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Sub-100 nm Confinement of Magnetic Nanoparticles Using Localized Magnetic Field Gradients

Adam R. Urbach,[†] J. Christopher Love,[†] Mara G. Prentiss,[‡] and George M. Whitesides*,[†]

Department of Chemistry and Chemical Biology, Harvard University, 12 Oxford Street, Cambridge, Massachusetts 02138, and Department of Physics, Harvard University, 9 Oxford Street, Cambridge, Massachusetts 02138

Received August 8, 2003; E-mail: gwhitesides@gmwgroup.harvard.edu

This paper describes the generation of intense (10^6-10^7 T/m) magnetic field gradients at the interface between segments of nanorods comprising ferromagnetic and diamagnetic sections, and the localization of magnetic nanoparticles to those small (20−100 nm), high-gradient regions. We used metallic rods (~80 nm diam) prepared by electrochemical deposition in polycarbonate membranes using procedures pioneered by Martin,[1] Mallouk,[2] and others.[3] These rods comprise long (~350 nm) sections of ferromagnetic alloy (CoNi) separated by short sections (20−100 nm) of diamagnetic metal (Au). When the rods are magnetized, high magnetic field gradients form at the boundaries between these sections; the regions attract and trap magnetic nanoparticles.

Magnetic nanoparticles are becoming important in biochemistry and biology.[4,5] They are used to separate biomolecules and cells from multicomponent mixtures, for stimulating cells mechanically, and for enhancing contrast in magnetic resonance imaging. While the synthesis and derivatization of magnetic nanoparticles has advanced rapidly,[6] there is a lack of methods for positioning particles with submicron resolution. This resolution would allow the use of magnetic nanoparticles for chemical or mechanical stimulation of biological processes at the subcellular level.

To confine magnetic particles to a region of space, the magnetic force attracting the particles also must be confined to that region. The force exerted on a magnetic particle in an inhomogeneous magnetic field is given by eq 1

$$F = \Delta\chi V(\nabla\cdot\mathbf{B})\mathbf{B}\mu_o^{-1} \quad (1)$$

where **B** is flux density (~0.5 T for a NdFeB magnet), $\Delta\chi$ is the difference in susceptibility between an object and its surroundings (10^3-10^5 m^{-3} for paramagnetic materials in air),[7] V is volume (10^{-18} cm^3 for a 20 nm particle), and μ_o is the vacuum permeability constant. For particles of a given size, the gradient term in the force equation, $\nabla\cdot\mathbf{B}$, is the only term that depends on distance. For example, if **B** is 1 T, then a gradient of 10^7 T/m reduces **B** by several orders of magnitude over a distance of 100 nm. Confining magnetic particles to small volumes, therefore, requires methods for fabricating structures that generate large magnetic gradients.

In a homogeneous magnetic field, the field lines are parallel; that is, there is no gradient. If a cylindrical ferromagnet is placed in this field with its length parallel to the field lines, then the field lines converge into the ferromagnet. This convergence forms a shallow magnetic field gradient at the pole (Figure 1). The diameter of the rod (d) determines the distance over which this gradient extends; this distance is roughly equal to the diameter. Each corner of the ferromagnet also produces a field gradient; the size of the gradient depends on the radius of curvature. Magnetic particles attract to the poles but do not confine to the corners due to the long-range gradient emanating from the pole.

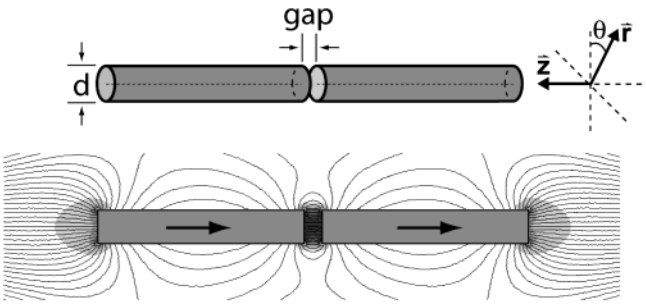

Figure 1. (top) Schematic of a metallic rod of diameter d comprising two ferromagnetic regions (gray) separated by a gap. To the right is a coordinate system representing the axial (**z**) and radial (**r**) directions. (bottom) Magnetic simulation of the field surrounding a cross section of the rod. The contours represent the field lines; the shading represents magnetic flux density, **B**.

If a second ferromagnet is placed next to the first, such that the gap between magnets is smaller than their diameter, then, to minimize the magnetic potential energy, the field lines exiting one magnet converge into the other magnet, rather than diverging into free space (Figure 1). In the center of the gap, the field lines are parallel, but they diverge at the edges and form gradients; the size of the gap determines the intensity of the gradient. Reducing the size of the gap increases the intensity of the gradient and decreases the distance over which the gradient extends.

Magnets configured in this manner should localize small magnetic particles to the gradients formed at the edges of the gap. To confine the gradient and, therefore, the particles to regions smaller than 100 nm, the gap between ferromagnets needs to be smaller than 100 nm. There are, however, few methods available for positioning magnets at this resolution. If the gap between ferromagnets were filled with air, mechanical instability would result from strong attraction of the two magnets. Filling the gap with a diamagnetic metal provides mechanical stabilization and has a negligible effect on the shape of the magnetic field.[8]

We hypothesized that metallic nanorods (diameter < 100 nm) comprising long ferromagnetic sections (350 nm) separated by short diamagnetic sections (20−100 nm) would generate high gradients close to the interfaces between ferromagnetic and diamagnetic sections and would attract magnetic nanoparticles to these regions (Figure 2a). The size of the ferromagnetic sections and the magnetic susceptibilites of the materials determine the size and shape of the gradient and, thus, the spatial confinement of magnetic nanoparticles attracted to these regions.

We used FEMM software[9] to calculate the magnetic field of a cross section of a rod containing alternating ferromagnetic and diamagnetic sections (see Supporting Information). The two-dimensional calculation approximates the three-dimensional rod

[†] Department of Chemistry and Chemical Biology.
[‡] Department of Physics.

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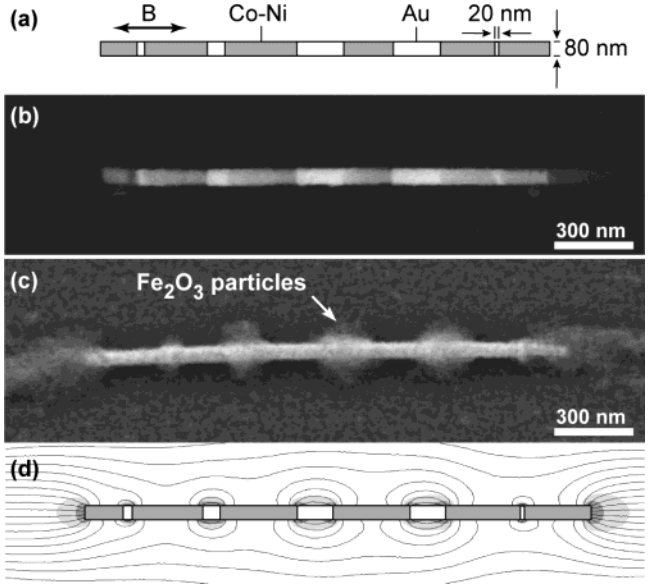

Figure 2. (a) Schematic of a metallic rod containing five diamagnetic sections (white). The thicknesses of the diamagnetic sections, from left to right, are approximately 40, 80, 160, 160, and 20 nm. (b) Scanning electron micrograph (SEM) of a metallic rod. The diameter of the rod is 80 nm. (c) SEM of a metallic rod after treatment with 8 nm γ-Fe_2O_3 particles. (d) Magnetic simulation of the field surrounding the rod. The contours represent field lines; the shading represents flux density, **B**.

because of its radial symmetry. The magnetic behavior of a ferromagnetic object scales to all sizes if the object can be treated as a bulk material. We assume that our rods obey this criterion and, therefore, that the FEMM calculations are meaningful. Based on these calculations, the rods should generate large field gradients ($\sim 10^6-10^7$ T/m) between ferromagnetic and diamagnetic sections of the rod; these gradients diminish by at least 1000-fold in any direction over distances of ~80 nm from the surface. Magnetic gradients as large as 10^6-10^7 T/m form adventitiously at asperities on ferromagnetic materials (steel wool) used in magnetic separations.[4] We generate these gradients by design.

Rods of alternating layers of Co−Ni and Au were electrodeposited in porous polycarbonate filters and then released.[1−3] We fabricated rods with long (350 nm) ferromagnetic sections (Co−Ni alloy) separated by short (20−100 nm) diamagnetic sections (Au) (Figure 2a).[10] The aspect ratio of the ferromagnetic sections (ratio = thickness/diameter) results in an easy axis of magnetization parallel to the axis of the rod.[11] The rods were suspended in dichloromethane by ultrasonication (the suspensions were stable for minutes) and then deposited onto a Si wafer. During deposition, a magnet was placed underneath the Si wafer with its dipole parallel to the plane of the Si surface to magnetize the rods on their easy axis. The structure of the rods was characterized by scanning electron microscopy (Figure 2b). Magnetic force microscopy was used verify that the rods were polarized along the long axis (see Supporting Information).

The magnetized rods, deposited on a surface, were treated for 5 min with a dispersion of 8 nm γ-Fe_2O_3 particles. These nanoparticles were chosen for three reasons: (1) they are superparamagnetic—that is, they have magnetizations characteristic of ferromagnetic materials, but they have negligible remanence; (2) their synthesis is convenient; and (3) they are smaller than the diamagnetic sections. The γ-Fe_2O_3 particles clustered predominantly near the diamagnetic sections in a radially symmetric fashion (Figure 2c).

The sizes and shapes of the clusters closely matched that of the gradients in the **z** and **r** directions (as defined in Figure 1) predicted by magnetic calculations (Figure 2d). In the **r** direction, the size of the clusters depended on the ratio of the size of the gap to the diameter of the rod. If the gap is equal to or larger than the diameter, then the gradients at the edge of the gap are due to the small radius of curvature at the corners. For the 80 and 160 nm diamagnetic sections, we observe clusters of nanoparticles extending outward in **r** to a distance of 80 nm. If, however, the gap is smaller than the diameter, then the shape and intensity of the gradients depend on the size of the gap. For the 20 and 40 nm diamagnetic sections, we observe clusters of nanoparticles extending in **r** to ~20 and ~40 nm, respectively. We can, therefore, control the shape of the gradient and the localization of particles in both **z** and **r** dimensions depending on the design of the rod. In addition, particles localize on the rods when the rods are free from the surface. This characteristic suggests that these structures should be stable when free in a liquid.

This work describes a simple, inexpensive, and widely accessible technique for generating intense magnetic gradients by design. The gradients are used to localize magnetic nanoparticles to attoliter volumes of space on mobile magnetic microstructures. The pattern of alternating sections in the rod determines the size and shape of the clusters of nanoparticles and their positions along the rod. The positioning of nanoparticles with precise location and separation may have broad potential in cell biology for stimulating single cells, either chemically or mechanically, with magnetic nanoparticles at multiple, fixed positions on the surface or interior of a single cell.

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Supporting Information Available: Experimental details (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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