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Manipulation of superparamagnetic beads using on-chip current lines placed on a ferrite magnet

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Manipulation of superparamagnetic beads in a static solution is demonstrated using on-chip current striplines placed on a ferrite magnet. The ferrite magnet fits the requirement to enhance the bead's magnetic moment while still keeping beads randomly dispersed in the liquid, so allowing easy and selective manipulation of single beads. By applying currents up to hundreds of milliampere, the tapered stripline first attracts the beads to its edge, then the magnetic force along the edge drives the trapped beads moving continuously towards the chip center. On arriving into the chip central area (a square zone which acts as a site to collect the arriving beads), fine manipulation of selected single beads is further performed by switching on/off and/or tuning the current passing through the nearby quadruple striplines. We suggest that the present system may provide a simple but effective platform for handling magnetic tags for biological and biomedical applications. © *2006 American Institute of Physics*. [DOI: 10.1063/1.2151824]

Superparamagnetic beads have played an important role in current bioscience and clinical practice.[1,2] In recent years, with the rapid development of the biochip technique for fast and efficient bioassays,[3] methods for realizing successful on-chip bead manipulation are urgently needed.[4,5] Generally the microsized bead encapsulates iron oxide nanoparticles within a polymer layer that can be functionalized to attach certain molecules and living cells. Although the internal nanoparticles are superparamagnetic, they can be magnetized and thus the bead entity forms a magnetic dipole, which can be manipulated by an external magnetic field. To date, a variety of on-chip current lines used as microelectromagnets have been exploited for manipulating the superparamagnetic beads: for example, gold ring for bead trapping,[6] tapered Al lines,[7] serpentine circuits,[8] and array of planar coils[9] for bead transport; and a gold wire matrix for bead positioning.[6]

Note that uniform magnetic field only exerts a torque on a magnetic dipole. The translation force for bead displacement is actually produced by the gradients of the magnetic potential when a bead is placed in a nonuniform magnetic field. It can be written as $\mathbf{F}=\nabla(\mathbf{m}\cdot\mathbf{B})$, where $m \propto B$ is the magnetic dipole moment carried by a single bead in an external magnetic field (B). Obviously, both a large magnetic field and field gradient are necessary for generating sufficient force to move beads. If the magnetizing field is only generated by the current line, a large current needs to be applied. However, the consequent Joule heating especially for thin metal film structure would be serious in this case, which could even break the current line. In order to avoid this, a background field may be supplied by a permanent magnet, providing that the convenience of the biochip environment would not be compromised.

Here, we report a simple but effective platform using on-chip current striplines placed on a ferrite magnet for bead manipulation. Figures 1(a) and 1(b) show the schematics of the experimental setup and the stripline design. The on-chip metal strips are made of copper films (200–250 nm) evaporated on Cr-seeded Si/SiO_x substrates ($25\times25\times1\ mm^3$) and then capped by Au. The pattern formation is fabricated by optical lithography followed by a lift-off process. In order to create the magnetic-field gradient, the current lines have a tapered geometry[7] with width varied from $\sim$2 mm at the

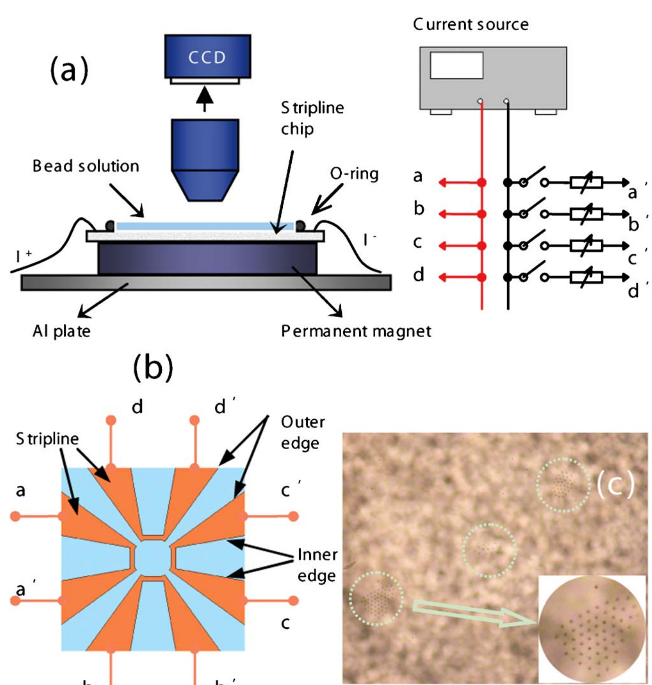

FIG. 1. (Color online) Schematics of the experimental setup (a) and the stripline chip design (b)(not scaled). Fig. 1(c) shows the self-assembled bead clusters (highlighted in circles) in an out-of-plane field ($\sim$3.4 kG) supplied by a rare-earth permanent magnet. The inset of (c) illustrates the internal ordered hexagonal lattice.

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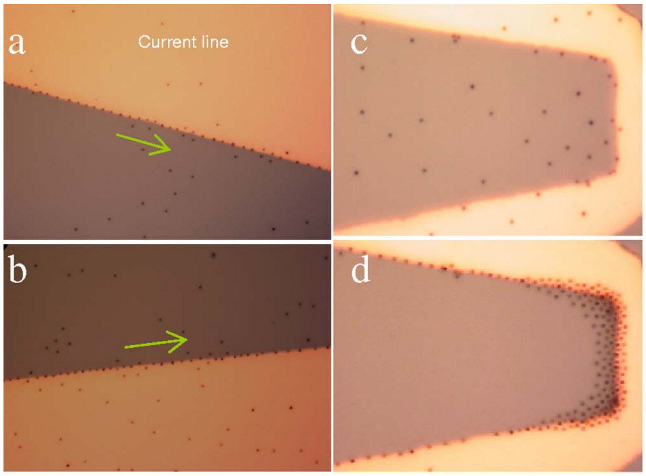

FIG. 2. (Color online) With the current switched on, beads are attracted to the inner up (a) and down side (b) edges of the stripline and then moved along the edge to the chip central area. The arrows indicate the moving direction. Notably, due to the repulsive dipole interaction between beads, the front and successively followed beads would not contact with each other but space with a certain distance along the edge. (c,d) Close to the chip central area where the stripline becomes narrowest, bead arrangement before (c) and after (d) applying current (~250 mA) for ~100 s.

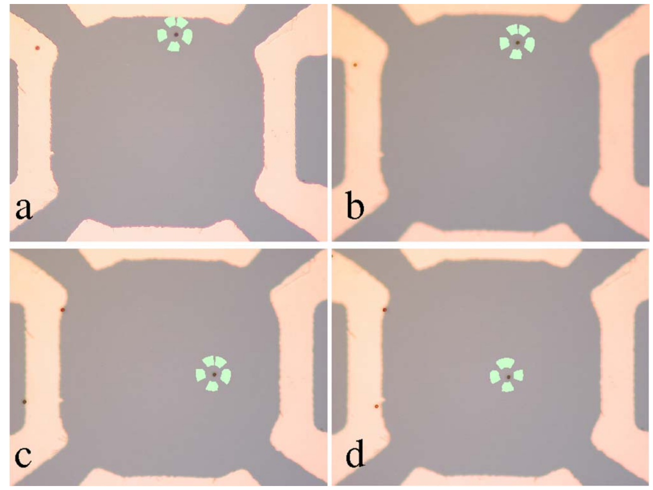

FIG. 3. (Color online) Manipulation events, (a)→(b)→(c)→(d), in which a single bead (highlighted) is first intentionally moved downwards and then finely tuned or corrected a little to leftwards.

electrical contacts to 40 μm near the chip central area. The striplines are quadruple (aa′, bb′, cc′ and dd′). By using only one current source but with external electrical circuits, the current passing through each stripline can be simply switched on/off or finely tuned by adjusting the variable resistors. The superparamagnetic beads used in this experiment are Dynalbeads-M450 with a diameter of 4.5 μm.

Prior to experiment, the bead solution is prepared by dispersing the beads into deionized water, in which <1% (by volume) Triton X-100 was added in order to stabilize the beads in suspension and prevent them from aggregating.[8] We use a small O-ring (inner diameter $\oslash$=14 mm) to surround the bead solution on the stripline chip. To insulate the current lines from the liquid, the chip surface was coated with a thin polymer layer (AZ9260). The chip is placed on a ferrite magnet ($\oslash$=30 mm, height=6 mm), which provides an out-of-plane stray field $B^{\mathrm{pm}}=160$ G at the chip. We note that, in comparison with using in-plane external magnetic field, this vertical magnet arrangement has little influence on the biochip lateral environments, which is crucial for observation under a microscope. Moreover, in this configuration, the out-of-plane electromagnetic field from all striplines are easily aligned with B^{pm}. We also find that, although a rare-earth permanent magnet can provide even stronger field in kilogauss, the beads in the solution tend to form ordered superstructures because of the strong magnetic repulsive dipole interaction between beads that confined by a finite boundary [see Fig. 1(c)]. This sort of self-assembly makes the movement of a bead cluster difficult, and a selective manipulation of single beads becomes essentially impossible. Hence, we use a ferrite magnet instead, which provides a moderate field but satisfies the need to enhance the bead's magnetic moment, while, importantly, still keeping beads randomly dispersed.

The chip-magnet system is easily mounted on the stage plate under an optical microscope (Eclipse ME600), and the manipulating events were captured by an equipped digital camera. At the starting point, we use a single stripline to test transporting beads to the chip central area. Since the chip-magnet system is fixed on the stage plate, the electromagnetic field being parallel to $\mathbf{B}^{\mathrm{pm}}$ at either inner or outer edge of the stripline [see Fig. 1(b)], can be obtained by applying reversed currents. As a consequence, when the current is switched on, the superparamagnetic beads are first attracted to only one stripline edge where the energy potential is the local minimum. After the beads get trapped at the edge, they are then continuously transported towards the chip central area by the magnetic force which is directed along the edge of the tapered stripline [see Figs. 2(a) and 2(b)]. In the present prototype design, the liquid solution and the large metal pad at the electrical contacts help to dissipate away the generated heat from the stripline, allowing currents applied up to hundreds of milliampere. In the scenario when beads are attracted to, and transported along the inner edge of the stripline, an applied current of 200 mA, causes a bead at about 530 μm away from the chip center move at a speed $v \approx 1$ μm/s along the edge. The electromagnetic field B^{em} at the bead's place is about 10 G. Adding the background field B^{pm} from the ferrite magnet, the total external field B is $\approx$170 G. The yielded field gradient is $\partial B_z/\partial x=\partial B_z^{\mathrm{em}}/\partial x \approx 1$ T/m. The magnetic susceptibility χ_{eff} for a single Dynal-M450 bead is about 7.0×10^{-11} Am^2/T.[10] Thereby, the driving force $F=2\chi_{\mathrm{eff}}B\,\partial B_z^{\mathrm{em}}/\partial x$ for moving this bead is in the order of 10^{-12} N, being significantly larger than the Brownian stochastic force $kT/a\sim10^{-15}$ N (kT is the thermal energy at room temperature, and a is the bead's diameter), and which is also larger than the hydrodynamic drag force $F=3\pi\eta v a\sim10^{-14}$ N [η is the viscosity coefficient of the medium liquid, for water, $\eta=8.9\times10^{-4}$ Ns/m^2 (Ref. 9)]. With beads approaching to the central area, the narrowing stripline creates larger field and field gradient, therefore inducing a faster bead moving. For instance, a bead ~190 μm away from the chip center moves at a speed of ~20 μm/s. Figures 2(c) and 2(d) show the area close to the chip center before and after applying current (~250 mA) for ~100 s. It can be

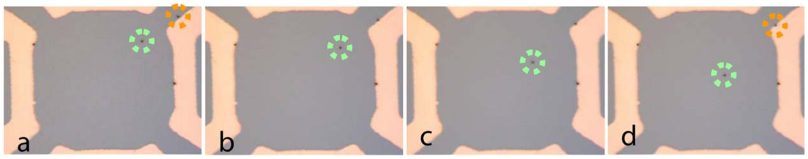

FIG. 4. (Color online) Another manipulation event: controlled motion of a single bead in a diagonal direction, (a)→(b)→(c)→(d). The selected single bead is highlighted in all figures (dashed circles in light green), while one nearby bead which moves rather slowly is only highlighted in (a) and (d) for reference.

seen that the beads are transported to this area at an average rate of ~1.5 beads/s. Additionally, the beads being mostly collected near the inner edge of the narrowest stripline, directly reveals the maximum strength of the global field distribution.

In the following, we exploited a combination of the striplines to perform single bead manipulation. For this purpose, the solution with a low bead concentration was used. Again, as described above, a single bead is first transported close to the chip central area. Depending on how close the bead locates to the two edges of a stripline, bead transport along the inner edge or outer edge of the stripline was performed. Since the quadruple striplines spread over the chip surface, it is convenient to transport a selected bead to the chip center from any direction. When a single bead comes close to the square center, fine controlled motion of the bead is carried out by switching on/off and/or tuning the current passing through the nearby striplines. The currents are now basically applied to cause the electromagnetic field at the outer edge of the stripline to be parallel to the background field. Figure 3 shows the manipulation events in which the highlighted bead was intentionally moved downwards (a)–(c) and then tuned or corrected a little to leftwards by applying larger current in the left stripline (d). Figure 4 shows another manipulation event, in which a single bead was moved to the chip center along a diagonal direction by giving equivalent currents in the left and bottom striplines, while applying relatively less currents in the top and right striplines. Note that in the captured views, there are other beads remaining fixed or only moving locally. They illustrate that the single bead manipulation was indeed selective. The square region ($\sim 160 \times 160\ \mu\mathrm{m}^2$) can be regarded as the analysis zone. If a magnetic sensor ($\sim 10\ \mu$m) is integrated in the center, the manipulating capability demonstrated above would ensure controlled biosensing by positioning a single bead of interest exactly over the sensor.

In summary, on-chip current striplines placed on a ferrite magnet have been used for transport of beads and fine controlled motion of selected single beads. This combined chip-magnet system may provide a simple but effective platform for handling magnetic tags in biological and biomedical applications.

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