Method for trapping and manipulating nanoscale objects in solution

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We present a device that allows a user to trap a single nanoscale object in solution at ambient temperature, and then to position the trapped object with nanoscale resolution. This anti-Brownian electrophoretic trap (ABEL trap) works by monitoring the Brownian motion of the particle (via fluorescence microscopy), and then applying a feedback voltage to the solution so that the electrophoretic drift exactly cancels the Brownian motion. The ABEL trap works on any object that can be imaged optically and that acquires a charge in water. The ABEL trap is noninvasive, is gentle enough to handle biological molecules, and can trap objects far smaller than can be trapped with laser tweezers. Our proof-of-principle device can trap fluorescent polystyrene nanospheres with diameters down to 20 nm. © *2005 American Institute of Physics*. [DOI: 10.1063/1.1872220]

One of the outstanding challenges of nanotechnology is to develop a means to trap and manipulate individual nanoscale objects in solution. Laser tweezers[1] and ac dielectrophoresis[2–4] have been used to trap micrometer-scale objects, but fail for smaller objects because the trapping force is proportional to the volume of the object. Quasi-dc magnetic fields have been used in conjunction with digital feedback to cancel the Brownian motion of 4.5 μm magnetic particles, but here, too, the force scales with the volume of the trapped particle.[5] We demonstrate a trap that uses quasi-dc electric fields and digital feedback to manipulate individual nanoscale objects in solution at ambient temperature. Unlike other trapping schemes, the trapping performance of the device presented here scales favorably for small particles (in a manner discussed below).

The anti-Brownian electrophoretic trap (ABEL trap) works by monitoring the Brownian motion of the particle (via fluorescence microscopy), and then applying a time-dependent feedback voltage to the solution so that the electrophoretic drift exactly cancels the Brownian motion. The ABEL trap consists of four microfabricated electrodes on a glass slide, arranged on the corners of a diamond [Fig. 1(a)]. An arbitrary in-plane electric field is generated by independently controlling the voltages on the four electrodes. A CCD camera connected to a fluorescence microscope and a computer provides a real-time image of a particle diffusing above the electrodes. Using the particle's position at the end of each video frame, the computer generates a feedback voltage so that the electrophoretic drift returns the particle to the target position during the subsequent frame.

How tightly can the ABEL trap confine a particle? The rms distance d between the actual and target locations has two components: d_f due to the finite restoring force of the trap, and d_r due to the response time of the feedback loop. We now show that typically $d_r \gg d_f$.

Consider the scenario where the feedback is instantaneous. If the maximum possible field (set by the electrode geometry and the electrolysis of water) is applied counter to the instantaneous displacement of the particle, then the particle "sees" a conical potential well whose walls have a slope of $qE_{\max}$, where q is the charge of the particle. Elementary thermodynamics then implies that the fluctuations of the particle along each axis have an amplitude of $d_f = 2k_BT/(qE_{\max})$. For a 20 nm polystyrene particle in the ABEL trap, $q \sim 3000e$ and $E_{\max} \sim 10^4$ V/m (taking into account the dielectric constant of water), so that $d_f \sim 1.7$ nm.

Now we consider the effect of the finite response time t_r of the feedback loop. During each iteration of the feedback loop, the particle diffuses a rms distance $d_r = (2Dt_r)^{1/2}$ along each axis. In the present embodiment, t_r is set by the 60 Hz frame rate of our camera. A particle of diameter 20 nm in water has $D = 22$ μm^2/s, and thus in 1/60 s diffuses a rms distance $d_r \sim 860$ nm. We see that $d_r \gg d_f$, so the ABEL trap is limited by the feedback latency rather than by the electric field strength.

Electrodes were fabricated on 22 mm square low-fluorescence glass coverslips (Fisher) using standard contact photolithography and a bilayer liftoff process. The electrodes consisted of a 40 nm chromium adhesion layer capped by 200 nm of gold. Four-electrode arrays were formed with gaps between opposing electrodes of 3, 5, 10, and 15 μm.

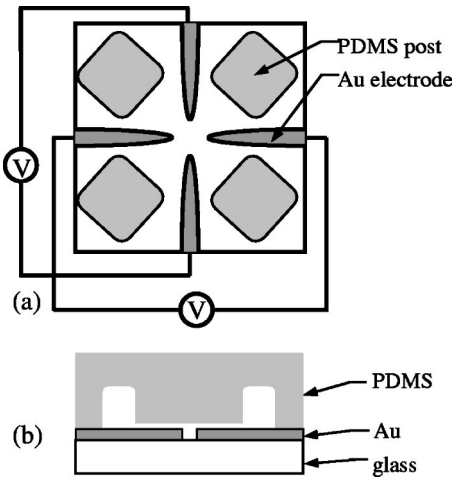

FIG. 1. Schematic diagram of the sample cell of the ABEL trap. (a) Top view. (b) Side view (not to scale).

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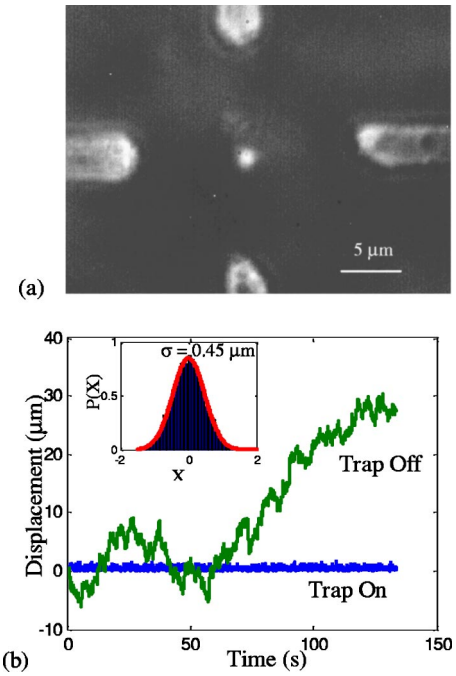

FIG. 2. (Color online) Trapping of a 200 nm particle. (a) Average of 30 video frames showing a single trapped particle. The trapping electrodes are visible protruding from the edges of the image. (b) Comparison of trajectories of a 200 nm diameter particle with the trap on and with the trap off. Inset: histogram of displacements from equilibrium.

The trapping results reported here were obtained with the 10 and 15 μm arrays.

The ABEL trap does not provide confinement in the z direction (although a variant with eight electrodes placed at the corners of a cube is conceivable). To provide z confinement, we formed a thin disk-shaped fluid volume in the z direction using a polydimethylsiloxane (PDMS) stamp. The PDMS stamp consisted of a checkerboard array of square posts 1.5 μm high and 95 μm wide, separated by 105 μm [Fig. 1(b)]. In spite of the low aspect ratio, the recessed regions of the stamp did not collapse onto the coverslip, provided that the assembly was handled gently. An annular "pressure relief" trench in the PDMS, ~1 mm inner radius, ~2 mm outer radius, and ~0.5 mm deep, surrounded the array of posts. Fluid inlet and outlet holes were punched through the top of the stamp into the pressure relief trench. This trench was crucial to the success of the experiment: without it, minute pressure differences between the inlet and outlet ports led to large flow velocities in the thin layer of solution above the electrodes.

In a typical experiment, the coverslip and PDMS stamp were cleaned by sonication in a solution of deionized water and Alconox detergent. After sonication, both surfaces were hydrophobic, so that water would not fill the thin channels. The coverslip was rendered hydrophilic by exposing it to a rf plasma of room air for 1 min. This treatment was sufficient to cause water to fill the channels, without necessitating any special surface treatment of the PDMS. If the PDMS was subjected to the same plasma treatment, it became hydrophilic as well, but also on contact it bonded irreversibly to the coverslip. We typically did not plasma-treat the PDMS so that the PDMS and coverslip could be separated and cleaned between experiments. The PDMS stamp and coverslip were assembled by hand under a dissecting microscope.

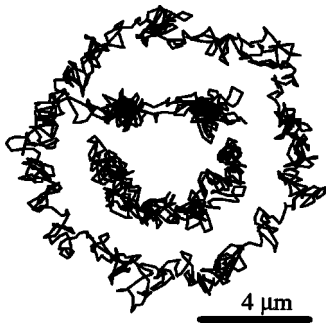

FIG. 3. Trajectory of a 200 nm particle over the course of 1 min, as it was manipulated to draw out a smiley face. The trajectory was specified by a file containing 1800 target positions, updated at 30 Hz. (Two of the 1800 data points—those joining the eyes and mouth—are not plotted.)

The assembled sample cell was mounted in an inverted fluorescence microscope (Nikon TE 300), and filled with a solution of the particles to be trapped. The inlet and outlet holes were then capped with a slab of PDMS. Once capped, the cell could be used for days without need for disassembly. Fluorescently labeled polystyrene nanospheres (FluoSpheres, Molecular Probes) dissolved in deionized water were excited with a 1 mW 633 nm HeNe laser, and fluorescence emission was detected with a Genwac 902H Si CCD camera operating at a 60 Hz frame rate. Images from the camera were fed to a 2.8 GHz Pentium™ 4 computer, where they were processed in real time using custom software written in Visual Basic. The coordinates of particles were extracted using the IMAQ Vision library (National Instruments). The offset between the desired location of a particle and its actual location was turned into a feedback voltage, which was applied to the electrodes.

Figure 2 shows the displacement trajectories of a free and a trapped 200-nm-diameter particle. By fitting the histogram of displacements to a Gaussian of width σ, we extract a spring constant of $k=20$ nN/m from the relation $k=k_BT/\sigma^2$. We could move the target position of the particle either by dragging with the computer mouse, or by reading values from a file. Figure 3 shows the trajectory of a 200 nm particle automatically manipulated to trace out a smiley face. Figure 4 shows a histogram of the displacements of a 20 nm particle with a fixed target position, from which we extract a spring constant of $k=1.7$ nN/m.

Fluorescence imaging of single molecules has become commonplace.[6] We expect that future versions of the ABEL trap using higher speed cameras—and ultimately an array of

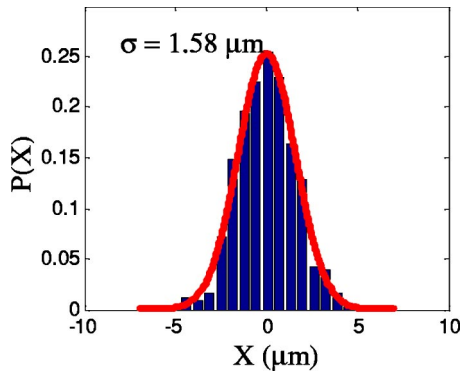

FIG. 4. (Color online) Histogram of displacements of a trapped 20 nm fluorescent particle.

avalanche photodiodes or a scanning excitation source[7]—should be able to trap individual fluorophores. The fundamental limit to trapping an individual fluorophore is the finite rate of photon detection: it is impossible to know the position of a fluorophore in between photon detection events. To confine a fluorophore with $D \sim 300\ \mu m^2/s$ to a distance $d \sim 1\ \mu m$ requires a photon detection rate, and a feedback bandwidth, of ~ 500 Hz. If the fluorophore has a charge of $1e$, then the field must be $E_{max} \sim 5 \times 10^4$ V/m. All these conditions are attainable in a system with a 3 μm interelectrode gap and avalanche photodiode detection of fluorescence. We note that, as for all single-molecule fluorescence studies, photobleaching can limit the observation time. In addition, water is a challenging trapping medium because its dielectric constant of 80 significantly screens the voltages applied to the electrodes. For nonbiological particles, it would be advantageous to work in solvents with lower dielectric constants, yet sufficiently polar for the particles to develop free charges.

The ABEL trap has potential applications in single-molecule spectroscopy, nanomanufacturing, and the identification of biological particles. The basic idea—using feedback to counter molecular motion—could be implemented with other means of generating deterministic motion, such as electro-osmotic flow or pressure-driven flow, or with other means of optical detection of the nanoparticle.

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