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Loss-based optical trap for on-chip particle analysis†

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Abstract

Optical traps have become widespread tools for studying biological objects on the micro and nanoscale. However, conventional laser tweezers and traps rely on bulk optics and are not compatible with current trends in optofluidic miniaturization. Here, we report a new type of particle trap that relies on propagation loss in confined modes in liquid-core optical waveguides to trap particles. Using silica beads and *E. coli* bacteria, we demonstrate unique key capabilities of this trap. These include single particle trapping with micron-scale accuracy at arbitrary positions over waveguide lengths of several millimeters, definition of multiple independent particle traps in a single waveguide, and combination of optical trapping with single particle fluorescence analysis. The exclusive use of a two-dimensional network of planar waveguides strongly reduces experimental complexity and defines a new paradigm for on-chip particle control and analysis.

Introduction

The possibility of using light to manipulate small objects was first exploited by Ashkin for moving and trapping inorganic micron-scale beads.^{1,2} The subsequent use of optical tweezers to trap bacteria and viruses created an entire field for studying biological objects with the help of light-induced forces.³ Indeed, optical tweezers are widely applied in cell biology, immunology, genetics and other areas due to their numerous desirable properties. These include exquisite spatial resolution, noninvasive nature, and independence of the charge state of the particle or the surrounding medium.⁴ Microfluidic approaches towards miniaturization of chemical and biological analysis exploit minute sample volumes, short reaction times, and versatile designs of chemical and physical microenvironments. Recently, microfluidic devices have started to incorporate integrated optical methods. These optofluidic approaches have already resulted in the demonstration of on-chip light sources, detectors, liquid-core waveguides, and biological Raman and fluorescence sensing down to the single particle level.^{5–7} What has been missing from this integrated optofluidic toolbox is the equivalent of bulk optical tweezers, *i.e.* a universal means for optical particle manipulation in integrated form. Several steps in this direction have recently been taken, including particle pushing in hollowcore photonic crystal fibers⁸ and planar waveguides,⁹ and particle trapping in fluidic channels either *on top of*¹⁰ or *across*¹¹ an optical waveguide. Since conventional optical tweezers cannot easily be implemented in a waveguide due to the requirement for beam foci with high numerical aperture, on-chip traps have relied on

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gradient forces in evanescent fields and conventional dual beam traps created by diverging beams exiting opposing waveguides. These approaches are limited by the inefficient use of power in evanescent trapping¹⁰ or by being restricted to a few points along the liquid channel.¹¹ Dielectrophoresis, a related technique using alternating quasi-static electrical fields, has been used successfully to trap and manipulate sub-micron bio-particles.^{12,13} However, this technique requires specific electrical properties of buffer and particles, is restricted to the vicinity of electrodes and is hard to reconcile with optofluidic detection schemes.

We introduce a new method for on-chip optical particle control that does not suffer from these restrictions and serves as a genuine manipulator for trapping and actuating particles *within and along* a liquid waveguide channel. This technique takes advantage of using waveguide loss to form a stable dual beam trap and provides maximum flexibility for controlling the particle location on an optofluidic chip. In addition to characterizing this trapping method, we demonstrate the key attributes for complete on-chip particle control and analysis: (1) control of particle location with micron-scale precision over large distances of several millimeters, (2) definition of multiple, independent traps inside the same fluidic channel, and (3) simultaneous trapping and fluorescence detection of a single particle in fully planar beam geometry.

Experimental

The ARROW[‡] optofluidic analysis platform

Fig. 1a shows a schematic overview of the planar optofluidic analysis platform in which the waveguide-based trap was implemented. It is constructed from two types of ARROW[‡] waveguides: solid-core rib waveguides and fluid-filled hollow-core waveguides. Both types confine light in a low-index medium by wave interference in dielectric multilayers of silicon dioxide and silicon nitride deposited on a silicon substrate.¹⁴ Typical waveguide cross sections, modes, and a complete chip are shown in Figs. 1b–d. The ARROWs form two-dimensional geometries that allow for independent optical and fluidic access to the hollow-core channels.¹⁴ Light beams for both particle manipulation and analysis are delivered *via* solid-core ARROWs from the ends of the chip to the desired location in the liquid-core waveguide channel. The fluidic channel is terminated by attached reservoirs filled with analyte solution.

Materials and methods

The ARROW chips were built with a previously described process,^{15,16} combining plasma-enhanced chemical vapor deposition of dielectric layers (SiO₂ and SiN) under low-stress conditions and patterning of a sacrificial core layer (SU-8 3005, Microchem). Solid-core waveguides for excitation and collection were formed by a contact photolithography step (MA150, Karl Suss America) to define the solid-core ridge in the top oxide layer with a 1 μm -deep reactive ion etch (Anelva Corp.) in a CF₄ atmosphere. The ends of the SU-8 core were exposed using the same reactive ion etcher to locally remove the SiO₂ and SiN coating layers. The SU-8 core was then removed in a selective chemical etch (Nanostrip, Rockwood Electronic Materials). After cleaving the chip to the desired size, metal cylinders were glued with epoxy resin over the two open ends to create fluid reservoirs. The hollow-core dimensions of the waveguide were $5 \times 12 \mu\text{m}^2$, and the solid-core waveguide width was 12 μm . The refractive index was 1.46 for the oxide layers and 2.05 for the nitride layers. The dielectric layer sequence for the ARROW waveguides had been used in previous single-

[‡]ARROW: AntiResonant Reflecting Optical Waveguide.³⁰

particle fluorescence studies¹⁷ and is given in the ESI.[†] The sequence was designed for high transmission in the region of 500 to 900 nm with a typical loss of ~2–5/cm (see ESI[†]).

The optical measurements were carried out on a home built microscope which consisted of an objective (Olympus: ULWD 50×, NA 0.45) and an EM-CCD camera (Andor: Luca b/w) operated at up to 10 frames per second. Trapping light was delivered from the laser system (Coherent: Verdi V10 at 532 nm, Mira 900F at 820 nm in cw-mode) through single mode optical fibers and coupled end-to-end to the waveguides. Fluorescence was alternatively excited using a HeNe laser at 632 nm and powers of a few milliwatts at the chip facet. Fluorescence light was collected from the trapping fibers using a beamsplitter and directed onto a single photon counting module (Perkin-Elmer, model AQR-14).

Microparticles (Invitrogen: 1 μm “Tetraspek” dye impregnated, and 2 μm sulfate-modified, and Duke Scientific: 1 μm neat polystyrene) were diluted by 100× to 1000 in ultrapure water with 0.1% Triton X. *Escherichia coli* bacteria (Coli Genetic Stock Center, K12-D21) were grown at 37 °C in LB-broth, washed in 10× PBS buffer and re-suspended in ultrapure water containing 5 μM Acridine Orange dye for staining.

The fill level was controlled using a syringe pump and a tube inserted into the reservoirs.

Particle control and manipulation in a loss-based optical trap

Fig. 2a illustrates the principle of the new loss-based dual beam trap that enables efficient particle trapping at any point inside and along the liquid waveguide channel. Conventional dual beam traps rely on an asymmetry in the beam area of two counter-propagating beams along the beam axis. Since the mode profile in a waveguide is independent of propagation direction, this principle cannot be implemented here. Instead, trapping is based on the presence of waveguide propagation loss α as illustrated in Fig. 2a. Here, scattering forces from two counter-propagating beams act on a particle. These are given by

$$F_{r/l}^{Sca}(z) = \mp Q \frac{c}{n} P_{r/l}^0 \text{Exp}\left(-\alpha\left(\frac{L}{2} \pm z\right)\right) \quad (1)$$

(Q : radiation pressure efficiency, c : speed of light, n : index of the embedding medium, L : waveguide length, $P_{r/l}^0$: input beam power at the ends of the liquid core). Usually an unwanted property, here, α introduces the asymmetry of the scattering forces that is required for establishing a dual beam trap.¹⁸ Thus, the two forces cancel only at the trapping point $z = z_1$. For all practical cases in the ARROW waveguide geometry ($\alpha \sim 3\text{cm}^{-1}$, elongation $\Delta z = z - z_1 \lesssim 10 \mu\text{m}$, $\alpha\Delta z \ll 1$), the trapping potential is of the form

$$U(z) \approx 1/2 k_{eff} \Delta z^2 \quad (2)$$

with an effective spring constant

$$k_{eff} = 2 \alpha F_{r/l}^{Sca}(\Delta z=0) \quad (3)$$

as illustrated in Fig. 2b. In addition to optical forces, fluidic flow can arise in microfluidic channels. The resulting viscous drag force acting on the particles should then be added to the

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force balance to find the point of zero force. Even though flow does not prevent trapping, it was carefully eliminated in the experiments to simplify the analysis (see ESI [†]). Since both particles and fluid are transparent at the trapping wavelengths heating effects do not occur. Figs. 2c and 2d depict the particle trajectory and trapping potential of the loss-based trap (LB-trap) for typical experimental parameters (see ESI [†]). The particle is trapped within an area of $\sim 1 \times 4 \mu\text{m}^2$ in a potential of ~ 5 kT depth. Other relevant trap parameters include $F_r^{\text{Sca}}(\Delta z=0) \approx 143 \text{ fN/m}$ for the scattering force at the trapping location z_1 , and $k_z \approx 13 \text{ nN/m}$ and $k_x \approx 44 \text{ nN/m}$ for the trap stiffness along and perpendicular to the beam propagation direction, respectively. The value of k_z was determined using a dynamic relaxation measurement to avoid the influence of long-time drift along z (see ESI [†]). These values are comparable in magnitude to conventional divergence-based traps (DB-traps).^{2,11,19} As in other optical traps, the behavior of particle ensembles is governed by complex optical mutual interactions.²⁰ Nevertheless, particles will agglomerate at the same location as in the single-particle case.

The LB trap has several unique properties that are relevant to on-chip particle manipulation. The first is the ability to optically vary the trap center along the entire physical length of the waveguide. The trapping location z_1 is related to the power ratio of the trapping beams by

$$z_1 = \frac{1}{2\alpha} \text{Log} \left(\frac{P_r^0}{P_l^0} \right) \quad (4)$$

Note that the loss coefficient α determines the sensitivity on the power balance. In Fig. 2e, we demonstrate this relation by plotting the trapping locations for a microbead against different power ratios for constant total power. It is evident that the particle can be propelled to and stabilized with micron-scale accuracy at any location z_1 along the fluidic channel. This opens the possibility to manipulate and study the properties of a particle successively with various tools at different points along the liquid-core waveguide that may be subject to different local conditions, *e.g.* in temperature, pH value, or reagent concentration. The second unique property of the LB-trap is the dependence of the particle confinement $\langle \Delta z^2 \rangle$, defined as average deviation of the particle from the trapping point, on the waveguide loss α . Equating the potential $U(z)$ to the thermal energy of the particle, and substituting eqn (1) into the expression for k_{eff} yields

$$\langle \Delta z^2 \rangle = \text{const} \frac{\exp\left(\alpha \frac{L}{2}\right)}{\alpha} \quad (5)$$

Differentiation of eqn (5) yields a condition of $\alpha = 2/L$ for tightest particle confinement (minimum $\langle \Delta z^2 \rangle$ and maximum k_{eff}) resulting in

$$\sqrt{\langle \Delta z^2 \rangle} = \sqrt{KT/k_{\text{eff}}} \approx 5 \mu\text{m} \quad (6)$$

for $F_{r/l}^{\text{Sca},0} \approx 0.14 \text{ pN}$ and $\alpha = 5.2 \text{ cm}^{-1}$. L and α can be varied independently during waveguide design and can be optimized for specific applications. The optimum loss value for the $L = 4 \text{ mm}$ liquid-core ARROW shown in Fig. 1d is $\alpha = 5 \text{ cm}^{-1}$ which is very close to the experimental value of $\alpha = 5.2 \text{ cm}^{-1}$ at $\lambda = 532 \text{ nm}$ found from the slope of the fit to eqn (4) (solid line) in Fig. 2e.

Independent operation of loss- and divergence-based traps

Fig. 3 illustrates a second key functionality of the LB trap: the establishment of independent particle traps along the waveguide channel and the ability to vary the relative distance between trapped particles. Fig. 3a shows a top view of the region around a waveguide intersection where two polystyrene beads (diameter: 1 μm) are simultaneously and independently trapped at different locations z_1 and z_2 inside the liquid-core ARROW. The particle at z_2 sits inside a conventional DB (divergence-based) dual beam trap that is formed by the two beams that are delivered by solid-core waveguides along the x-direction and that diverge once they enter the liquid channel.¹¹ The particle at z_1 , on the other hand, is trapped in the LB trap formed by two beams along the waveguide axis.

Dual traps as shown in Fig. 3a are commonly used for the application and the measurement of differential forces in bio-physical and polymer physics studies, typically by attaching a linear molecule between the two beads and changing their relative distance.²¹⁻²³ Fig. 3b shows how the particle in the LB-trap is independently moved (*via* P_r^0/P_l^0) with respect to the particle in the DB-trap over a wide range and approaching to less than 14 μm . For the parameters used here (see ESI[†]), the DB-trap has a stiffness of $k_z = 32$ nN/m. Therefore, it acts as a position clamp on one particle while the comparatively shallow potential of the longitudinal LB-trap acts as a force clamp for another particle. Such a force clamp can be used to determine variations in the length of molecular or polymeric tethers, or the action of biomolecular motors.²¹⁻²³ The two traps can be described by a double-well potential (see Fig. 3c) and a minimal particle separation $s_{\min} = |z_1 - z_2|_{\min}$ may be defined by the condition of having a barrier of 1 kT in-between the two potential minima. This quantity depends on the liquid-core waveguide loss, the solid core mode waist, and the beam powers. A statistical analysis of the particle locations z_i yields a Gaussian potential with a depth of 18 kT. Combined with the potential for the LB-trap (stiffness ~ 50 nN/m) we estimate a minimal distance of $s_{\min} \approx 7.4$ μm . Potential depth and gradient of both traps scale with the powers of the trapping beams. An increase of the powers would therefore allow bringing particles to a closer distance while still maintaining the 1 kT barrier (details are available in the ESI[†]).

Fluorescence detection on single, trapped particles

The third capability afforded by the LB trap is to deliver and hold single particles in an optical interrogation region on the chip for prolonged analysis. This is essential for taking full advantage of the single-particle sensitivity of ARROW-based optofluidic chips that had been established using stochastic methods.^{24,25}

Fig. 4a shows a microbead, initially held next to the waveguide intersection in a longitudinal LB-trap using infrared light. An excitation beam of 633 nm was then activated along the intersecting solid core as shown in Fig. 4b and the power ratio of the trapping beams adjusted to move the particle into the intersection. The fluorescence signal was collected from the end facet of the chip (see Fig. 1a) using a beamsplitter in the trapping light delivery system, a fluorescence bandpass filter (Omega: 670BP40) and two IR blockers (Semrock: 550BP220), and a single photon detector. A time trace of the fluorescence signal is shown in Fig. 4c. During the first 30 seconds the particle was still outside the excitation region at the intersection and no fluorescence was excited. At $t = 30$ s, a sharp increase in the fluorescence signal can be observed. The subsequent slow decline of the signal is due to a slight positional drift of the trapping point along the liquid core until a stable regime was reached at 60 seconds. Recovery of the full signal after adjustments of the trapping beams also rules out photobleaching as the source of the temporal decay. We note that fluctuations in the pump light delivery system as well as of the longitudinal particle position in the perpendicular excitation beam cause the noise in the fluorescence signal to grow above the

statistical photon counting noise limit. The principle was then applied to analyzing relevant biological particles using the bacterium *Escherichia coli* as a model system. Mie theory shows that despite its appreciable volume of $V \approx 6 \mu\text{m}^3$, trapping would require 50 times the beam power used with the latex particles due to the low index contrast with water of $\Delta n \approx 0.03$. To alleviate this problem, we applied a technique frequently encountered in conventional bio-physical trapping experiments where latex particles serve as optical handles for the manipulation of biomolecules.^{4,26} Spontaneous attachment of *E. coli* was promoted by using sulfate-terminated polystyrene beads²⁷ and successful trapping of such a pair using the longitudinal LB-trap in the waveguide intersection is shown in Fig. 4d. The pairs tend to align along the optical axis under the influence of the gradient force acting on the elongated object which improves the detection efficiency. The compatibility of this LB-trap based trapping scheme with fluorescence detection was shown by staining the core of the bacterium with the intercalating dye Acridine Orange. Fluorescence from a single *E. coli* was excited with an Ar-ion laser at 488 nm through the intersecting solid core waveguide. The signal collected through a bandpass filter is shown in Fig. 4e.

Conclusion

We have introduced a new type of integrated all-optical particle trap that enables new methods for on-chip particle control and analysis using exclusively planar optical waveguides. Like other all-optical analysis methods, this on-chip approach is noninvasive, biocompatible, and versatile. The fact that the trapping mechanism relies on waveguide loss results in a large design flexibility. For example, the spatial loss profile, and consequently the trapping potential can be defined during the fabrication process. It could even be altered dynamically using other optofluidic methods.²⁸ The ability to combine different types of traps to independently hold and control single particles is of great interest to fundamental single molecule studies in biophysics and molecular biology. The combination of single molecule detection and optical trapping is very powerful,²⁶ but can be implemented here much more easily using integrated optics.

The use of planar waveguides in two-dimensional layouts opens numerous possibilities for future expansion. These include the use of additional single beams for particle selection or sorting, rapid optical transport of particles between regions with different micro-environments on the chip, and even the introduction of active feedback strategies²⁹ that would vastly increase the efficiency of the traps. Predefined waveguide alignment and fiber-optic delivery dramatically reduce the complexity of the experimental setups, in particular if trapping and fluorescence analysis are combined. Therefore, we expect that this new method for on-chip particle manipulation will be accessible to a large number of researchers and spawn a number of new experiments and applications in integrated optofluidic environments.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Fig. 1. Basic building blocks and architecture of the ARROW platform. (a) Schematic layout of optofluidic chip for all-optical particle manipulation and analysis, showing intersecting solid- and liquid-core ARROW waveguides and relevant optical beam paths. (b and c) Scanning electron microscope images of solid- and hollow core waveguide cross sections. (d) Photograph of fabricated chip.

Fig. 2.

Working principle and performance of the LB (loss-based) dual beam trap. (a) Schematic view of particle inside liquid-core waveguide subjected to scattering forces in the presence of waveguide loss. (b) Corresponding dependence of scattering forces, total force, and potential along the channel. (c and d) Typical particle trajectory and trapping potential, indicating micron-scale confinement. (e) Trapping location along the channel *versus* beam power ratio, symbols: experiment, solid line: fit to eqn (4).

Fig. 3.

Independent manipulation of trapped microbeads in a dual optical trap. (a) Top view of waveguide intersection region showing two microbeads trapped by two different dual beam traps; (b) Time-dependent locations of particles in traps shown in Fig. 1e, indicating independent particle movement; (c) Solid line: corresponding total potential along liquid channel, dotted line: DB-trap potential, dashed line: LB-trap potential.

Fig. 4. Optical interrogation of trapped particles. Fluorescence detection of trapped particles. (a) Top view of microbead near waveguide intersection. (b) Top view of fluorescence detection geometry and fluorescing particle in intersection. (c) Corresponding detector signal collected from chip edge. (d) *E. coli* bacterium attached to microbead, trapped in waveguide intersection. (e) Top view of fluorescing *E. coli* stained with intercalating dye.