Fabrication of magnetic microfiltration systems using soft lithography

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Arrays of nickel posts were used as magnetic elements in a microfiltration device that is compatible with microfluidic systems. The combination of microtransfer molding—a soft lithography technique—and electrodeposition generated nickel posts ~7 μm in height and ~15 μm in diameter inside a microfluidic channel. Once magnetized by a magnetic field from an external, permanent, neodymium–iron–boron magnet, these nickel posts generated strong magnetic field gradients and efficiently trapped superparamagnetic beads moving past them in a flowing stream of water. These nickel post arrays were also used to separate magnetic beads from nonmagnetic beads. © *2002 American Institute of Physics.* [DOI: 10.1063/1.1436282]

This letter describes the fabrication of a magnetic microfiltration system that consists of ~10-μm-scale posts of nickel positioned in microfluidic channels, and demonstrates the capture and release of magnetic beads suspended in aqueous solution using this system. Magnetic filtration is a powerful method for the removal of paramagnetic and ferri(o) magnetic particles from diamagnetic fluids.[1,2] It has been applied in a range of areas.[3–6] Magnetic filtration offers high filtration rates, low pressure drop across the filter, applicability to small (<1 μm) and soft particles that would plug most conventional filters, and the capability to release the captured material without disassembling the filter (by turning off the external magnetic field).[7]

Magnetic filtration has evolved rapidly in two areas: large-scale industrial separation,[2,5,8] and biotechnology.[9–12] One reason for this evolution has been the growth of technology for magnets—both superconducting and high-field permanent magnets.[6] Most large magnetic filtration systems consist of nonmagnetic canisters filled with ferromagnetic filter-matrix elements immersed in an applied magnetic field sufficient to saturate these elements magnetically.[8] Magnetic filtration for biotechnology has been much simpler in its implementation, and it is usually carried out simply by placing a test-tube containing a magnetic material, for example, superparamagnetic beads used to adsorb biomaterials, close to a permanent magnet.[9,10] The need for versatile systems for filtration in the fluidic microsystems that are increasingly important in biotechnology and biology is such that the development of magnetic filters compatible with these systems would contribute an important new capability.

Here we report the fabrication of a magnetic microfiltration system that uses arrays of micron-scale nickel posts in a microfluidic channel as filtering elements; the posts were fabricated by soft lithography and electrodeposition. These posts generated high magnetic field gradients when subjected to an external magnetic field, and rapidly captured 4.5-μm-superparamagnetic beads suspended in water flowing past the posts. The ability to control the geometry of the magnetic filter on the microscale by microfabrication opens the door to the design and fabrication of sophisticated magnetic filters for use in biology, biotechnology, and microanalysis.

Figures 1(a)–1(d) show the fabrication of the nickel posts. We have used a similar process in the fabrication of current-carrying circuits for the manipulation of magnetic

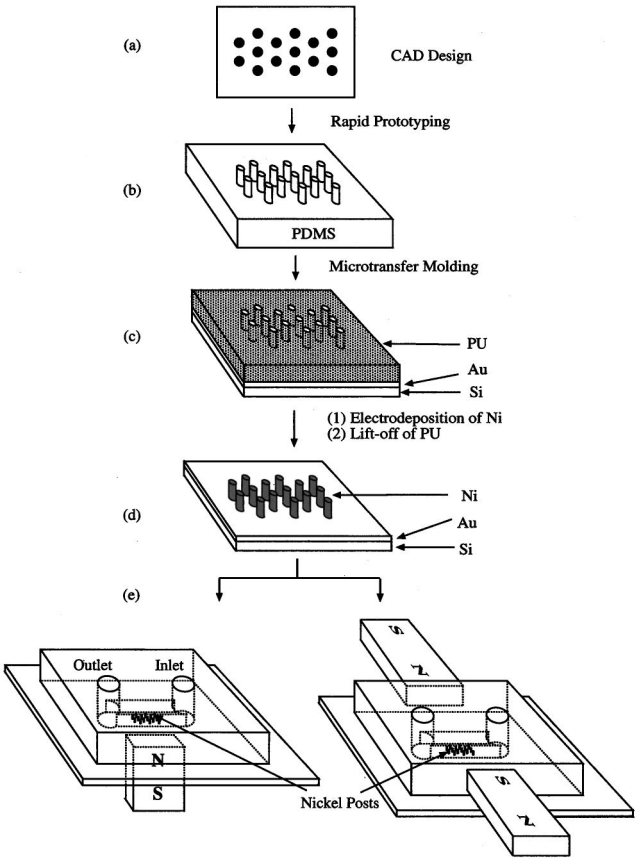

FIG. 1. Schematic outline of the fabrication of post arrays using soft lithography. (a) Pattern designed using Freehand™ software; (b) PDMS mold generated by rapid prototyping; (c) PU patterns transferred using microtransfer molding on a Si wafer coated with Ti (50 Å)/Au (500 Å); (d) nickel posts (~7 μm in height and ~15 μm in diameter) after electroplating of nickel, and liftoff of PU; (e) microfiltration system after the integration of the nickel posts into a PDMS fluidic channel. The channel was about 150 μm wide and 50 μm high. The external magnets were permanent neodymium–iron–boron magnets and the magnetic field generated from the magnet at the microfluidic channel was ~500 G. The left-hand side diagram shows the axial arrangement and the right-hand side shows the transverse arrangement of the external magnetic field with respect to the posts.

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beads.[13] We used the rapid prototyping process developed by Qin *et al.* for the fabrication of polydimethylsiloxane (PDMS, Sylgard 184, Dow Corning; Midland, MI) molds (~1 mm thick).[14] Using microtransfer molding (μ TM),[15] we transferred these patterns into features in polyurethane (PU, NOA73, Norland Products; New Brunswick, NJ) on a Si wafer coated with Ti (50 Å)/Au (500 Å); these PU features were ~7 μm thick. The PU was cured by exposure to UV light (Type 7825-34, Canrad-Hanovia 450 W medium-pressure Hg vapor lamp, Ace Glass; Vineland, NJ) for ~1 h, with samples placed at a distance of ~1–2 cm from the lamp. The electrodeposition of nickel was carried out using nickel sulfamate plating solution (Technic Inc., Providence, RI), and a chunk of bulk nickel as the anode. The current density was ~60 mA/cm^2 during the deposition. The solution used to liftoff the PU resist layer was CH_2Cl_2:CH_3OH:$NH_3 \cdot H_2O$, 100:25:3 (by volume). The ammonia solution is a concentrated solution (30% of NH_3 by weight in water).

Figure 1(e) is the magnetic microfiltration system after the integration of nickel posts into a PDMS microfluidic channel. The channel was about 50 μm high and 150 μm wide. The post arrays and the channels were aligned under a microscope using a micromanipulator. We used an external magnetic field generated from a neodymium–iron–boron magnet (Edmund Scientific, Tonawanda, NY; www.edmundscientific.com) to magnetize the nickel posts during the filtration. There are three possible geometrical configurations in terms of the arrangement of the external magnetic field: axial (the external magnetic field parallel to the axis of the post and perpendicular to the fluid flow), longitudinal (the external magnetic field perpendicular to the axis of the post and parallel to the fluid flow), and transverse (the external magnetic field perpendicular to both the axis of the post and the fluid flow). The axial and transverse arrangement [Fig. 1(e)] worked well for our system. In the longitudinal arrangement, however, it was impractical (using the configuration examined here) to place the face of the magnet as close to the nickel posts as in the axial and transverse cases, and the induced magnetic field was too low to be effective for filtration.

Figure 2(a) shows scanning electron micrograph (SEM) of a typical array of posts, and Fig. 2(b) shows a magnified view of one post. The nickel posts were ~7 μm in height and ~15 μm in diameter. Their surface roughness was ~0.5–1 μm. The height of the post (~7 μm) was much less than the height of the fluid channel (~50 μm); most bead solution flowed over the top of the post arrays. The high magnetic field gradient generated from the posts extended over most of this volume, so the posts could still trap the majority of the magnetic beads flowing by.

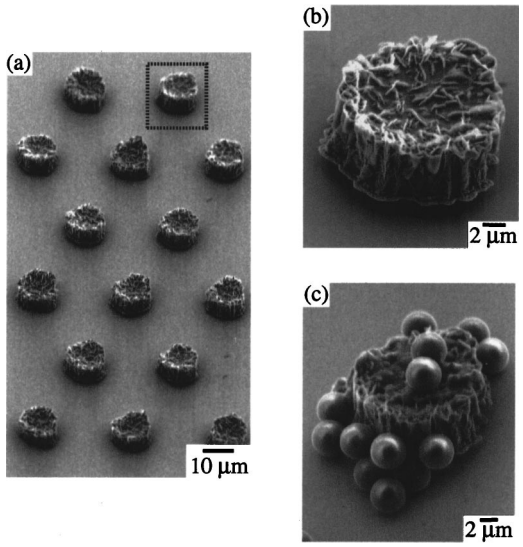

FIG. 2. Scanning electron micrographs of the nickel posts; (a) a typical array. The post was ~7 μm in height and ~15 μm in diameter. The spacing between two neighboring posts was ~40 μm and the spacing between two neighboring arrays was also ~40 μm; (b) magnified view of a post. The edge roughness was ~1 μm and the surface-roughness was ~500 nm; (c) same post attached with magnetic beads after drying and separation from the PDMS channel. The beads were ~4.5 μm in diameter.

To test the magnetic microfiltration system, a solution of magnetic beads was passed through the system. We used an aqueous suspension of Dynal (Dynal Inc., Lake Success, NY; www.dynal.no) M-450 uncoated beads with diameter of ~4.5 μm. The concentration of the beads was ~10^4 beads/mL and the solution also contained ~1% (by weight) Triton X-100 to prevent the beads from aggregating.[16] A syringe pump injected the bead solution into the PDMS channel through the inlet at the speed of ~2 μL/min. A CCD camera (NEC, Model Nx18A, Cambridge Instruments; Cambridge, UK) recorded the images of the posts and beads. The movement of the external magnets was controlled by micromanipulators. When moving the magnet close to the channel (~3 mm from the channel), the nickel posts were magnetized and generated strong magnetic field gradients. The magnetic beads passing by the posts in suspension felt the gradients and were bound to the posts magnetically. Removing the external magnetic field while keeping the flow velocity of the liquid unchanged released the beads.

Figure 3 shows the optical images of the system before the capture of the beads, with the captured beads, and after

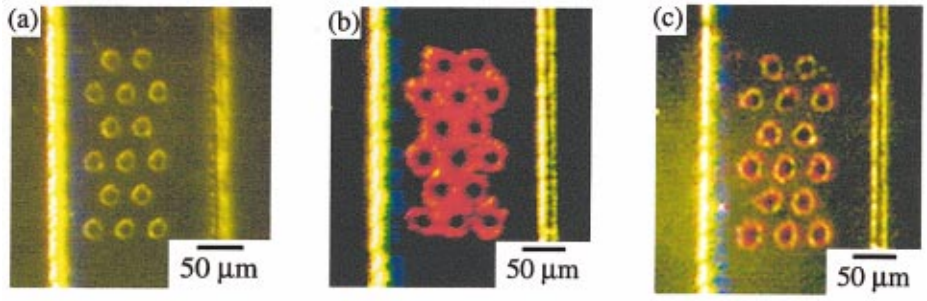

FIG. 3. (Color) Optical micrographs of the magnetic filtration system: nickel posts in a 150 μm wide channel: (a) before catching beads; (b) after applying an external magnetic field, beads caught; (c) releasing beads after removing the external magnetic field.

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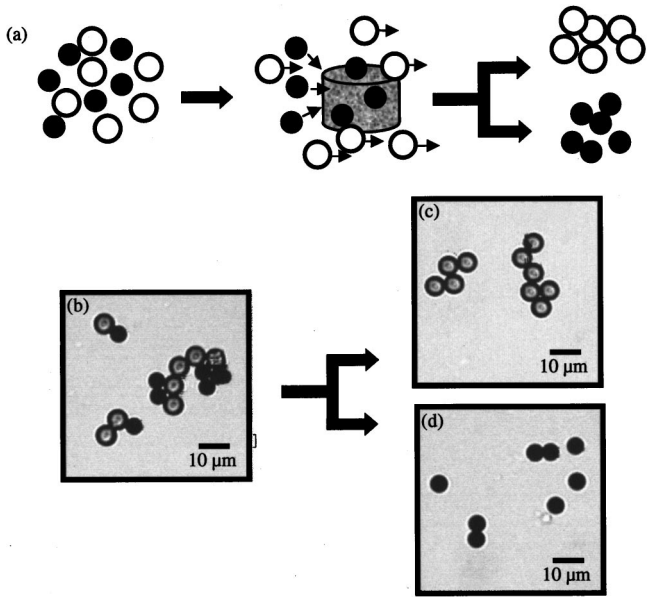

FIG. 4. Separation of magnetic and nonmagnetic beads. (a) Outline of the separation process; (b) optical micrograph of the original solution containing both magnetic beads ($\sim 10^4$ beads/mL, dark in the image) and nonmagnetic beads ($\sim 10^4$ beads/mL, light in the image); (c) optical image of the nonmagnetic bead solution ($\sim 10^4$ beads/mL); (d) optical image of the magnetic bead solution ($\sim 10^3$–10^5 beads/mL, depending on the amount of distilled water used for washing out the beads).

release of those beads. On average, each post can capture a maximum of ~50 beads. In Fig. 3(b) the magnet was in the axial arrangement; the transverse arrangement showed a similar capability for capturing beads. Figure 3(c) shows there were still some beads attached to the posts after removing the external magnetic field. The small remnant field left in the posts made it hard to release the beads quantitatively. Figure 2(c) also shows a SEM image of a post with magnetic beads attached. The SEM image shows the post after the capture of the beads, drying of the channel, and separation of the channel from substrate. Water evaporating through PDMS allowed the channel to dry; we did not disturb the external magnetic field during drying. Some beads were detached from the posts by interactions with the liquid–vapor interface as the aqueous solution retreated during drying.

We also demonstrated the separation of magnetic beads from a solution containing both magnetic beads and nonmagnetic beads. The magnetic beads were Dynal M-450 uncoated beads with diameter of ~4.5 μm. The nonmagnetic beads were dyed polybeads (Polysciences, Inc., Warrington, PA; www.polysciences.com) with diameter of ~6 μm. The aqueous solution contained $\sim 10^4$ beads/mL of magnetic beads, $\sim 10^4$ beads/mL of dyed polybeads, and ~1% (by weight) Triton X-100. After injecting the solution into the channel, we moved the neodymium–iron–boron magnet close to the channel (either in axial or transverse arrangement). The magnetic beads were bound to the posts and the nonmagnetic beads were collected at the outlet of the channel in solution 1. Then we replaced the bead suspension with distilled water containing ~1% Triton X-100. After flowing the water through the channel for several minutes, we removed the external magnetic field and collected the magnetic beads at the outlet in solution 2. Figure 4(a) summarizes the separation. Figures 4(b)–4(d) are the optical micrographs of the original solution, solution 1, and solution 2. All nonmagnetic beads were collected in solution 1. More than 95% of the magnetic beads were collected in solution 2 and less than 5% collected in solution 1 (a few magnetic beads remained attached to the posts because of the remnant magnetic field).

This letter describes a magnetic microfiltration system that has arrays of nickel posts as filtering elements. This magnetic filtration device is compatible with fluidic microsystems. Using magnetic filters integrated into microfluidic systems reduces the size of these systems substantially related to conventional magnetic filtration systems; these integrated microsystems also require only small quantities of sample. Compared to the magnetic filtration systems that use a random ferromagnetic wire matrix as a filtering element, the regularity of the placement of the ferromagnetic filtering elements in our systems makes the systematic design and fabrication of the magnetic matrix practical, and should allow more selective separation of materials differing in magnetic susceptibility and hydrodynamic drag. The in-channel design of the magnetic filtration system also enables more precise control of the filtering process, and a more compact system, than systems of the type reported by Ostergaard *et al.*, who used large (>5 mm) permanent magnets outside the fluidic channels for the separation of magnetic beads.[17] We believe microfabricated magnetic filters will expand the capabilities of biologists, chemists, and materials scientists to handle samples that require the separation of objects attached to magnetic beads. At present, we are still using external magnets to apply the magnetic field to the microfilter; the next step in miniaturization of this system would be to use electromagnets fabricated under these nickel post arrays. We are also exploring different designs and materials other than nickel for use in these systems.

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