On-Chip Manipulation of Levitated Femtodroplets

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Abstract

We report diamagnetic levitation of droplets and/or particles of pico–femtoliter volume and demonstrate their on-chip storage and high precision manipulation (translation, merging, assembling and rotation). We also demonstrate a levitation based microfluidic processor to process droplets/particles with up to a billion times smaller volume than in typical microfluidic devices. The levitated particles can be positioned with up to 300 nm accuracy and precisely rotated and assembled, providing a different physical approach for Micro-Electro-Mechanical-Systems. Force can be applied to the droplets/particles via magnetic, electric and gravitational fields with up to femto Newton accuracy, and potential energy can be controlled with up to 0.2 zepto J (0.05 $k_B T$) precision, thus providing experimental tools for fundamental studies.

The manipulation of droplets/particles that are isolated (levitated in gas/vacuum) from the environment (container walls) pure or loaded with chemicals, cells, bacteria or viruses, is of utmost importance[1,2] for both basic research in physics, chemistry, biology, biochemistry and colloidal science and for applications in nanotechnology, microfluidics, atmospheric chemistry, aerosol science, crystal growth and other fields. Among different levitation methods (optical, diamagnetic[3], electrostatic, electromagnetic, acoustic), only optical tweezers[4], based on powerful lasers, has demonstrated the ability for stable levitation of micron scale droplets in air. The ability to process (manipulate) single or several isolated pico-femtoliter volume particles/droplets and implementation in the Lab-on-a-Chip environment has not previously been demonstrated with existing levitation techniques. We have reduced the size of diamagnetic levitation devices from superconducting magnet size to computer processor size by using micron scale permanent magnets to create a Magnetic Micromanipulation Chip (MMC). MMC operates with droplets levitated in air (or an inert atmosphere/vacuum), thus providing isolation from container walls, very low viscous friction, the possibility for precise manipulation of levitated particles with electric, magnetic and gravitational fields and extremely small droplet size. A MMC based microfluidic processor can store and process droplets, which can be used as a pico-femtoliter size "beakers", on a "magnetic bench" created by permanent magnets. These "beakers" can be localized in magnetic potential wells or moved from one well to another by magnetic or electric fields. This first generation MMC can manipulate droplets and/or particles with a volume up to a billion times smaller than that recently reported[2,5] for on-chip manipulation of droplets floating on a denser, immiscible liquid layer. Pico–femtoliter volume droplets can be loaded with a fixed small number of cells, bacteria, viruses or molecules at nano-pico mole solution concentrations. It is thus feasible, by merging two femtoliter droplets (femtodroplets), to inject a single given molecule or a predefined sequence of molecules to a cell, or to initiate chemical reactions with only two reacting molecules available in a closed femtoliter volume (i.e. at nanomole solute concentrations). We have validated this program by demonstrating controllable droplet motion and merging including those loaded with red blood cells or micron size fluorescent microspheres. Furthermore, the ability to measure and apply forces with accuracy in the femto Newton range and to control the potential energy with 0.2 zJ (zepto Joule) or 0.05 $k_B T$ precision provides a powerful tool for fundamental physical studies of a broad range of phenomena from particle/droplet interactions to stochastic resonance and Brownian motors.

Lord Kelvin[6] showed that a diamagnetic body can have stable equilibrium in a magnetic field minima and that this does not contradict the Earnshaw theorem[7] that no stable equilibrium is possible if particles interact according to Coulomb's law (i.e. a R^{-2} dependence for the interaction force). Note, that electrostatic levitation cannot be stable according to the Earnshaw theorem[7]. Recently, diamagnetic levitation of centimeter scale bodies, even living species[3], has been elegantly demonstrated inside powerful magnets.

The core of MMC consists of two 10mm$\times$10 mm$\times$ h neodymium-iron-boron permanent magnets with height h in the range 100 μm – 2000 μm mounted on a steel substrate which contains a set of electrodes directed perpendicular to the slit between the magnets (Fig. 1, Supplement Figure S1). The magnetization of the permanent magnets is directed in-plane, normal to the slit of width $w \approx 0.25h - 0.4h$ and opposite in direction to each other. The magnetic field is estimated to be 0.5T on the magnet surface with a minimum that lies along a line between the magnets. The levitating droplets/particles have a small induced magnetic moment directed opposite to the magnetic field. Interaction of this moment with the magnetic field gradient provides the force which levitates the droplet/particle. Charged particles or droplets also experience the Coulomb interaction with the metal magnets and the substrate (image interaction). The presence of the Coulomb interaction makes the stable potential minimum provided by diamagnetism metastable. However, for relatively small charges, this interaction does not noticeably affect the stability. To create a set of potential wells for droplets we have fabricated grooves or electrodes 25 μm wide or larger and about 100 μm deep or less on the steel substrate. The potential minima are due to the magnetic interaction of the droplet/particle with the steel substrate and due to the Coulomb interaction for charged droplets. Figure 2(a-c) shows three sequentially timed snapshots of back and forth motion of a 30 micron diameter glycerine/water droplet levitated above a substrate with electrodes (3 are shown). The droplet has stable local energy minima between the electrodes. The magnetic field generated by current pulses in the electrodes (0.5s-2s duration, amplitude $\approx$5A-7A) moves the droplet along the slit from one potential minimum to another (Figure 2(a-c), Supplement Figure S2 and Video S3). The metal substrate prevents overheating of the current carrying electrodes. Use of a smaller current permits control of the droplet's average position with an accuracy of 300nm or better. Droplets can be merged (Figure 2(d-f), Supplement Video S4) and particles assembled into chains of particles (Supplement Figure S5). An AC electric field (up to10^5 V/m in the kHz range) can also be applied between neighboring electrodes to pull the dielectric droplet/particles along the slit into the higher electric field region (dielectrophoresis) thus providing another mechanism for precise droplet/particle manipulation. The levitated/manipulated objects include (but are not limited to) micron size droplets of diverse water and alcohol solutions, oils, polystyrene microspheres, microparticles of bismuth, antimony, multiwalled nanotube powder and red blood cells or fluorescent microspheres in droplets. The levitation time is virtually unlimited (the longest studied was two weeks). Dozens of droplets have been levitated and manipulated simultaneously. We have grown crystals of $NaCl$, KCl, $AlSO_4$ and $NaHCO_3$ from droplets of corresponding water solutions. Crystal anisotropy of the levitated particles permits their precise rotation by application of an AC electric field ($\approx 10^4$ V/m) between the two permanent magnets (for demonstration purposes we have used an in situ grown salt crystal) in the trap (Figure 3, Supplement Video S6).

The detailed physical characterization and the theory of the MMC go far beyond the scope of this letter. Here we only briefly evaluate typical forces acting on droplets, the amplitude of their fluctuations and their relaxation times. The forces, acting on the diamagnetic body in the MMC, include gravity, the Coulomb force (if charged), the magnetic force due to the magnetic field gradient, viscous friction described by Stokes's law and the random force ζ which is assumed to be of thermal origin. Detailed analysis of the origin and correlation properties of ζ will be presented elsewhere. This, however, does not affect our results. To measure forces acting on a droplet/particle, we have used gravity, similar to experiments by Millikan[8]. The microscope with its MMC was mounted on a vibration isolated platform which can be tilted by $\pm 30^\circ$ about axis perpendicular to the slit between magnets with accuracy in the range 1×10^{-4} - 3×10^{-4} radian, thus creating a "magnetic incline". The motion of a droplet/particle suspended in the MMC and oscillating in the local potential minima can be described by the equation:

$$3\pi D\eta \dot{R}_i - \kappa_i R_i + mg\sin(\alpha)\delta_{ix} + \zeta_i = 0 \qquad (1)$$

where η is the air viscosity, $i = x, y$, R_i are coordinates in the xy-plane with the x-coordinate directed along the slit, κ_i are effective "spring constants" which characterize the local energy (magnetic and Coulomb) minimum, D the droplet diameter, m its mass, g the acceleration due to gravity and α the tilt angle from the original position. In Eq.1 we neglect the z dependence, which is a reasonable approximation for small (compared to potential well width) displacements along the slit. Droplets were injected by a method similar to that of Millikan[8], i.e. with an atomizer. The droplet diameters were typically in the 1 μm -80 μm range. The droplet position was recorded with a video camera (maximum resolution of 10 pixels per micron), connected to a computer. Data were recorded as a series of uncompressed, 640×480 pixel size frames with capture time 20ms and a time interval of 10s between shots with a total acquisition time of 3-5 minutes. The droplet position as a function of tilt angle was calculated by averaging data from 10-20 frames, which was sufficient for evaluation purposes. For measurements we have used typical potential well about 100 μm in width and glycerin/water (15% glycerin by volume) mixture droplets of 6 ± 0.3 μm, 9 ± 0.3 μm and 14 ± 0.3 μm in diameter. The average droplet displacement due to the tilt was independent on droplet size within 10% accuracy. This means that the force acting on a droplet in that set of measurements was predominantly diamagnetic. The linear restoring force dependence on displacement was confirmed within 10% accuracy in the displacement range ±7.0 μm. The value of κ_x for a 6.0 ± 0.3 μm diameter was found to be 3.0 ± 0.6 fN/μm. With this value of κ_x the fluctuation amplitude x_0 can be estimated from the Fluctuation-Dissipation Theorem (FDT) as $x_0=\sqrt{k_B T/\kappa_x}$, where k_B is the Boltsmann constant and T the temperature. For the 6 μm diameter droplet, the measured fluctuation amplitude is about 1.0 ± 0.3 μm in the x-direction and is no more than 0.3 μm in the y-direction. The value of x_0 calculated from FDT is reasonably close to the value from the direct measurements. The energy E_V of a diamagnetic object of volume V and with susceptibility χ_o in a magnetic field B is given by: $E_V = -\chi_o VB^2/2\mu_0$, where χ_o is -8.8×10^{-6} for water. The value of κ_y can be estimated as $\kappa_y\approx4|E_V|w^{-2}$, where $w\approx80$ μm is the distance between magnets. The magnetic field B is about 0.5T. This gives $\kappa_y\approx60$fN/μm which is consistent with the FDT lower bound on κ_y. The levitation threshold (∇B^2) for water[3] is 1.4×10^3 T^2/m. The parameter (∇B^2) for this MMC is estimated to be 5×10^3 T^2/m. According to Eq. 1 the characteristic relaxation time is $\tau_i=3\pi D\eta/\kappa_i$. This gives $\tau_x\approx0.3$ s for the 6 μm size droplet, which fits well with the observed oscillation pattern. Visual control (0.3 μm accuracy) of the droplets position in the potential well permits control of the force acting on the 6 μm diameter droplet with at least $0.3\,\mu\times\kappa_x\approx1$fN accuracy, and its potential energy can be controlled with at least 0.2zJ or $0.05\,k_B T$ precision. Control of the tilt angle (1×10^{-4} accuracy) permits control of the force of gravity on the 6 μm diameter droplet with weight 1.2 ± 0.2pN with an accuracy of up to 0.1fN which corresponds to the 0.03 μm average displacement in the potential well studied. The force and potential energy control can be significantly improved by using shallower traps (2-3 orders of magnitude) and/or better data acquisition and processing techniques (1-2 orders of magnitude).

These experiments establish a technology with enormous potential for application in physics, fluid mechanics, chemistry, biochemistry, atmospheric chemistry, biology, pharmaceutical, microfluidics, MEMS and aerosol studies.

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Figure Captions:

Fig.1 Diagram of the MMC. Two permanent magnets are mounted on a substrate (grey) with opposite magnetization directions shown by arrows. A levitating droplet/particle (black) is moved by current pulses through electrodes (dark grey).

Fig. 2 (a-c): Three sequentially timed snapshots (top view) of back and forth motion of a 30 micron diameter glycerine/ water droplet moved by currents in the electrodes (3 are shown); (d-f): Three sequentially timed snapshots (top view) of a controllable merging of 22 μm and 24 μm diameter glycerine/ water droplets moved by currents in the electrodes (3 are shown). The resulting combined droplet is 29 μm in diameter.

Fig. 3. Four sequentially timed snapshots of the orientation of a 20 $\mu m \times 20 \mu m \times 12 \mu m$ salt crystal rotated by an AC electric field applied between the magnets (top view). The crystal was grown in situ from a levitated droplet of a $NaCl$ water solution.

FIGURES

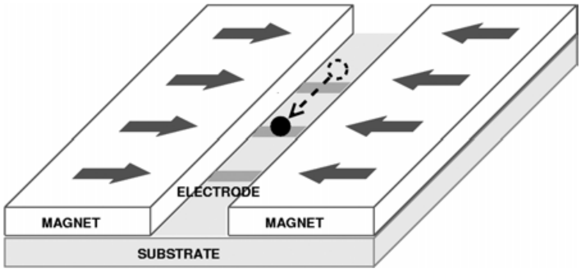

Figure 1.

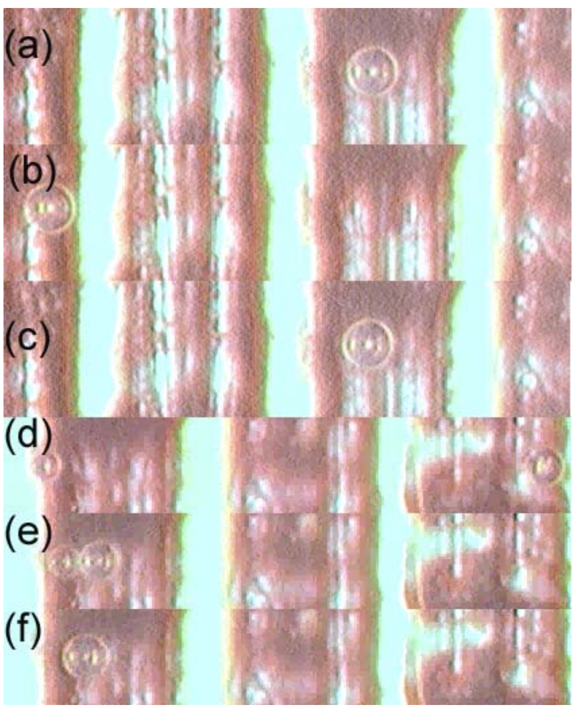

Figure 2.

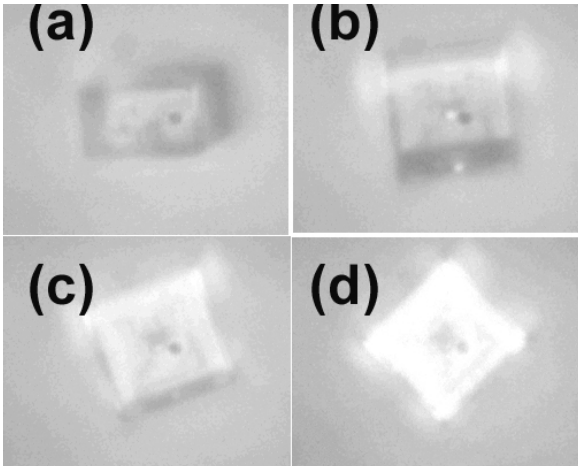

Figure 3.