer the most precise check on the Mie–Debye theory (12, 13) and give a two to three order of magnitude improvement in absolute and relative size and index of refraction measurement of spheres (11, 14). More recently, drops have served as extremely high Q dye laser and Raman laser resonators and as a medium for studying and enhancing a wide range of linear and nonlinear optical interactions (15).

Origins of Optical Atom Trapping. Following the early work on light forces on atoms (1, 2), experiments were performed demonstrating atomic beam deflection (16, 17) and isotope separation (18) using the scattering force. In 1975, Hänsch and Schawlow made the important suggestion that it was possible to use the strong velocity dependence of the scattering force due to Doppler shift for the optical cooling or damping of atomic motions (19). For example, in one dimension with a pair of identical opposing beams tuned below resonance, any atomic motion along the axis meets a net opposing force due to the strong Doppler shifts of the absorption. Three pairs of such opposing beams should damp all degrees of freedom. This cooling process, however, is based only on the average behavior of the forces. Because of quantum fluctuations, there are random departures from average behavior that correspond to a constant heating process. The equilibrium temperature finally achieved is a balance of the optical cooling rate and the quantum heating rate. Letokhov and Minogin (20, 21) were the first to estimate the equilibrium temperature based on the fluctuations of the scattering force. For a tuning $\gamma_n/2$ below resonance, which gives the optimum cooling rate, they estimate an equilibrium energy of $\approx h\gamma_n$. They also then proposed that one could use the same 6-beam cooling geometry for stably trapping atoms on the intensity maxima of the three-dimensional standing wave pattern by virtue of the gradient force. Unfortunately, they estimated a trap depth that was also $\approx h\gamma_n$, which implies a very leaky trap.

In 1978, I decided to address the problem of saturation of the gradient force using the same semi-classical rate–equation approach used earlier for understanding saturation of the scattering force (2). The key points were the realizations that the classical value of the polarizability α in the formula $\frac{1}{2}\alpha\nabla E^2$ applies to an atom in its ground state and that an atom in its excited state contributes polarizability of the opposite sign in proportion to the fraction of time f it spends in the excited state. With this rate equation approach (22), one finds for the potential energy U of the gradient force, $U = h/2\ (\nu - \nu_o)\ \ln\ (1 + p)$ where p is an intensity-dependent saturation parameter. It is seen that one can greatly increase U and the forces by factors of 10^2 or more for a given intensity by keeping the saturation modest ($p \approx 1$) and greatly increasing the detuning ($\nu - \nu_o$) to values of $\approx 10^2\ \gamma_n$ or more. For the first time, trapping geometries were possible for atoms that were stable in the Boltzman sense, i.e., $U/kT \gg 1$. A 2-beam trap was proposed at this time in analogy with the first macroscopic particle trap. Also suggested was the simplest of all traps, the optical tweezers trap (22) consisting of a single strongly focused Gaussian beam. Although the thought of using tweezers at first sight seems counter intuitive, tweezers are axially stable because of the dominance of the backward axial gradient force over the forward scattering force. These new strongly detuned atom traps require use of optimally tuned auxiliary cooling beams to keep the atom temperature at $\approx h\gamma_n$ (23).

An experiment was performed demonstrating large gradient forces with detuned light (24). An atomic beam was injected into the core of a Gaussian laser beam and strong focusing and defocusing of the atomic beam was seen depending on tuning below or above the resonance frequency. This experiment was the first experimental demonstration of the gradient force on atoms. It also represents a demonstration of two-dimensional trapping of atoms using light forces, and, furthermore, it marks the beginning of the so-called "field of atom optics." Additional work studying the variation of the atomic beam focal spot size with light intensity gave the first evidence of quantum heating of atoms by light (25).

Prospects for optical atom trapping were bolstered by a theoretical analysis by Gordon *et al.* (26) entitled "motion of atoms in a radiation trap." This work derived the basic optical forces on atoms, their saturation, and their fluctuations from first principles using a fully quantal theory and applied the results to traps. It confirmed the correctness of the earlier derived scattering and gradient force components, which were deduced in part from experiment, intuition, and semi-classical analysis. A new result was the derivation of the fluctuations of the gradient or dipole force. This is conceptually more difficult to understand than the scattering force fluctuations, but it contributes equally with the scattering force fluctuations to the quantum heating rate and the equilibrium temperature. This paper has become a standard reference for questions about the basic optical forces on atoms.

A further big experimental step on the way to atom trapping was the gross slowing of atomic beams using the scattering force of an opposing laser beam by Phillips *et al.* (27, 28). The major problem here was to compensate for the large Doppler shifts that occur as the atoms are slowed. This was done by magnetically tuning the resonant frequency of the atoms with a properly tapered magnetic field to keep the peak of the distribution of slowing atoms in resonance with the light. Chirping the light frequency also was suggested by Letokhov *et al.* (29) and subsequently demonstrated (30). Although these one-dimensional techniques could slow the peak of the axial velocity distribution to 0, there was no transverse cooling, and the lowest average temperature achieved was ≈0.1 K. At this temperature, relatively few atoms are available for filling small volume atom traps. One solution actively pursued at that time by experimenters at the National Bureau of Standards was a different type of trap (31) in which atoms were confined in a relatively large volume solely by the scattering force from mildly diverging beams. Unfortunately, this proposal was flawed. A theorem called the "Optical Earnshaw theorem" was proven (32) showing that any trap based solely on scattering forces, which are strictly proportional to the light intensity, is inherently unstable. This was proven in analogy with the Earnshaw Theorem in electrostatics.

In 1984, an experiment was started at Bell Laboratories in Holmdel, NJ, on optical trapping of atoms. This was stimulated

by new department head Steve Chu, who arrived with interest in trapping atoms. The initial plan was to combine slowing, cooling, and trapping in a single experiment. Chu argued for a simpler first step, to first study the three-dimensional cooling scheme using the Doppler cooling technique (19) now referred to as "optical molasses." This was wise because molasses cooling succeeded so well it affected our subsequent choice of traps. The molasses experiment (33) produced a roughly 1-cm^3 volume of atomic vapor at a density of 10^9 atoms/cm^3, viscously confined at a temperature of $\approx$250 μK, close to the Doppler limit (20, 21, 23, 26), which persisted for times up to 1 s before diffusing away. Indeed, with this remarkable sample of cooled atoms, it became possible to demonstrate the first three-dimensional stable atom trap (34) using the very simple tweezers trap consisting of just a single strongly focused Gaussian beam. Despite its small volume, tweezers placed anywhere within the sample of cold atoms proceeded to fill up to densities of $\approx 10^{11}$ atoms/cm^2 by diffusion from the surrounding vapors, in analogy to the filling of the first particle trap by diffusion from the surrounding latex spheres (1). Trapped atoms persisted in the trap after molasses atoms diffused away and could be freely manipulated in space. The success of these cooling and trapping experiments marked the beginning of a new era of experimentation that has revolutionized experimental atomic physics.

Origins of Optical Trapping in Biology. Although the optical tweezers trap was originally designed as an atom trap and was used in the first optical atom trapping experiment (34), that experiment did not represent the first use of tweezers. During the atom trapping experiment, at a time of temporary difficulty, it was decided to try the tweezers trap on simpler Rayleigh dipole particles such as submicron silica spheres. Trapping of single submicron colloidal silica particles in water was indeed demonstrated (35) with sizes as small as $\approx$250 Å. It was also possible to trap fixed arrays of charged colloidal particles. Trapping of micron-sized spheres, large compared with the wavelength, was likewise demonstrated at this time. This extended the notion of a backward gradient force to large particles as well. The origin of the backward light force for tweezers in the ray-optics regime (36) is shown in Fig. 2*B*. For many applications with macroscopic particles, tweezers is superior to the levitation trap. Levitation traps depend on gravity and have forces of $\approx$mg, where m is the mass and *g* is the acceleration of gravity. Tweezers, however is an all optical trap and can have forces of thousands of times mg, limited only by the optical power. This is useful for confining submicron particles in situations in which gravity plays a minor role and Brownian motion dominates. The compact tweezers trap is also more tolerant of particle shape irregularities than the levitation trap.

Our next experiment involved tweezers trapping of colloidal tobacco mosaic virus (37). Tobacco mosaic virus is a rugged, rod-like protein that traps easily and orients itself within the trap. Then some puzzling observations were made. With time we noticed the appearance of increasing numbers of strange, relatively large, apparently self-propelled particles. Some occasionally were trapped and gave rise to a wild display of light scattering before settling down to a steady state. Suspecting accidental bacterial contamination, we introduced the trap into a microscope, thus combining trapping with high resolution viewing. This confirmed the trapping of live motile bacteria and their subsequent "opticution" (death by light) (37). A change from our previous green (5145 Å) argon laser to an infrared yttrium/aluminum garnet laser at 1.06 μm made a dramatic difference (38). It became possible to hold *Escherichia coli* bacteria and yeast cells for hours in isolation and observe cell reproduction within the trap. This proved the ability of infrared lasers to manipulate cells under damage-free conditions. Damage-free trapping of pigmented red blood cells, green plant cells, and algae also was shown. Remarkably, manipulation also was possible on organelles and particles deep within plant cells and protozoa, without damaging the cell wall. Deformations and evidence of the elastic behavior of cells was seen. Using pairs of traps, one could orient cells in space and transfer selected bacteria from one sample to another.

Further work on internal cell manipulation in plant cells (39) showed that one can probe the cytoplasmic streaming of internal particles. By pulling out long cytoplasmic filaments, one can also probe the elastic and viscoelastic properties of the cytoplasm. A form of internal cell surgery is possible using the viscoelastic flow of cytoplasm with gross movements of large organelles. These papers (37–39) on damage-free trapping marked the beginning of the new field of optical trapping in biology.

Recent Work on Atom Trapping and Manipulation. The achievement of optical cooling and trapping of a dense cloud of atoms in 1986 greatly stimulated interest in optical manipulation techniques. A new large volume magneto-optical trap was developed using the scattering force (40). A quadrupole Zeeman splitting field was used that made both the resonance frequency and α position-dependent. When combined with a 6-beam cooling geometry this results in a stable scattering force trap that does not violate Earnshaw's theorem. This robust, large volume, deep trap is widely used as a workhorse trap despite some poorly understood behavior (41).

Although the initial molasses temperature of 240 μK was close to the Doppler cooling limit for a 2-level atom (33), disagreements soon arose. Unexpected tolerance to beam misalignments and long storage times were seen (42). Also, temperatures almost 10 times less than the Doppler limit were observed (43). Explanations of this additional damping are based on the multi-level nature of the cooling transition used. The inability of optical pumping processes to adiabatically follow the polarization gradients leads to an increased cooling force (44, 45). Molasses cooling in one dimension using multi-level atoms directly shows the additional cooling due to polarization gradients (46).

One might think that the minimum possible temperature of cooled atoms would be T_r, which is the temperature due to the recoil of a single photon. For sodium, the recoil velocity is $\approx$3 cm/s with a temperature T_r of $\approx$2 μK. However, cooling below even T_r can be achieved. For example, one can dramatically cool a trapped sample by simply letting the high energy atoms escape. Turning off a trap momentarily (47) or evaporative cooling (48–50) are two such possibilities. Further cooling of trapped atoms is also possible by adiabatic expansion of a trap (51). Cooling below T_r also occurs using velocity selective coherent population trapping. In this technique, atoms randomly scatter photons until they fall into a superposition ground state with close to zero velocity, where they are decoupled from the light. Accumulation of He metastable atoms in such a "dark state" was seen in one dimension (52) and later in three dimensions (53). Another practical scheme for cooling below T_r involves selective Raman cooling (54). Sodium atoms in dipole traps have been Raman cooled (55) to $\approx$0.4 T_r in three dimensions with this method.

An early use of cold atoms was in the achievement of a practical "atomic fountain" (56). Chu *et al.* showed that atoms optically launched vertically from a magneto-optical trap could interact with a microwave cavity for long times. This implies narrow resonances and large potential increases in accuracy of atomic clocks. Improved clocks using fountains are currently under development (57). Another growing use of cold atoms is in the study of ultra-cold atomic collisions in which one can explore processes not seen at higher temperatures (58, 59). This is due to the long collision times and large deBroglie wavelength of cold atoms and the sharpness of spectra of photoassociative molecules formed during collision (60, 61). Previously inaccessible high lying levels of the Na_2 and Rb_2 have been experimentally resolved during associative ionizing collisions (62, 63). Ultra-cold collisions play a role in optical traps where they are one of the principal loss mechanisms (59, 60). Of interest, it was shown that one can suppress photoassociative collisions in traps (64).

A subfield of optical manipulation has been developed called "atom optics." It loosely refers to the optical manipulation of atoms in ways similar to manipulation of light by conventional optical elements like lenses, mirrors, beam splitters, gratings, and interferometers. At times it makes use of the wave properties of atoms. The first experiments showed guiding and focusing of atoms using the distributed lens action of the gradient force in a long thin laser beam (24). Other single optical lenses were demonstrated (65, 66), but all suffer from chromatic aberration. Nevertheless, focusing to spot sizes of 20 Å has been seen (67). Achromatic lenses have been considered (68). A form of distributed lens based on the magneto-optical trap has been used to focus and increase the density of atomic beams by factors of 10^3 (69). Optical mirrors for atoms have been developed using reflection from the dipole force of evanescent waves of laser fields (70, 71). Atomic beam splitters based on the "phase grating" formed by the dipole force in optical standing waves were used first by Pritchard *et al.* to diffract atoms (72). A new type of "blazed grating" using standing waves (73) gives a more practical beam splitter, more generally usable on He, Rb, and Cs. Another elegant beam splitter, using adiabatic passage, transfers momentum to atoms without populating the excited states of atoms, using the so-called "superposition dark state" (74). Chu *et al.* (75) applied this general technique to transfer 140 photon momenta to sodium and thereby make a precision measurement of the fine structure constant. Atom optics techniques also have potential uses in technology. Standing wave lenses have focused sodium and chromium atoms onto surfaces, making grating patterns with 20-nm features (76, 77). Cooled beams could reduce this line width considerably. Neutral atom lithography has advantages over e-beam and x-ray lithography. Atom interferometers are an important class of devices for making precision measurements in which one detects fringe shifts due to phase changes in one of the interferometer arms. Chu *et al.* (78) used their fountain and Raman techniques to make an interferometric measurement of the acceleration of gravity with an accuracy of 1 part in 10^6. Increases in accuracy to 10^{-10} *g* are anticipated. Applications to geology, search for net charge on atoms, fifth force experiments, and test of general relativity are suggested. Another atom optic device demonstrated recently (79) is a flexible hollow optical fiber, acting as a grazing incidence light guide that channels atoms along the center of the fiber. Such a guide is useful for atom interferometers and delivering atoms to surfaces in microfabrication.

As atoms get colder and the trap depths needed get shallower, perturbations due to gravity increase. Trapping in space is being considered to eliminate gravity (80). However, gravity is being used for possible interferometers involving "trampolines" whereby atoms are dropped onto atom mirrors and bounce repeatedly before dissipating (81). An interesting consequence of the achievement of low temperatures is the ability to trap atoms on the high intensity peaks of three-dimensional standing waves, forming atomic lattices (82). At temperatures of $\approx$70 μK, so-called "Dieke narrowing" of the fluorescence was seen, indicating trapping in distances less than λ. Later, using one-dimensional molasses at a temperature of $\approx$10 μK, it was possible to resolve the vibrational levels of Rb atoms localized to $\lambda/15$ on the standing wave peak (83). In three-dimensions, optical Bragg reflections were observed off the lattice of Cs atoms that collected on lattices (84). Atomic lattices may be useful in the context of photonic bandgaps and photon localizations. Recently, using the precision made possible by laser-cooled atoms, Hall *et al.* (85) measured the line width of Na resolving a previous 1% discrepancy with theory.

The most important recent development in the field has been the final achievement of Bose–Einstein condensation of atomic vapors. This was made possible by the realization of a combination of sufficiently cold and dense vapors of atomic bosons in which the deBroglie wavelength of atoms becomes large enough so that individual atomic wave functions overlap and become coherent in a single ground state extending over the sample. This was accomplished by using evaporative cooling and specially designed magnetic traps (49, 50). This newly formed, weakly interacting condensate is the cleanest macroscopic quantum system yet achieved. Its poorly understood properties are now being explored in a nondestructive way (86). Bose–Einstein condensation can be considered the first step toward an "atomic laser" source of coherent atoms (87).

Another approach to Bose–Einstein condensation being studied uses far off–resonance dipole traps (88, 89). Such traps give an environment unperturbed by magnetic fields or spontaneous emission. One such trap consists of four repulsive sheet beams formed into a large inverted pyramid that relies on gravity for vertical confinement. This "dark," large volume, noninteracting levitation trap is close to the ultimate ultra-cold optical atom trap. Raman cooling of large numbers of atoms to 1.0 μK has been observed.

In a recent, beautiful experiment, Ketterle *et al.* showed the coherence of the Bose–Einstein condensate by splitting it into two parts with a far off–resonance laser beam and observing atom wave interference, with a period of 15 μm, as the parts recombined (90). They also succeeded in coupling pulses of atoms out of their magnetic trap to give a crude form of atom laser (91).

Recent Work on Optical Trapping and Manipulation in Biology. As seen above, use of traps in biology resulted from the accidental discovery of trapping of bacteria by tweezers and the later demonstration of damage-free trapping of cells using infrared lasers. An early application of tweezers in biology involved the measurement of the torsional compliance of bacterial flagella by twisting a bacterium about a tethered flagellum (92). It was shown that this compliance was located within the bacterial motor itself (93). Tweezers helped show that the flagella of spirochete bacteria also work by the rotary action of their motors (94). Greulich and Berns were the first to use the tweezers technique in combination with the so-called "microbeam" technique of pulsed laser cutting (sometimes called "laser scissors" or "scalpel") for cutting and moving cells and organelles. Greulich's early work involved UV cutting and tweezers manipulation of pieces of chromosomes for gene isolation (95). Tweezers also was used to bring cells into contact with one another to effect cell fusion by cutting the common wall (96). Berns and his group used tweezers, often combined with optical scissors, to manipulate chromosomes during cell division (97) as a new way to study the complexities of mitosis.

Experiments were performed with tweezers to manipulate live sperm cells in three dimensions (98, 99) and to measure their swimming forces (100). Applications of tweezers and scissors to all-optical *in vitro* fertilization are being considered (101). UV drilling of channels in the zona pellucida of oocytes was shown to assist sperm penetration (101). Tweezers was used to insert selected sperm into channels to effect fertilization (102, 103). However, fertilization efficiency and questions of possible genetic damage must be further studied. Important experiments by Berns' group measured the effects of the wave length on optical damage processes in sperm and in other contexts using tunable Ti sapphire lasers (104).

One of the most important biological applications of tweezers is in the study of molecular motors. These mechano-enzymes interact with the microtubules or actin filaments of the cell to generate the forces responsible for cell motility, muscle action, cell locomotion, and organelle movement within cells. In early work using the "handles technique," Block *et al.* (105, 106) attached single kinesin motor molecules to spheres and placed them directly onto microtubules where they could be activated by ATP. This new technique greatly improved on earlier *in vitro* motility assays that used many motors and relied on random diffusion for attachment to filaments. Ashkin and colleagues (107), using a related *in vivo* technique, estimated the force generated by a few dynein motors attached to mitochondria as they moved along microtubules in the giant amoeba *Reticulomyxa*. Kuo and Sheetz (108), working *in vitro* with tweezers and handles

attached to a microtubule filament, estimated the force generated by a single kinesin molecule.

A major advance in the field was the resolution by Svoboda *et al.* (109) of the detailed motion of a single kinesin molecule into a sequence of 8-nm steps as it advanced along a microtubule. This first observation of this previously postulated stepping motion was made possible by the development of an optical trapping interferometric position monitor with subnanometer resolution (109). Proper damping of the Brownian motion of the sphere by the trap also was needed to see the steps (110). Later, Svoboda and Block (111) measured the complete force–velocity relationship of single kinesin motors as a function of ATP concentrations. A maximum force of ≈5–6 pN was observed. Finer *et al.* (112, 113) shortly thereafter introduced a new feedback-enhanced tweezers trap with a detection capability of subnanometers in position, piconewtons in force, and milliseconds in time response. They studied the interaction of actin with myosin in a dual trap scheme that suspended the actin filament over a single myosin molecule. They observed stepwise motion of ≈11 nm and forces of ≈3–4 pN. Malloy *et al.* (114) also used feedback to study the interaction of myosin with mutant *Drosophila* actins. The unbinding force of a single myosin molecule and actin filaments in the absence of ATP was measured with tweezers by Nishizaka *et al.* (115). Single motor molecule experiments have triggered work on detailed models of motion, the ATP hydrolysis cycle, and single enzyme kinetics (110, 116–118). One speculative model of motor motion is the so-called "thermal ratchet model" (119). The principle of a thermal ratchet was demonstrated convincingly recently using optical trapping techniques (120).

A recent exciting advance in the field was the extension of tweezers force measuring techniques to a new class of motors, nucleic acid motor enzymes. Using a handles technique, the force generated by a single RNA polymerase enzyme was measured as it pulled itself along a DNA molecule while synthesizing an RNA transcript (121). The motion is slow, but the motor is surprisingly powerful. It was observed to stall reversibly at 14 pN. This assay opens a new way of studying the transcription process (122). Increasingly, tweezers is becoming the technique of choice for the study of the mechanics of the many types of motor molecules.

Tweezers also has been used to examine the mechanical properties of microtubules, actin filaments, and DNA biopolymers. Kurachi *et al.* (123) measured the flexural rigidity of microtubules by attaching polystyrene beads and bending them with tweezers. Feigner *et al.* (124) studied the rigidity directly by manipulating free-floating single microtubules. The torsional rigidity of actin was deduced from a measurement of the rotational Brownian motion of a single actin filament suspended from a freely rotating sphere held in a tweezers trap (125). Chu *et al.* (126) made the first direct observation of the tube-like motion of a single, extended, fluorescently labeled DNA polymer strand as it relaxed through a dense entangled polymer solution. The behavior supports the reptation model of deGennes. The model explains the observed viscoelastic behavior of many biological materials (38). Relaxation of a model DNA polymer strand in a dilute aqueous solution was observed and compared with theories of dynamic scaling (127). The stretching of double-stranded DNA was studied with optical forces. At 70 pN of force, a reversible transition to a single-stranded, unraveled form of DNA was seen (128). This result may be important for understanding the energetics of DNA recombinations.

The ability of tweezers to separate single bacteria from a mixed sample in a chamber was used recently in a new assay for separating selected archaea bacteria under high temperature anaerobic conditions for cloning purposes (129). This is a major improvement over previous techniques and has already yielded a new species of hyperthermophilic archaeum from the hot springs of Yellowstone Park. The hope is to find new high temperature enzymes, possibly as valuable as *Taq* polymerase used in PCR (130, 131). There are vast numbers of unidentified water and soil bacteria that could be separated by similar tweezers techniques (132).

Burkhardt, J. K. *et al.* (133) used tweezers in a study to identify the mechanisms within killer cells and T lymphocytes by which so-called "lytic particles" move to attack target cells. They developed an *in vitro* assay that showed kinesin-dependent motility of these particles on microtubules. Sheetz *et al.* studied the cell–substrate adhesive process (134) using the ability of tweezers-manipulated, coated microspheres to stick to the surface of moving fibroblast cells. They identified increased integrin–cytoskeleton adhesive interactions at the front of moving cells and increased deformability of the cell membrane at the rear of such cells. Measurements of changes in plasma membrane lipid structure during hypoxia were made by Kuo *et al.* (135) with tweezers. They monitored changes in membrane viscoelasticity by pulling coated spheres from the membrane. Results showed a transition to a more rigid state and the loss of membrane viscoelasticity during hypoxia. Sheetz *et al.* (136) made the first study of the mechanical properties of membranes on the leading edges of migrating neuronal growth cones by pulling out membrane tethers with tweezers. The force to extend the membrane and the membrane surface viscosity were determined. This was a considerable advance in technique over earlier methods using pipettes and very simple cells.

The early work of Ashkin *et al.* (38) showed the ability of tweezers to distort the shape of red blood cells. Svoboda and Block (137) measured the elastic properties of isolated red blood cell membrane skeletons. Recently, using three tweezers traps, Brakenhoff *et al.* (138) developed a new assay to sensitively measure the shape recovery time of single red blood cells using physiologically relevant shapes and conditions. The "parachute" type distortion used closely resembles conditions in small capillaries. Significant differences in relaxation times were found for old and young cells (162 vs. 350 ms). Measurements were possible in blood plasma and gave markedly different results from previous assays using pipettes in buffer solution. With automation, this may be a powerful technique for study of subpopulations of pathological cells. The three computer-controlled tweezers traps used are an application of a multiple scanning trap system developed by Visscher *et al.* (139). Greulich *et al.* have used tweezers to simulate the effect of gravity on the growing tips of algal cells (140). Dragging the statoliths or gravity sensors of the cell to one side can induce the cell to reorient its growth in that direction.

A new assay to study the collision of two particles or cells under controlled biologically relevant conditions, called "OPTCOL," was developed with two tweezers traps (141). The adhesion of influenza virus-covered spheres to erythrocytes during collision with controlled velocities and controlled geometry was studied in the presence of various attachment inhibitors. The new technique is orders of magnitude more sensitive than previous assays. In those experiments it identified the most potent known inhibitor of the adhesion process. The authors foresee wide usage of OPTCOL for studies of collisions of biological particles such as bacteria, viruses, T cells, ribosomes, liposomes, and even nonbiological objects.

Other Recent Work on Optical Trapping and Manipulation in Physics and Chemistry. Interesting applications of optical manipulation techniques exist in other diverse areas of physics and chemistry. In the field of statistical physics and nonlinear dynamics, Simon and Libchaber (142) used stochastic resonance to synchronize the escape of a Brownian particle from a pair of coupled tweezers traps. Weilert *et al.* (143) showed that optical losses were low enough to allow optical levitation of superfluid helium. Ackerson *et al.* (144) studied phase transitions and crystallization of a random two-dimensional colloidal suspension to a colloidal crystal using the optical forces of a standing wave beam. Higurashi *et al.* (145) observed optically induced torques and rotations of micromachined, micron-sized anisotropic particles held in a tweezers trap. Svoboda and Block (146) showed that small metallic Rayleigh

particles have polarizabilities larger than dielectric particles and can be trapped by tweezers. Ghislain and Webb (147) have built a novel scanning force microscope based on a tweezers-trapped stylus particle having a much lower spring constant than a mechanical cantilever. Applications to imaging soft samples in water are anticipated. Malmqvist and Herz (148) propose using trapped submicron particles as light sources for an optical scanned probe microscope. Tweezers was used to help measure the entropic forces of ≈40 fN that control motion of colloidal particles at passive surface microstructures (149). Laser light has been used to cool heavy ion beams in three dimensions for use in accelerators and storage rings (150).

There has been extensive use of optical trapping techniques in the field of microchemistry, which studies the spectroscopy and chemistry of small micron-sized domains. Experiments combining trapping with fluorescence, absorption spectroscopy, photochemistry, and electrochemistry were performed. Polymerization, ablation, and other microfabrication techniques were demonstrated with micrometer samples. Beam-scanning techniques were developed for trapping of micron-sized metal particles, low index particles, and moving of particle arrays in complex patterns. These experiments are described by Masuhara *et al.* (151), summarizing the results of a 5-year Exploratory Research for Advanced Technology project. Bar-Zvi *et al.* (152, 153) have used tweezers to study the physical properties of membranes and vesicles. The local unbinding of pinched membranes (152) and pressurization and entropic expulsion of inner vesicles from large vesicles (153) was studied. Direct measurements using tweezers showed that an attractive force can exist between like-charged particles in a colloidal suspension near a surface, contrary to theory (154). Metastable colloidal crystals were made based on this attractive potential. This has importance on theoretical and possibly practical grounds (155).

CONCLUSION

The precise degree of control made possible by optical trapping and manipulation of small neutral particles has caught the imagination of experimentalists in diverse areas of science, especially atomic physics and biology. Many ingenious and previously impossible experiments have been devised, some having revolutionary impact. The field is still young, and the scope of applications is still growing. Advances in laser technology should further stimulate adoption of these novel manipulation methods. The future looks bright.

1. Ashkin, A. (1970) *Phys. Rev. Lett.* **24,** 156–159.
2. Ashkin, A. (1970) *Phys. Rev. Lett.* **25,** 1321–1324.
3. Askar'yan, V. S. (1962) *Zh. Eksp. Teor. Fiz.* **42,** 1567–1569.
4. Letokhov, V. S. (1968) *Zh. Eksp. Teor. Fiz.* **7,** 348–351.
5. Ashkin, A. & Dziedzic, J. M. (1971) *Appl. Phys. Lett.* **19,** 283–285.
6. Ashkin, A. & Dziedzic, J. M. (1980) *Appl. Opt.* **19,** 660–668.
7. Ashkin, A. & Dziedzic, J. M. (1974) *Appl. Phys. Lett.* **24,** 586–588.
8. Ashkin, A. & Dziedzic, J. M. (1976) *Appl. Phys. Lett.* **28,** 333–335.
9. Ashkin, A. & Dziedzic, J. M. (1977) *Appl. Phys. Lett.* **30,** 202–204.
10. Ashkin, A. (1980) *Science* **210,** 1081–1088.
11. Ashkin, A. & Dziedzic, J. M. (1977) *Appl. Phys. Lett.* **38,** 1351–1354.
12. Chylek, P., Kiehl, J. T. & Ko, M. K. W. (1978) *Phys. Rev. A At. Mol. Opt. Phys.* **18,** 2229–2233.
13. Ashkin, A. & Dziedzic, J. M. (1981) *Appl. Opt.* **20,** 1803–1814.
14. Chylek, P., Ramaswamy, V., Ashkin, A. & Dziedzic, J. M. (1983) *Appl. Opt* **22,** 2302–2307.
15. Barber, P. W. & Chang, R. K. (1988) *Optical Effects Associated with Small Particles* (World Scientific, Teaneck, NJ).
16. Schieder, R., Walther, H. & Woste, L. (1972) *Opt. Commun.* **5,** 337–340.
17. Jacquinot, P., Liberman, D. Pigne, J. L. & Pinard, J. (1973) *Opt. Commun.* **8,** 163–165.
18. Bernhardt, A. F. (1976) *Appl. Phys.* **9,** 19–34.
19. Hänsch, T. W. & Schawlow, A. L. (1975) *Opt. Commun.* **13,** 68–69.
20. Letokhov, V. L., Minogin, V. G. & Pavlik, B. D. (1977) *Zh. Eksp. Teor. Fiz* **72,** 1328–1341.
21. Letokhov, V. L. & Minogin, V. G. (1978) *Appl. Phys.* **17,** 99–103.
22. Ashkin, A. (1978) *Phys. Rev. Lett.* **40,** 729–732.
23. Ashkin, A. & Gordon, J. P. (1979) *Opt. Lett.* **4,** 161–163.
24. Bjorkholm, J. E., Freeman, R. R., Ashkin, A. & Pearson, D. B. (1978) *Phys. Rev. Lett.* **41,** 1361–1364.
25. Bjorkholm, J. E., Freeman, R. R., Ashkin, A. & Pearson, D. B. (1980) *Opt. Lett.* **5,** 111–113.
26. Gordon, J. P. & Ashkin, A. (1980) *Phys. Rev. A At. Mol. Opt. Phys.* **21,** 1606–1617.
27. Phillips, W. D. & Metcalf, H. (1982) *Phys. Rev. Lett.* **48,** 596–599.
28. Prodan, P., Migdall, A., Phillips, W. D., So, I., Metcalf, H. & Dalibard, J. (1985) *Phys. Rev. Lett.* **54,** 992–995.
29. Letokhov, V. S. & Minogin, V. G. (1981) *Phys. Rep.* **73,** 1–65.
30. Ertmer, W., Blatt, R., Hall, J. L. & Zhu, M. (1985) *Phys. Rev. Lett.* **54,** 996–999.
31. Minogin, V. G. & Javanainen, J. (1982) *Opt. Commun.* **43,** 119–122.
32. Ashkin, A. & Gordon, J. P. (1983) *Opt. Lett.* **8,** 511–513.
33. Chu, S., Holberg, L., Bjorkholm, J. E., Cable, A. & Ashkin, A. (1985) *Phys. Rev. Lett.* **55,** 48–51.
34. Chu, S., Bjorkholm, J. E., Cable, A. & Ashkin, A. (1986) *Phys. Rev. Lett.* **57,** 314–317.
35. Ashkin, A., Dziedzic, J. M., Bjorkholm, J. E. & Chu, S. (1986) *Opt. Lett.* **11,** 288–290.
36. Ashkin, A. (1992) *Biophys. J.* **61,** 569–582.
37. Ashkin, A. & Dziedzic, J. M. (1987) *Science* **235,** 1517–1520.
38. Ashkin, A., Dziedzic, J. M. & Yamane, T. (1987) *Nature (London)* **330,** 769–771.
39. Ashkin, A. & Dziedzic, J. M. (1989) *Proc. Natl. Acad. Sci. USA* **86,** 7914–7918.
40. Raab, E. L., Prentiss, M., Cable, A., Chu, S. & Pritchard, D. E. (1987) *Phys. Rev. Lett.* **59,** 2631–2634.
41. Walker, T., Sasko, D. & Wieman, C. (1990) *Phys. Rev. Lett.* **64,** 408–411.
42. Chu, S., Prentiss, M., Cable, A. & Bjorkholm, J. E. (1987) *Laser Spectroscopy VIII*, eds. Swanberg, S. & Perssow, W. (Springer, Berlin), p. 58.
43. Lett, P. D., Watts, R. N., Westbrook, C. I., Phillips, W. D., Gould, P. L. & Metcalf, H. J. (1988) *Phys. Rev. Lett.* **61,** 169–172.
44. Ungar, P. J., Weiss, D. S., Riis, E. & Chu, S. (1989) *Opt. Soc. Am. B* **6,** 2058–2071.
45. Dalibard, J. & Cohen-Tannoudji, C. (1989) *Opt. Soc. Am. B* **6,** 2023–2045.
46. Weiss, D. S., Riis, E., Shevy, Y., Unger, P. J. & Chu, S. (1989) *Opt. Soc. Am. B* **6,** 2072–2083.
47. Chu, S., Bjorkholm, J. E., Ashkin, A., Gordon, J. P. & Holberg, L. (1986) *Opt. Lett.* **11,** 73–75.
48. Hess, H., Kochenski, G. P., Kleppner, D. & Greytak, T. J. (1987) *Phys. Rev. Lett.* **59,** 672–675.
49. Anderson, M. H., Ensher, J. R., Mathews, M. R., Wieman, C. E. & Cornell, E. A. (1995) *Science* **269,** 198–201.
50. Davis, K. B., Mewes, M.-O., Andrews, M. R., vanDruten, N. J., Durfee, D. S., Kurn, D. M. & Ketterle, W. (1996) *Phys. Rev. Lett.* **75,** 3969–3973.
51. Kastberg, A., Phillips, W. D., Falston, S. L. & Spreeuw, R. J. C. (1995) *Phys. Rev. Lett.* **74,** 1542–1545.
52. Aspect, A., Arimondo, E., Kaisor, R., Vansteenkiste, N. & Cohen-Tannoudji, C. (1988) *Phys. Rev. Lett.* **61,** 826–829.
53. Lawall, J., Kulin, S., Saubamea, B., Bigelow, N., Leduc, M. & Cohen-Tannoudji, C. (1995) *Phys. Rev. Lett.* **75,** 4194–4197.
54. Kasevich, M. & Chu, S. (1992) *Phys. Rev. Lett.* **69,** 1741–1744.
55. Lee, H. J., Adams, C. S., Kasevich, M. & Chu, S. (1996) *Phys. Rev. Lett.* **76,** 2658–2661.
56. Kasevich, M. A., Riis, E., Chu, S. & DeVoe, R. G. (1989) *Phys. Rev. Lett.* **63,** 612–615.
57. Drullinger, R. (1996) *APS News* **5,** 4.
58. Prentiss, M., Cable, A., Bjorkholm, J. E., Chu, S., Raab, E. & Pritchard, D. E. (1988) *Opt. Lett.* **13,** 452–454.
59. Sesko, D., Walker, T., Monroe, C., Gallagher, A. & Wieman, C. (1989) *Phys. Rev. Lett.* **63,** 961–964.
60. Thorsheim, H. R., Weiner, J. & Julienne, P. S. (1987) *Phys. Rev. Lett.* **58,** 2420–2423.
61. Julienne, P. S. & Frederick, H. M. (1989) *J. Opt. Soc. Am. B* **6,** 2257–2269.
62. Lett, P. D., Helmerson, K., Phillips, W. D., Ratliff, L. P., Ralston, S. L. & Wagshul, M. E. (1993) *Phys. Rev. Lett.* **71,** 2200–2203.
63. Miller, J. D., Cline, R. A. & Heinzen, D. J. (1993) *Phys. Rev. Lett.* **71,** 2204–2207.
64. Zilio, S. C., Marcassa, L., Muiz, S., Horowicz, R., Bagnato, V., Napolitano, R., Weiner, J. & Julienne, P. S. (1996) *Phys. Rev. Lett.* **76,** 2033–2036.
65. Sleator, T., Pfau, T., Balykin, V. & Mlynek, J. (1992) *Appl. Phys. B* **54,** 375–379.
66. Balykin, V. Letokhov, V. S., Sidorov, A. I. & Orchinnikov, Y. B. (1988) *J. Mod. Opt.* **35,** 17–34.
67. Gallatin, G. M. & Gould, P. L. (1991) *J. Opt. Soc. Am. B* **8,** 502–508.
68. Pritchard, D. E. (1991) XII International Conference on Atomic Physics, eds. Zorn, J. & Lewis, R. (American Institute of Physics, New York), p. 65.
69. Riis, E., Weiss, D. S., Moler, K. A. & Chu, S. (1990) *Phys. Rev. Lett.* **64,** 1658–1661.
70. Cook, R. J. & Hill, R. K. (1982) *Opt. Commun.* **43,** 258–260.
71. Kaiser, R., Levy, Y., Vansteenkiste, N., Aspect, A. Seifert, W. Leipold, D. & Mlynek, J. (1994) *Opt. Commun.* **104,** 234–240.
72. Martin, P. J., Oldaker, B. G., Miklich, A. H. & Pritchard, D. E. (1988) *Phys. Rev. Lett.* **60,** 515–518.
73. Johnson, K. S., Chu, A., Lynn, T. W., Berggren, K. K., Shahriar, M. S. & Prentiss, M. (1995) *Opt. Lett.* **20,** 1310–1312.
74. Lawall, J. & Prentiss, M. G. (1994) *Phys. Rev. Lett.* **72,** 993–996.
75. Weitz, M., Young, B. C. & Chu, S. (1994) *Phys. Rev. Lett.* **72,** 2563–2566.

76. Timp, G., Behringer, R. E., Tennant, D. M., Cunningham, J. E., Prentiss, M. & Berggren, K. (1992) *Phys. Rev. Lett.* **69,** 1636–1639.
77. McClelland, J. J., Scholten, R. E., Palm, E. C. & Celotta, R. J. (1993) *Science* **262,** 877–880.
78. Kasevich, M. & Chu, S. (1991) *Phys. Rev. Lett.* **67,** 181–184.
79. Renn, M. J., Montgomery, D., Vdovin, O. V., Anderson, D. Z., Wieman, C. E. & Cornell, E. A. (1995) *Phys. Rev. Lett.* **73,** 3253–3256.
80. Freedman, D. H. (1993) *Science* **262,** 1376–1378.
81. Aminoff, C. G., Steane, A. M., Bouyer, P., Desbiolles, P., Dalibard, J. & Cohen-Tannoudji, C. (1993) *Phys. Rev. Lett.* **71,** 3083–3086.
82. Westbrook, C. I., Watts, R. N., Tanner, C. E., Ralston, S. L., Phillips, W. D. & Lett, P. D. (1990) *Phys. Rev. Lett.* **65,** 33–36.
83. Jessen, P. S., Gerz, C., Lett, P. D., Phillips, W. D., Ralston, S. L., Spreeuw, R. J. C. & Westbrook, C. I. (1992) *Phys. Rev. Lett.* **69,** 49–52.
84. Birkl, G., Gatzke, M., Deutsch, I. H., Ralston, S. L. & Phillips, W. D. (1995) *Phys. Rev. Lett.* **75,** 2823–2926.
85. Oats, C. W., Vogel, K. R. & Hall, J. L. (1996) *Phys. Rev. Lett.* **76,** 2866–2869.
86. Andrews, M. R., Mewes, M.-O., van Druten, N. J., Durfee, D. S., Kurn, D. M. & Ketterle, W. (1996) *Science* **273,** 84–87.
87. Kleppner, D. (1996) *Phys. Today* **49,** 11–13.
88. Miller, J. D., Cline, R. A. & Heinzen, D. J. (1993) *Phys. Rev. A* **47,** 4567–4570.
89. Lee, H. J., Adams, C. S., Kasevich, M. & Chu, S. (1996) *Phys. Rev. Lett.* **76,** 2658–2661.
90. Andrews, M. R., Townsend, C. G., Miesner, H.-J., Durfee, D. S., Kurn, D. M. & Ketterle, W. (1997) *Science* **275,** 637–641.
91. Mewes, M.-O., Andrews, M. R., Kurn, D. M., Durfee, D. S., Townsend, C. G. & Ketterle, W. (1997) *Phys. Rev. Lett.* **78,** 582–585.
92. Block, S. M., Blair, D. F. & Berg, H. C. (1989) *Nature (London)* **338,** 514–518.
93. Block, S. M., Blair, D. F. & Berg, H. C. (1991) *Cytometry* **12,** 492–496.
94. Charon, N. W., Goldstein, S. F., Block, S. M., Curci, K. & Ruby, J. D. (1992) *J. Bacteriol.* **174,** 832–840.
95. Seeger, S., Manojembaski, S., Hutter, K. J., Futterman, G., Wolfrum, J. & Greulich, K. O. (1991) *Cytometry* **12,** 497–504.
96. Steubing, R. W., Cheng, S., Wright, W. H., Namajiri, Y. & Berns, M. W. (1991) *Cytometry* **12,** 505–510.
97. Liang, H., Wright, W. H., He, W. & Berns, M. W. (1993) *Exp. Cell Res.* **204,** 110–120.
98. Tadir, Y., Wright, W. H. Vafa, O., Ord, T., Asch, R. H. & Berns, M. W. (1989) *Fertil. Steril.* **52,** 870–873.
99. Colon, J. M., Sarosi, P., McGovern, P. G., Ashkin, A., Dziedzic, J. M., Skurnick, J., Weiss, G. & Bonder, E. M. (1992) *Fertil. Steril.* **57,** 695–698.
100. Bonder, E. M., Colon, J. M., Dziedzic, J. M. & Ashkin, A. (1990) *J. Cell Biol.* **111,** 421a.
101. Tadir, Y., Wright, W. H., Vafa, O, Liaw, L. H., Asch, R. & Berns, M. W. (1991) *Hum. Reprod.* **6,** 1011–1016.
102. Schütze, K., Clement-Sengewald, A. & Ashkin, A. (1994) *Fertil. Steril.* **61,** 783–786.
103. Clement-Sengewald, A., Schütze, K., Ashkin, A., Palma, G. A., Kerlen, G. & Brem, B. (1996) *J. Assist. Reprod. Genet.* **13,** 259–265.
104. Liang, H., Vu, K. T., Krishnan, P., Trang, T. C., Shin, D., Kimel, S. & Berns, M. W. (1996) *Biophys. J.* **70,** 1529–1533.
105. Block, S. M., Goldstein, L. S. B. & Schnapp, B. J. (1990) *Nature (London)* **348,** 348–352.
106. Svoboda, K. & Block, S. M. (1994) *Ann. Rev. Biophys. Biomol. Struct.* **23,** 247–285.
107. Ashkin, A., Schütze, K., Dziedzic, J. M., Eutenauer, U. & Schliwa, M. (1990) *Nature (London)* **348,** 346–348.
108. Kuo, S. C. & Sheetz, M. P. (1993) *Science* **260,** 232–234.
109. Svoboda, K., Schmidt, C. F., Schnapp, B. J. & Block, S. M. (1993) *Nature (London)* **365,** 721–727.
110. Block, S. M. (1995) *Trends Cell Biol.* **5,** 169–175.
111. Svoboda, K. & Block, S. M. (1994) *Cell* **77,** 773–784.
112. Finer, J. T., Simmons, R. M. & Spudich, J. A. (1994) *Nature (London)* **368,** 113–119.
113. Simmons, R. M., Finer, J. T., Chu, S. & Spudich, A. (1996) *Biophys. J.* **70,** 1813–1822.
114. Molloy, J. E., Burns, J. E., Sparrow, J. C., Tregear, R. T., Kendrick-Jones, J. & White, D. C. (1995) *Biophys. J.* **68,** 2985–3055.
115. Nishizaka, T., Miyata, H., Yoshikawa, H., Ishiwata, S. & Kinosita, K., Jr. (1995) *Nature (London)* **377,** 251–254.
116. Maddox, J. (1994) *Nature (London)* **368,** 278.
117. Levi, B. G. (1995) *Phys. Today* **48,** 17–19.
118. Svoboda, K., Mitra, P. P. & Block, S. M. (1994) *Proc. Natl. Acad. Sci. USA* **91,** 11782–11786.
119. Asturmian, R. D. & Bier, M. (1994) *Phys. Rev. Lett.* **72,** 1766–1769.
120. Faucheux, L. P., Bourdieu, L. S., Kaplan, P. D. & Libchaber, A. J. (1995) *Phys. Rev. Lett.* **74,** 1504–1507.
121. Yim, H., Wang, M. D., Svoboda, K., Landick, R., Block, S. M. & Gelles, J. (1995) *Science* **270,** 1653–1657.
122. O'Brien, C. (1995) *Science* **270,** 1668.
123. Kurachi, M., Hoshi, M. & Tashiro, H. (1995) *Cell Motil. Cytoskeleton* **30,** 221–228.
124. Feigner, H., Frank, R. & Schliwa, M. (1996) *J. Cell Sci.* **109,** 509–516.
125. Tsuda, Y., Yasutake, H., Ishijima, A. & Yamagida, T. (1996) *Proc. Natl. Acad. Sci. USA* **93,** 12937–12942.
126. Perkins, T. T., Smith, D. E. & Chu, S. (1994) *Science* **264,** 822–825.
127. Perkins, T. T., Quake, S. R., Smith, D. E. & Chu, S. (1994) *Science* **264,** 819–822.
128. Smith, S. B., Cui, Y. & Bustamante, C. (1996) *Science* **271,** 795–799.
129. Huber, R., Burggraf, S., Mayer, T., Barns, S. M., Rossnagel, P. & Stetter, K. O. (1995) *Nature (London)* **376,** 57–58.
130. Milstein, M. (1995) *Science* **270,** 226.
131. Barker, S. (1996) *Nature (London)* **381,** 455.
132. Mitchell, J. G., Weller, R., Beconi, M., Sell, J. & Holland, J. (1993) *Microb. Ecol.* **25,** 113–119.
133. Burkhardt, J. K., McIlvain Jr., J. M., Sheetz, M. P. & Argon, Y. (1993) *J. Cell Sci.* **104,** 151–162.
134. Schmidt, C. E., Horwitz, A. F., Lauffenburger, D. A. & Sheetz, M. P. (1993) *J. Cell Biol.* **123,** 977–991.
135. Wang, X. F., Lemaster, J. J., Herman, B. & Kuo, S. (1993) *Opt. Eng.* **32,** 284–290.
136. Dai, J. & Sheetz, M. P. (1995) *Biophys. J.* **68,** 988–996.
137. Svoboda, K., Schmidt, C. F., Branton, D. & Block, S. M. (1992) *Biophys. J.* **63,** 784–793.
138. Bronkhorst, P. J. H., Streekstra, G. J., Grimbergen, J., Nijhof, E. J., Sixma, J. J. & Brakenhoff, G. J. (1995) *Biophys. J.* **69,** 1666–1673.
139. Visscher, K., Brakenhoff, G. J. & Krol, J. J. (1993) *Cytometry* **14,** 105–114.
140. Leitz, G., Schnepf, E. & Greulich, K. O. (1995) *Planta* **197,** 278–288.
141. Mammer, M., Helmerson, K, Kishore, R., Seok-Ki, C., Phillips, W. D. & Whitesides, G. M. (1996) *Chem. & Biol.* **3,** 757–763.
142. Simon, A. & Libchaber, A. (1992) *Phys. Rev. Lett.* **68,** 3375–3378.
143. Weilert, M. A., Whitaker, D. L., Maris, H. J. & Seidel, G. M. (1995) *J. Low Temp. Phys.* **98,** 17–35.
144. Choudhury, A., Ackerson, B. J. & Clark, N. A. (1985) *Phys. Rev. Lett.* **55,** 833–836.
145. Higurashi, E., Ukita, H., Tanaka, H. & Ohguchi, O. (1994) *Appl. Phys. Lett.* **64,** 2209–2210.
146. Svoboda, K. & Block, S. M. (1994) *Opt. Lett.* **19,** 930–932.
147. Ghislain, L. P., & Webb, W. W. (1993) *Opt. Lett.* **18,** 1678–1680.
148. Malmqvist, L. & Hertz, H. M. (1992) *Opt. Commun.* **94,** 19–24.
149. Dinsmore, A. D., Yodh, A. G. & Pine, D. J. (1996) *Nature (London)* **383,** 239–242.
150. Miesner, H., Grimm, R., Grieser, M., Habs, D., Schwalm, D., Wanner, B. & Wolf, A. (1996) *Phys. Rev. Lett.* **77,** 623–626.
151. Masuhara, H., deSchryver, F. C., Kitamura, N. & Tamai, N. (1994) *Micro-Chemistry-Spectroscopy and Chemistry in Small Domains* (North–Holland, Amsterdam).
152. Bar-Ziv, R., Menes, R., Moses, E. & Safran, S. A. (1995) *Phys. Rev. Lett.* **75,** 3356–3359.
153. Bar-Ziv, R., Frisch, T. & Moses, E. (1995) *Phys. Rev. Lett.* **75,** 3481–3484.
154. Larsen, A. E. & Grier, D. G. (1997) *Nature (London)* **385,** 230–233.
155. Murray, C. A. (1997) *Nature (London)* **385,** 203.