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Manipulation of magnetic microbeads in suspension using micromagnetic systems fabricated with soft lithography

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Current-carrying microcircuits can generate strong magnetic-field gradients; these gradients, in turn, can control the position of magnetic microbeads in aqueous suspension. Micromagnetic systems were prepared using two representative soft lithography techniques—micromolding in capillaries and microtransfer molding—combined with electrodeposition. They can capture microbeads from solution, hold them in a fixed position, and move them along complex paths. Simply changing the current flowing in the systems can dynamically reconfigure the paths. The manipulation of magnetic microbeads using microfabricated circuits should expand current sample handling capabilities for biotechnology and combinational technology with or without the presence of net fluid flow and microfluidic channels. © *2001 American Institute of Physics.* [DOI: 10.1063/1.1356728]

This letter describes the use of soft lithography[1] to fabricate current-carrying circuits that can generate strong local magnetic-field gradients, and demonstrates that these fields and field gradients can manipulate magnetic microbeads of types commonly used in biological and chemical applications.[2] Magnetic microbeads suspended in water move towards magnetic-field maxima generated by current-carrying wires (Fig. 1). We fabricated structures with wires that were 50–100 μm wide and 10–20 μm high; these wires could carry continuous direct current (dc) of at least 10 A at room temperature. Such currents resulted in peak magnetic fields of hundreds of gauss, and generated field gradients of several G/μm.

Separating, transporting, storing, and positioning 1–100 μm objects (for example, microbeads supporting immobilized chemical reagents and cells) are important generic processes in biotechnology, microanalysis, and microsynthesis.[3,4] Most approaches to handling microbeads involve flows driven by pressure[5] or electro-osmosis.[6] Systems designed for these processes require sophisticated pumps and valves; these components are subject to failure. They are also limited in the types of motion they can generate in suspended microbeads. Oestergaard and Blankenstein[7] have described a magnetic system for the manipulation of magnetic microbeads based on permanent or electromagnets with dimensions >5 mm. The size of these magnets made it impractical to obtain magnetic field localized over microscale regions. To change the position of the magnetic microbeads, they needed to move the magnets to reconfigure the magnetic field. There are commercial devices for separating and sorting of magnetic microbeads,[8] but all of them use either permanent magnets or electromagnets, and have limited capability for performing complex manipulations of these beads.

The micromagnetic systems reported here employed microfabricated circuits rather than permanent magnets or electromagnets to generate local magnetic field. These microfabricated systems offer five useful characteristics: (i) They can quickly generate peak fields of several hundred gauss, and magnetic-field gradients of several G/μm. (ii) They generate magnetic fields that are localized within 100-μm-scale regions of the wires. This localization offers tight confinement of magnetically labeled microspheres, and enables the parallel processing of many different spheres (or packets of spheres) on the same microchip. (iii) They are tunable: it is straightforward to obtain different magnetic forces by reconfiguring or adjusting the magnetic fields. (iv) Coating of the circuits with different magnetic or nonmagnetic materials can also tailor their properties. These coatings allow the control of both the local magnetic characteristics and the surface chemistry of the circuits required for biotechnological and chemical applications. (v) The processes used to fabricate these systems are compatible with those used in the fabrication of microfluidic systems and microelectromechanical

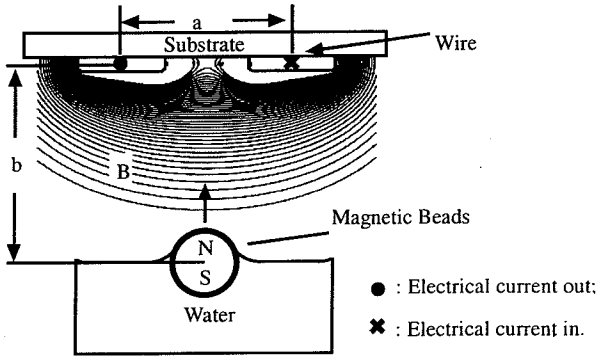

FIG. 1. Schematic of a system using magnetic field generated by current-carrying wires to manipulate magnetic microbeads (not to scale). The beads are suspended in water and they move towards the field maxima generated by the current. The distance between the two wires is "*a*" and the distance between the wires and the beads is "*b*;" *b* should be larger than 0.5*a* and smaller than several *a* for an observable bead movement. In most of this work, *a* is ~100 μm.

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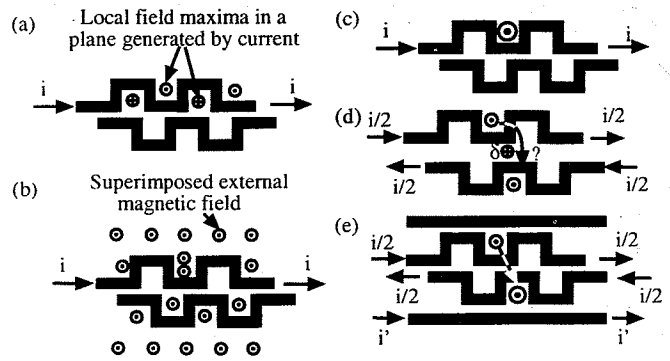

FIG. 2. (a) Magnetic-field maxima generated by passing current through a serpentine wire. The maxima appear in every turn with opposite directions in neighboring turns. (b) Magnetic field by superimposing an external magnetic field on the field from the current-carrying wire. The superimposed field cancels the maxima created by the wire with the opposite direction and enhances the ones with the same direction. (c) Simplified version of (b), omitting the superimposed field and only showing field maxima. (d) Negative magnetic-field barrier generated between two serpentine wires when moving the beads across both wires. When the current in the top wire decreases (assuming to $i/2$) and in the bottom wire increases (assuming to $i/2$), the negative magnetic field between the two wires will be large enough to block the movement of the beads from top to bottom. We intentionally make the two serpentine wires further apart in the drawing to show the negative magnetic field. (e) Negative-field barrier canceled by passing a current (i') through the bottom-side wire. The beads can move from top to bottom.

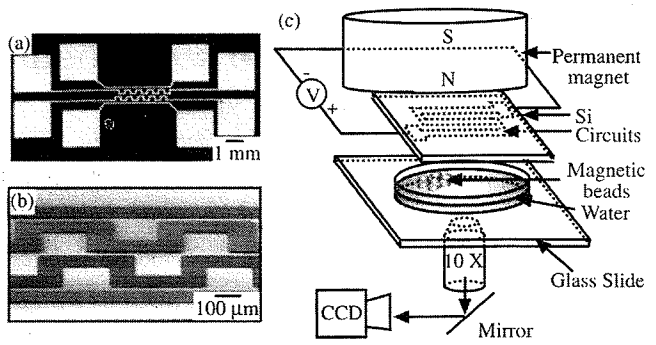

FIG. 3. (a) Optical micrograph of the system. The wires were ~100 μm wide and 10 μm high. The turns of the serpentine wires had an inner dimension of 200 μm×200 μm. The closest vertical spacing between the two serpentine wire was ~50 μm. The closest horizontal distance between two turns of different wires was ~100 μm. The contact pads were 1 mm ×1 mm. (b) Magnified view of the system by SEM. (c) Setup for the manipulation of superparamagnetic microbeads using the micromagnetic system (not to scale). The distance between the circuits and the air–water interface was ~50–400 μm, and the permanent magnet was ~2–4 cm away from the circuits during the experiment. The container of the solution of the magnetic microbeads was a rubber O ring (with inner diameter of ~1 cm, width of ~2 mm, and height of ~1 mm) attached to a glass slide (22 ×40 mm). The magnetic field from the permanent magnet (with a diameter of 2 cm and height of 4 cm) is ~20–50 G at the water–air interface.

systems, and integration should be straightforward.

By engineering the magnetic field generated by current-carrying wires (Fig. 1), we designed a current-carrying wire system that can generate local maxima in the magnetic field, and use these maxima to trap the microbeads. When the field maxima change locations, these microbeads will follow those maxima. A similar principle also works in the bubble memory system, in which magnetic bubbles follow the movement of local magnetic-field maxima.[9] Figure 3(a) (an optical micrograph) is the general design we used to transfer microbeads along a zigzag path.[10] Such a design was originally suggested by Haensch and co-workers for manipulating atoms that are attracted to the B-field minimum[11] and the system we show here is a modification of his scheme for manipulating beads that are attracted to the B-field maximum. The major electrical components of our system are two serpentine wires that are shifted linearly in phase by $\pi/3$. By combining the magnetic field generated from the current-carrying serpentine wires and the superimposed magnetic field, we can generate local field maxima and trap magnetic microbeads at these maxima [Figs. 2(a)–2(c)]. When changing the input current through the serpentine wires, we can change the position of these maxima, and thus move microbeads from one place to another.

We used the rapid prototyping process developed by Qin, Xia, and Whitesides[12] for the fabrication of polydimethylsiloxane (PDMS, Sylgard 184, Dow Corning; Midland, MI) molds (~1 mm thick). Using microtransfer molding (μTM) or micromolding in capillaries (MIMIC),[1] we transferred these patterns into features in polyurethane (PU, NOA73, Norland Products; New Brunswick, NJ) on a Si wafer coated with Ti (50 A)/Ag (800 Å); these PU features were ~10–50 μm thick. The electrodeposition of gold was carried out using Gold 25-E plating solution (Technic Inc.; Providence, RI), and a platinum electrode as the anode. The current density was ~5 mA/cm^2 during the deposition. After lift-off of the PU (using a solution of CH_2Cl_2:CH_3OH:NH_4OH, 100:25:3), and wet-chemical etching to remove silver [using an aqueous solution of 0.1 M $Na_2S_2O_3$/0.01 M $K_3Fe(CN)_6$/0.001 M $K_4Fe(CN)_6$] and titanium (using a 1% HF aqueous solution) in regions not covered by gold, we obtained gold wires, having rectangular cross sections, with height controlled by the conditions of electrodeposition. Figures 3(a) and 3(b) show optical and scanning electron micrographs (SEM) of a typical system. All the wires in the system had uniform dimensions, as verified by measurements of a profilometer. The wires can carry continuous dc current of at least 10 A (at which our power supply reaches maximum power) at room temperature for hours.

Figure 3(c) shows the experimental system used to manipulate the magnetic microbeads, using the serpentine wire systems. The superparamagnetic microbeads used in this experiment were DYNAL M-450 uncoated microbeads (Lake Success, NY; www.dynal.no) with a diameter of 4.5 μm. Prior to the experiment, we dispersed the microbeads in water containing 1% (by weight) Triton X-100 (~10^2–10^4 microbeads/mL). Triton X-100 was used to stabilize the beads in suspension and to prevent them from aggregating.[13] A charge-coupled-device camera (NEC, model N×18 A, Cambridge Instruments; Cambridge, U.K.) recorded the images of the microbeads. The working current used to generate the B field was 3 A during the experiments. The air in the interface separates the circuits and the suspension, and also acts as an insulator that reduces the heat transferred to the suspension from the wires.

Figure 2 shows that superimposing an external magnetic field on the field generated from a current-carrying serpentine wire generates local field maxima. By arranging the relative positions of two serpentine wires and changing the current in the order shown in Fig. 4, we can move the magnetic-

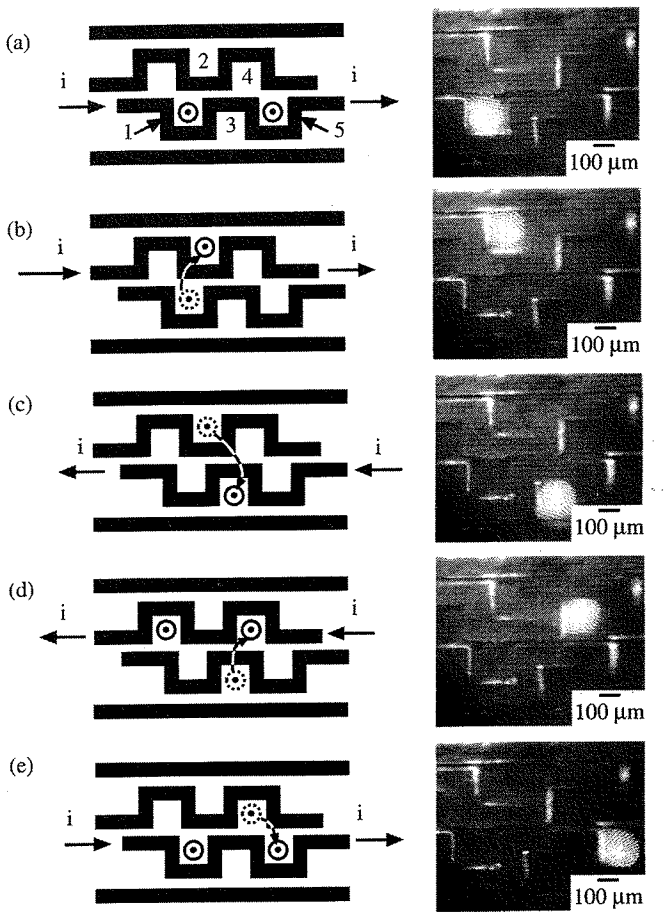

FIG. 4. Manipulation of magnetic microbeads using the micromagnetic system.

field maxima along the wires; the magnetic microbeads follow these maxima. In schematic drawings on the left side of Fig. 4, we show only the field maxima [using the same simplified notation of Fig. 2(c)]. Using the sequence of currents shown in these drawings, we moved the superparamagnetic beads (~200 microbeads with hexagonal ordering) through a sequence of positions (1, 2, 3, 4, 5, in Fig. 4). When moving the beads from 2 to 3, we passed current in the lower-side wire of Fig. 4(c) to overcome a negative-field barrier. Reversing the sequence of currents made the microbeads walk backwards (5, 4, 3, 2, 1). The time required to move the microbeads from a position to the neighboring position was less than 1 s, depending on the number of beads moved and the switching speed of the current.

This letter demonstrates the controlled movement of superparamagnetic microbeads along a magnetic track generated by a combination of microfields produced by small wires and a superimposed external field. Although the design we used here allows only limited motion, it demonstrates the principle; extensions of this design will allow the beads to be moved along more complex paths. Using soft lithography, we can quickly generate the current-carrying circuits in a broad range of geometries, and create either periodic or aperiodic structures. Compared with other methods that transfer microbeads in microfluidic channels[14] or that use large, movable external permanent or electromagnets,[7] this method offers a simpler method to generate complex movement of microbeads, with step sizes at the 100 μm scale, without moving parts or physical channels. At the current state of development, the heat generated by the current prevents us from moving labile biological entities such as mammalian cells. Integrating an element that acts as a heat sink into the system should reduce this heat. Coating permanent magnetic materials on top of the wires to enhance the magnetic field generated by the wires may make it possible to reduce the operating current, and thus also to reduce the heat generated. This methodology should be useful in a range of microsystems that require transfer of beads among storage, reaction, and detection microcells; it also is another step in the automation and miniaturization of biological, analytical, and synthetic devices and systems.

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