Optical trapping force reduction and manipulation of nanoporous beads

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We studied the interaction of infrared optical traps with controlled-pore glass (CPG) beads in aqueous medium. The lateral optical trapping force and stiffness were experimentally found considerably smaller than those of their solid counterparts. The simulation using an average refractive index revealed significant losses of effective trapping efficiency, which quantitatively agreed well with experimentally fitted curves. This effect was ascribed to the reduced relative refractive index of medium-filled CPG beads with respect to the medium. Combining optical trapping with mechanical confinements, we demonstrated a microfluidic platform allowing for the synthesis of multiple DNA oligonucleotide sequences on individual beads of interest. © 2012 American Institute of Physics. [<http://dx.doi.org/10.1063/1.3703604>]

Micro- and nano-sized beads are becoming increasingly important solid mobile carriers in biochemical and biological assays and diagnostics due to their tunable surface functionality, high specific surface area, free flow characteristics, rigidity, and chemical compatibility. At present, several major approaches, e.g., electroosmotic,¹ electrophoretic,² dielectrophoretic,³ magnetic,⁴ acoustic,⁵ or hydrodynamic⁶ mechanisms, are often employed to trap and transport thousands or millions of beads in an ensemble fashion and, therefore, necessitate both tedious experimental protocols to multiplex the data and complicated algorithms to interpret the statistical results. To drastically increase the efficiency and productivity as well as minimize diagnostic ambiguity, the ability to manipulate beads in a “one-bead one-compound” or “OBOC” (Refs. 7–9) fashion in a lab-on-a-chip system is highly desired. Such OBOC libraries have demonstrated significant advantages because they are spatially separable, enabling high-throughput combinatorial testing concurrently and independently without necessary deconvolution faced in the aforementioned ensemble approaches. Indeed, this concept has already led to advances in chip-based multifunctional high-throughput manipulation and detection systems. For example, Takeuchi and Tan¹⁰ recently demonstrated a multifunctional bead microarray using hydrodynamic confinement and optical-based microbubbles, which permitted immobilization, transfer, and retrieval of particles, infusion of reagents, and monitoring of reaction on a single chip. We have previously reported a microfluidic approach in which combinatorial deoxyribonucleic acid (DNA) oligonucleotides were directed by optical tweezers^{11,12} and chemically synthesized on selected controlled-pore glass (CPG) beads.¹³

However, the meaningful implementation of this challenging concept has still been severely hampered mainly due to the lack of effective, combinatorial single bead manipulation tools and systems.

In this letter, we examine the interaction of optical traps with CPG beads in aqueous medium. Because of their even higher surface area (2–3 orders of magnitude compared to their solid counterparts), CPG beads are highly sought after in many lab-on-a-chip applications. We thus design and test a combinatorial CPG bead manipulation approach on a microfluidic chip by combining optical trapping and mechanical confinement.

An ytterbium fiber laser (IPG Photonics YLR-10-1064-LP) provided a continuous wave TEM₀₀ mode beam ($\lambda = 1064$ nm) as the optical source for the trapping experiment. After passing through two pairs of telescopes, the light was directed upwards into the back aperture of an objective lens mounted on an Olympus 1 × 71 inverted microscope.¹³ The sample chamber, in which the beads were suspended in deionized water, was mounted to the motorized stage over the objective that was used for both trapping and video recording. For comparison, two types of beads were used: CPG beads (silica, 31–40 μ m diameter with 100 nm pores and density 0.486 g/cm³) and solid beads (soda lime, 30 μ m, NIST size standard). The inset of Fig. 1(a) shows both the optical trapping configuration and a SEM micrograph of the CPG beads. A more detailed experimental setup was described elsewhere.¹³

The behavior of the beads was investigated with drag force method,^{14,15} in which the optical trapping force and trap stiffness were determined from the drag force and displacement of the bead at varied fluid velocities and laser powers. For a *solid* spherical bead at low Reynolds numbers ($Re < 1$), the drag force was calculated from a modified Stokes' equation¹⁶

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FIG. 1. Maximum trapping forces (a) and trap stiffnesses (b) obtained from the solid glass and CPG beads at different incident laser powers on a 20 $\times$ objective lens. All four curves are second-order polynomial fittings to the experimental data (open circles and squares). The inset in (a) shows the optical trapping configuration and a SEM micrograph of the CPG beads.

$$F_d = \frac{6\pi\eta rv}{1 - 1.004\left(\frac{r}{h}\right) + 0.418\left(\frac{r}{h}\right)^3 + 0.21\left(\frac{r}{h}\right)^4 - 0.169\left(\frac{r}{h}\right)^5}, \quad (1)$$

where η is dynamic viscosity, r is radius of the bead, v is velocity of the bead, and h is half height of the inner chamber or microchannel.

For a *porous* bead, it is well known that the drag force is smaller as compared to that experienced by solid beads of the same size due to their high permeability to fluid flow.¹⁷ To correlate this effect to the solid counterpart, a dimensionless correction factor Ω defined as the ratio of the resistance experienced by a porous sphere to that by an equivalent solid sphere, was coined by Neale and co-workers.¹⁷ Thus, the drag force experienced by an isolated highly porous sphere in a steady creeping flow F_p is less than that for the corresponding solid sphere F_d , namely,

$$F_p = F_d \Omega, \quad (2)$$

where the correction factor $\Omega < 1$. To assess this factor, a normalized radius of sphere β is used,

$$\beta = \frac{r}{\sqrt{p}}, \quad (3)$$

where p is permeability. For $\beta > 5$, Ω can be expressed as¹⁷

$$\Omega = \frac{2\beta^2(1 - \beta^{-1})}{2\beta^2 + 3(1 - \beta^{-1})}. \quad (4)$$

For a high-porosity permeable sphere, e.g., CPG beads, β is typically in the range of 5–20,¹⁸ and this yields $0.764 < \Omega < 0.947$. This suggests that the drag force on a highly porous bead is 5.3%–23.6% smaller than the solid counterpart. In the case of CPG beads with 100 nm pores, Ω is predicted as 0.888, assuming $\beta = 10$.

Fig. 1 shows the maximum lateral trapping forces and trap stiffnesses obtained from Eqs. (1) and (2) for the solid and porous beads, respectively. For the solid beads, the measured maximum trapping force increased monotonically from 17 pN to 180 pN as the incident laser power was varied from 0.4 W to 1.2 W. In contrast, for the porous beads, the forces were smaller than that of the solid counterparts even with no Ω correction. With the correction of $\Omega = 0.888$, the force further dropped to approximately 130 pN at 1.2 W, which represented around 28% reduction with respect to the case of solid bead. Moreover, the two fitted curves in Fig. 1(a) suggested a force reduction of approximately 32% at an incident laser power > 0.4 W. Similarly, the trapping stiffnesses of the porous beads were also considerably smaller than those of the solid beads, for example, 4 pN/ μ m vs. 12 pN/ μ m at 1.2 W laser power (Fig. 1(b)).

To better understand these discrepancies, we simulated the transverse optical trapping efficiencies of both solid and nanoporous beads using a Gaussian beam model implemented in a modified MATLAB computational tool box.¹⁹ The parameters were set as $\lambda = 1064$ μ m, refractive index of medium $n_{\text{water}} = 1.25$, and diameter of the bead 30 μ m. For solid glass beads, $n_{\text{solid}} = 1.45$. For the CPG bead, which was comprised of three-dimensional glass networks with medium-containing nanometer pores, an average refractive index n_{porous} was used instead, and it was estimated as²⁰

$$n_{\text{porous}} = \sqrt{V_{\text{solid}} n_{\text{solid}}^2 + V_{\text{water}} n_{\text{water}}^2}, \quad (5)$$

where V_{solid} is the volume fraction of glass, 0.22 and V_{water} the fraction of medium, 0.78, as derived from the densities of CPG 0.486 g/cm³ and silica 2.20 g/cm³. This equation yielded $n_{\text{porous}} = 1.36$, and the corresponding relative refractive index was, therefore, reduced by 6.2% from 1.160 (solid bead) to 1.088 (porous bead). As a result, the simulation revealed that the transverse optical trapping efficiencies on the nanoporous beads were $\sim 36\%$ smaller than those of the solid counterparts, and therefore, the effective trapping forces were lower for porous beads at the same incident laser power. This reduction was mainly caused by the medium-filled pores distributed inside the CPG bead, which reduced the relative refractive index of beads with respect to the medium. This finding, i.e., 36% trapping force decline as predicted by the simulation, agreed quantitatively well with the experimentally fitted force reduction on the nanoporous beads around 32%.

To perform combinatorial operation, we designed and microfabricated a fluidic chip by combining two trapping mechanisms, namely, optical trapping/transfer and mechanical confinement for reconfigurable manipulation of a bead array in a two-stream laminar flow (Fig. 2). The main channel contained two parallel sets of physical confinement features that could retain beads in reagent 1 stream for one

FIG. 2. Schematic configuration of the microfluidic chip that combining optical trap and mechanical confinements in a two-stream laminar flow condition (bottom) and close-up micrographs showing details of open-ended “V”- and fenced “cage”-shaped confinements along with a two-stream flow highlighted by red and blue dyes (top).

reaction and also allowed the beads to be optically trapped and transferred between the two streams of the reagents 1 and 2 for another reaction. Thus, desired reaction sequences could be achieved by spatially and temporally positioning the beads in the desired stream. The channel devices were constructed using soft lithography,²¹ in which a patterned polydimethylsiloxane (PDMS) layer was bonded to a 170 μm -thick glass coverslip. The confinements took the open-ended “V” or fenced “cage” shapes (top of Fig. 2), which permitted the confined CPG beads to expose to the free reagent flow of each stream. Fig. 3 shows a complete movement of a trapped bead across the channel from the one cage to another with a laser trap generated from a 20 $\times$ objective lens at 800 mW incident power.

As an initial demonstration, we performed a 4-bead experiment that involved the synthesis of three oligonucleotide sequences, i.e., a target 25-nt, a deletion-containing sequence, a substitution-containing sequence, and a control group on four selected beads in a single run.¹³ Subsequent *in-situ* hybridization with Cy-3 fluorescently labelled complementary oligonucleotides confirmed that these products were indeed comparable to their counterparts synthesized in a standard column method and can also function as a single mismatch biosensor.

In conclusion, we examined the interaction of optical traps with nanoporous beads in a microfluidic environment and observed that the lateral trapping force and stiffness were considerably smaller than what in the case of their solid counterparts under the same conditions. The reason for the force reduction is due to the effect of reduced relative refractive index of medium-filled CPG beads with respect to the medium. Our simulation with an average relative refractive index also revealed significant losses of the effective trapping efficiency, which quantitatively agreed well with the second-order polynomial regressions of the experimental data. Finally, we demonstrated a microfluidic platform that

FIG. 3. Motion path of the optically manipulated CPG bead across the channel from position 1 inside one “cage” to position 9 inside another using a 20 $\times$ lens at 800 mW laser power: (a) a cartoon and (b) an actual complete path reconstructed from collaged real-time video snapshots (dashed circle for illustrating bead position).

combines optical and mechanical confinements for synthesizing multiple oligonucleotide sequences on selected beads. When scaled up, this strategy may offer a unique approach for combinatorial molecular processing, detection, and sensing.

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