2-D MICROMANIPULATION OF SINGLE NANOPARTICLES IN FREE SOLUTION USING A MICROFLUIDIC TRAP

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ABSTRACT

In this study, we describe the confinement and two-dimensional (2-D) manipulation of single micro- and nanoscale particles in free solution using an integrated microfluidic device. The trapping mechanism is based solely on fluid flow, whereby individual particles are confined at the stagnation point of an extensional flow created at the junction of two perpendicular microchannels. Particle confinement and manipulation is performed by active and independent control of the stagnation point position along orthogonal directions in the microchannel junction using two integrated membrane valves. This new technique enables particle trapping and micromanipulation without the use of electrical, magnetic, optical and acoustic force fields.

KEYWORDS: hydrodynamic trap, microfluidic trap, micromanipulation, nanoparticles, free solution trapping

INTRODUCTION

Controlling the motion of small particles in free solution is an essential technology for nanoscience and engineering. However, fine scale manipulation of nanoparticles in microdevices remains a significant challenge. In the past, particle trapping methods based on acoustic, electrokinetic, magnetic and optical fields have been used, but these methods are limited to trapping particles with specific material properties and micron-scale dimensions[1, 2]. Recent efforts have focused on combining particle confinement and manipulation methods into integrated devices in order to capitalize on microfluidic technology. In particular, several methods have been developed based on a combination of patterned microstructures and tailored flows in order to confine particles in aqueous solutions[3-5].

Here, we present a new flow-based confinement method called the hydrodynamic trap, which enables free-solution trapping and manipulation of single micro- and nanoscale particles[6, 7]. The hydrodynamic trap is an automated, non-contact and high resolution confinement technique based on a stagnation point flow generated in a microfluidic device. Using this method, we demonstrate trapping and 2-D manipulation of single micro- and nanoscale particles (100 nm-15 μm polystyrene beads) in aqueous solutions.

THEORY

The hydrodynamic trap actively confines particles at the stagnation point of a planar extensional flow, which is generated by two opposing laminar streams converging at a cross-slot junction (Fig. 1). A planar extensional flow is a two-dimensional flow containing a fluid stagnation point (zero-velocity point) and consists of purely extensional and compressional components with no rotational flow character. The stagnation point represents a saddle point – a point of minimum (maximum) flow potential along the inlet (outlet) streams – in the velocity potential function. Therefore, a particle in a planar extensional flow experiences an attractive force toward the stagnation point along the inlet stream direction and a repulsive force along the outlet stream direction with respect to the stagnation point.

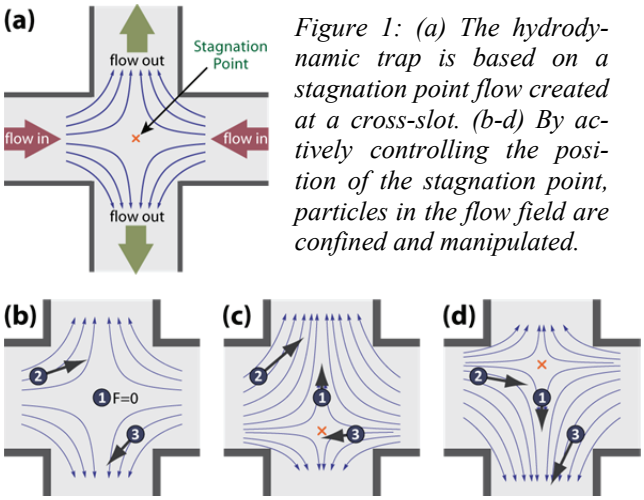

Figure 1: (a) The hydrodynamic trap is based on a stagnation point flow created at a cross-slot. (b-d) By actively controlling the position of the stagnation point, particles in the flow field are confined and manipulated.

The key concept behind hydrodynamic trapping is active control of the stagnation point position using an automated feedback control algorithm, thereby enabling dynamic and precise control of the hydrodynamic force exerted on a particle by the fluid. In order to confine a particle at a predetermined target location (trap center), the stagnation point is actively re-positioned such that a net hydrodynamic restoring force is exerted on the particle in the direction of the trap center. Two-dimensional particle trapping is achieved by active control of the flow field in extensional (outlet stream) and compressional (inlet stream) directions using two integrated valves.

EXPERIMENTAL

We built the hydrodynamic trap by designing and fabricating a hybrid poly(dimethylsiloxane) (PDMS)/glass microfluidic device using standard multilayer soft-lithography techniques (Fig. 2). The hydrodynamic trap is a two-layer microfluidic de-

vice consisting of two patterned layers in PDMS. A thin PDMS layer (fluidic layer) containing the flow channels (inlet and outlet microchannels) is positioned between a glass substrate and a thick PDMS layer (control layer). The control layer contains two elastomeric membrane valves, which are pressurized microchannels positioned above one of the inlet and outlet channels. By applying pressure to the control-layer microchannel, the valve opening is adjusted, thereby altering the flow resistance within the outlet stream situated beneath the valve. In this manner, the membrane valves are used as metering valves to adjust relative flow rates in the microchannels, which enables fine-scale control of the stagnation point position and facilitates particle confinement.

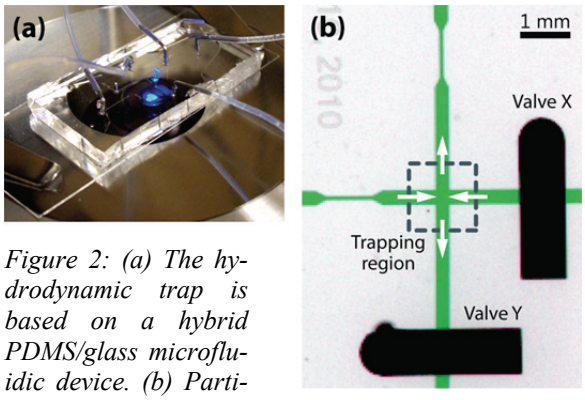

Figure 2: (a) The hydrodynamic trap is based on a hybrid PDMS/glass microfluidic device. (b) Particles are trapped and manipulated at the junction of two intersecting microchannels by controlling the planar extensional flow field via two integrated membrane valves (shown in black).

The experimental setup consists of the microfluidic device (hydrodynamic trap) mounted on the stage of an inverted microscope (Olympus IX-71) equipped with a CCD camera for image acquisition and a 10x or 40x high numerical aperture objective lens for particle detection. A syringe pump (Harvard Apparatus) is used to deliver fluid into the device, and an electronic pressure regulator (Proportion-Air) is used to actuate the membrane valve. Particles are confined at the trap center by successive iteration of the following steps comprising the automated feedback control mechanism: 1) capturing an image of the particles in the trapping region, 2) tracking and localizing the center-of-mass position of a "target" particle in the trapping region, 3) determining an updated stagnation point position (or an updated pressure value) using a linear feedback controller in order to exert a restoring hydrodynamic force on the particle directing it toward the trap center, 4) signaling the pressure transducers to apply the updated pressure to the on-chip valves, which adjusts the stagnation point position to steer the trapped particle towards the trap center.

RESULTS AND DISCUSSION

As a proof-of-principle experiment, we trapped micro- and nanoscale fluorescent beads and manipulated their position within the trapping region using the hydrodynamic trap. Fig. 3a shows the image of a 100 nm diameter fluorescent polystyrene bead trapped in free solution by the hydrodynamic trap. The hydrodynamic trap allows for confinement and manipulation of both fluorescent and non-fluorescent objects. The trapping mechanism relies on accurate determination of particle position. Therefore, particles smaller than the diffraction limit can be imaged, localized and trapped using fluorescence or dark-field microscopy.

2-D manipulation of particles in free solution is performed by active and independent control of the stagnation point position along orthogonal directions in the microchannel junction using two integrated membrane valves (Fig. 2b) positioned above the inlet and outlet channels. Fig. 3b shows a trajectory of a single particle that is manipulated with high-precision in free solution to draw the letter "a".

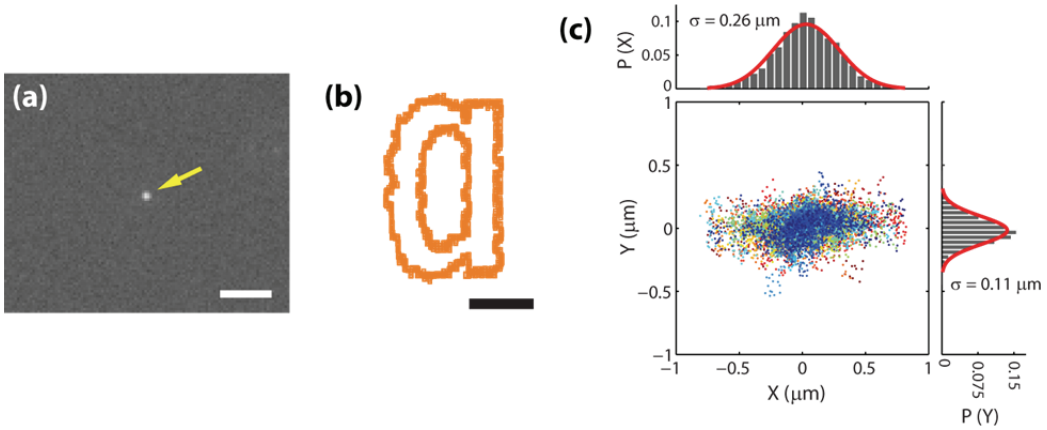

Figure 3: (a) Image of a trapped 100 nm diameter fluorescent polystyrene bead. Scale bar: 5 μm. (b) Two-dimensional trajectory of a 2.2 μm diameter fluorescent bead which is trapped and manipulated in free solution by the hydrodynamic trap to draw the letter "a". Scale bar: 10 μm. (c) 2-D trajectory of a trapped particle (2.2 μm diameter fluorescent bead). The particle is confined to within ±1 μm for several minutes from the trap center, as indicated by the histograms of particle displacement. X and Y correspond to the compressional (inlet stream) and extensional (outlet stream) flow directions, respectively.

In addition, we characterized the trap stiffness (tightness of confinement) by plotting the 2-D trajectory for a trapped particle (Fig. 3c). The particle is confined to within ±1 μm for several minutes from the trap center in the lateral direction, as indicated by the standard deviations of the histograms of particle displacement from the trap center along each axis (σ_x = 0.26 μm, σ_y = 0.11 μm). Trap stiffness depends on the strain rate and the feedback control parameters along each axis of manipulation and compares favorably to magnetic and electrophoretic traps.

The microfluidic trap offers several advantages for the confinement and manipulation of micro and nanoscale particles. First, particles are trapped in free-solution, thereby allowing for non-perturbative and non-contact confinement of single particles or cells. In addition, trapping is achieved by the sole action of hydrodynamic flow, which does not require the use of optical, electric, magnetic or acoustic fields. Importantly, hydrodynamic trapping is feasible for any arbitrary particle with no specific requirements on material composition or chemical/physical properties (e.g. surface charge, refractive index) of the trapped object. Furthermore, single particles may be hydrodynamically trapped in a concentrated solution of particles, which enables confinement, micromanipulation and isolation of a single target particle in a crowded solution, difficult to achieve using alternative force field trapping methods. In addition, hydrodynamic trapping allows for dynamic exchange of the surrounding medium (pH, temperature, ion concentration etc.) of a trapped particle, coupled with concomitant and direct imaging for real-time characterization of single nanoparticles or cells. Finally, hydrodynamically-trapped particles may be monitored using a wide variety of microscopy techniques including brightfield, phase contrast and fluorescence microscopy. Overall, the microfluidic-based hydrodynamic trap offers a powerful and versatile platform for non-perturbative, fine-scale confinement and manipulation of micro and nanometer-sized particles for long-time observation without surface immobilization.

CONCLUSION

In this work, we demonstrate confinement and 2-D manipulation of single micro- and nanoscale particles in free solution using an integrated microfluidic device Using the hydrodynamic trap, particles are confined in free-solution at a stagnation point, whereas the vast majority of existing microfluidic methods for particle manipulation relies on physical barriers (which necessitate particle-wall contact), circulating flows or microeddies. Unlike the existing methods such as optical or magnetic traps (where force scales with particle volume), the microfluidic trapping force scales linearly with particle radius, which holds strong promise to enable facile trapping of small nanoparticles (<50 nm) in free solution.

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