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# The fabrication of uniform cylindrical nanoshells and their use as spectrally tunable MRI contrast agents

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#### Abstract

A new form of tunable magnetic resonance imaging agent based on precisely dimensioned cylindrical magnetic nanoshells is introduced. Using top-down prepatterned substrates, the nanoshells are fabricated by exploiting what is usually regarded as a detrimental processing side-effect, namely the redeposition of material back-sputtered during ion-milling. The well-resolved nuclear magnetic resonance peaks of the resulting nanostructures attest to the nanoscale fabrication control and the general feasibility of such sputter redeposition for fabrication of a variety of self-supporting, highly monodisperse nanoscale structures.

## 1. Introduction

The impact of nanoparticles on biotechnology and biomedical imaging continues to grow rapidly [1-3]. Among others, magnetic resonance imaging (MRI) already employs a variety of bottom-up chemically synthesized nanoparticles [4, 5] for image contrast enhancement and cellular labeling and tracking [6–15]. More recently, top-down micro-engineered structures including the first microfabricated MRI contrast agent [16, 17] have also begun to emerge. Such top-down designed structures can exploit the enhanced geometrical and compositional control of lithographic patterning techniques, enabling tailor-designed labels or tags that offer greater encoding and probing functionalities than bottom-up chemically synthesized alternatives. However, with many nanoparticle applications depending on large ensembles of nanoparticles, the need for rapid fabrication of numerous structures can limit the nanoscale patterning resolution of top-down schemes. For example, while serial techniques such as electron beam or scanned probe writing offer high resolution patterning, they are less efficient than photolithographic processes, whose parallel nature affords much higher throughput.

Towards more efficient top-down nanoscale structuring, here we consider a simple, yet generalizable, resputtering technique on top-down photolithographically prepatterned substrates. Often regarded as an undesirable by-product of ion-milling, redeposited back-sputtered material is here instead exploited to yield scalable, large-area, parallel fabrication of accurately defined free-standing nanostructures. Demonstrating the added functionality that such top-down definition permits, a new form of MRI label is introduced: cylindrical magnetic nanoshells that can function both as conventional  $T_2^*$  and as new spectral shifting, or 'color', contrast agents. These labels, which are hollow cylinders formed from nanometer-thick shells of magnetizable material, can both modulate local magnetic resonance relaxivities as well as generate controlled, tunable nuclear magnetic resonance (NMR) shifts in the surrounding water through precise control of the shell heights, radii and wall thicknesses.

### 2. Theory

With function determined by form, the shell geometrical dependences are first explained before detailing the shell fabrication. The magnetic resonance physics behind the cylindrical shell structures can be viewed as an extension of earlier work that first demonstrated the spectral shifting of



**Figure 1.** Schematic of the fields generated by a magnetized hollow cylinder. (a) Cut-away schematic of the field (black arrows) of a hollow cylinder magnetized to saturation by background MRI field  $B_0$  (red arrows). (b) Calculated magnetic field magnitude profile with underlying field magnitude contour plot in a mid-plane through a magnetized hollow cylinder. Plane orientation shown in upper left corner. (c) As for (b) but for perpendicularly oriented mid-plane. (d) Histogram recording the frequency shifts that would be experienced by the water surrounding the hollow cylinder (see text). (e) Calculated cylindrical shell internal volume fraction falling within a bandwidth  $\delta\omega$ , about the shell's central frequency shift  $\Delta\omega$ . The inset cut-away schematic shows the characteristic spatial extent of the hollow cylinder's internal homogeneous field volume for a cylinder aspect ratio  $L/2\rho = 1.2$ : all points within the numerically calculated three-dimensional yellow surface contour have frequency shifts differing from  $\Delta\omega$  by no more than  $\pm 5\%$ .

NMR signals from water passing between a pair of magnetized disks [16]. Although hollow cylinders clearly differ from flat disks, the physical basis behind these new cylindrical nanoshells' spectral shifting properties can be understood, as described below, through a physical rotational transformation as approximately analogous to that behind the double-disk structures described elsewhere [16]. Therefore, this paper outlines only those details relevant to the new cylindrical structures.

For proton gyromagnetic ratio  $\gamma$ , the Larmor precession frequency  $\omega$ , of water hydrogen protons in a magnetic field of magnitude B, is given by  $\omega = \gamma B$ . In the vicinity of any magnetic structure, therefore, proton precession frequencies vary proportionally to the spatially varying magnetic fields produced by that structure. Accordingly, NMR spectra integrating over water proton signals from around that structure would typically integrate over broad frequency ranges, leading to broadened water lines. To yield instead a distinct frequency shifted NMR peak, the magnetic structure geometry must be such that it produces a water-accessible, extended spatial volume over which the total field from the magnetized structure's field, together with the applied magnetizing background MRI field  $B_0$ , is homogeneous and distinct in magnitude from the surrounding fields. It has been shown that the field between two suitably spaced magnetized disks possesses the necessary homogeneity to yield such shifted NMR peaks [16]. In such a double-disk system, the disks are assumed aligned such that the  $B_0$  field vector is parallel to the disks' planes. However, this alignment requirement restricts orientation about only a single axis; in particular, the doubledisk structure is free to rotate about a central axis parallel to  $B_0$ . Because the resulting NMR frequency shifts are invariant with respect to this rotation, a variety of alternative structures, each composed of what can be regarded as superpositions of rotated double-disk structures, should also possess the appropriate homogeneous field profiles. Although a hollow cylinder represents the surface of revolution of a radially offset thin rectangle, rather than that of a disk, its similarity to a rotated double-disk system means that its internal fields can likewise generate distinct spectrally shifted NMR peaks.

Figures 1(a)–(c) show a schematic of a cylindrical shell magnetized to saturation by  $B_0$ , together with resulting numerically calculated magnetic field magnitude profiles demonstrating the shell's homogeneous internal field. The histogram in figure 1(d) records the calculated field magnitudes (or equivalently, proton precession frequencies) throughout the space around the shell. By showing the relative volumes of space corresponding to each precession frequency, or field magnitude, the histogram approximates the resulting NMR spectrum from water in the shell's vicinity. The shifted spectral peak evident in the histogram is due to the shell's internal homogeneous field region whose spatial extent is delineated by the surface contour plot of figure 1(e).

The shifted resonance linewidth is determined by the internal field homogeneity, which depends on shell geometry, as shown in figures 2(a) and (b). Although the shell walls may have high aspect ratios, the overall cylindrical shell is fairly short, with an optimal length-to-diameter ratio just above unity. For such a shell the NMR frequency shift  $\Delta \omega$ , of the water within it can be analytically approximated from the field at its center. Assuming a magnetically saturated cylindrical shell of material with saturation magnetic polarization  $J_s$ , wall thickness t, diameter  $2\rho$ , and length L, the frequency shift is



**Figure 2.** Spectral linewidth dependence on cylinder geometry. (a) Vertically offset waterfall-style plot of calculated frequency histograms for thin-walled cylinders ( $t \ll L$ ), showing optimal aspect ratio,  $L/2\rho \approx 1.2$ . (b) Vertically offset waterfall-style plot of calculated frequency histograms for cylinders with non-uniform wall thickness. Labels indicate ratio of thickness change  $\Delta t$ , to average thickness t.

 $\Delta \omega = \gamma J_s L[(L^2 + (2\rho + t)^2)^{-1/2} - (L^2 + (2\rho - t)^2)^{-1/2}].$ Simplifying to a thin-walled structure ( $t \ll L \approx 2\rho$ ) gives

$$\Delta \omega \approx -4\gamma J_{\rm S} \left( \frac{L\rho t}{\left( L^2 + 4\rho^2 \right)^{3/2}} \right). \tag{1}$$

## 3. Geometrical scalability

Equation (1) above shows that shell frequency shifts can be engineered by varying shell lengths, radii, wall thicknesses, or material compositions. In this way, the different spectral signatures of different cylindrical shells can be regarded as MRI radio-frequency analogs to the different optical colors of different quantum dots [18, 19]. Here, however, it is shell geometry, rather than dot size, that determines the spectral response. Indeed with all geometrical parameters combining into a dimensionless ratio, the shells' magnetic resonance frequencies are controlled specifically by structure geometry but are independent of overall size. Provided all dimensions are scaled proportionally, therefore, nanoscale shells can shift the surrounding water NMR frequencies by just as much as can shells that may be far larger. A fabrication method that offers independent control over each dimension, and that is scalable across a wide size range, is therefore desirable for increasing the range of applications of the resulting frequency shifting agents. Particularly advantageous is scalability down to the nano-regime. Apart from smaller structures affording increased biological compatibility, relative to their size, smaller shells can amplify signals to a larger degree than can larger shells. This signal gain with structure miniaturization is due to water self-diffusion that, over typical proton relaxation periods, becomes appreciable on the micro- and nanoscales and that therefore enables signal amplification through magnetization transfer techniques [16, 20, 21] that exploit the continual exchange of water between inside and outside the shell. The smaller the structure, the more rapid is this water exchange. As such, for equal total quantities of magnetic material used to construct an ensemble of shells, an ensemble containing a greater number of smaller shells can interact with a larger volume of water than can an ensemble comprising a smaller number of larger shells. Provided the diffusional exchange is not so fast as to frequency-broaden the spectral peak by more than its shift, signals can increase quadratically as structure sizes shrink [16].

Beyond scalability, the fabrication method should also exhibit minimal cross-structure variation. If not, geometrical or compositional variations can induce unintended frequency shifts from one structure to the next, broadening and degrading the spectral peaks from signals integrated over ensembles of nanostructures. Indeed, ensuring optimally sharp magnetic resonances [17] demands monodispersity levels that are at odds with those of typical bottomup synthesized structures. As such, even though porous membrane templating techniques [22] commonly used for synthesizing various cylindrical nanostructures such as rings, cones, tubes, rods, wires, and core-shell or cable geometries [23-32], can sometimes yield what may be by bottom-up standards relatively monodisperse features, topdown patterning's enhanced dimensional control and interparticle uniformity render it a more favorable approach.

## 4. Fabrication by sputter redeposition

Because the nanoscale lateral definition demanded by the cylindrical shells' high-aspect-ratio walls is poorly suited to traditional planar microfabrication, we introduce an unconventional approach based on local resputtering of a prepatterned substrate. The key step to this fabrication method is straightforward, involving ion-milling away a thin magnetic layer previously evaporated onto a substrate patterned with an array of solid cylindrical posts. During this ion-milling, a fraction of the magnetic material emitted from the substrate redeposits on the post sidewalls, leaving cylindrical magnetic nanoshells once the post material has subsequently been While the process itself may be simple, less dissolved. simple is why it should be well suited to producing nanoshells with just the right properties to yield well-defined NMR spectral peaks. In particular, sharp resonances require shells with uniform wall thicknesses over their full lengths (see figure 2(b)).

Figure 3(a) sketches the geometry used for discussion of the sputter coated wall thickness as a function of height z, up



**Figure 3.** Local sidewall sputter coating. (a) Schematic of geometry used in sputtering calculation (see text). (b) Calculated sidewall coating thicknesses for  $\cos^{1/2} \theta$ ,  $\cos \theta$ , and  $\cos^2 \theta$  sputter distributions and associated calculated sidewall sputter coating thicknesses (labels indicate cosine powers). Dark gray indicates sidewall thickness profile for R/L = 2 (see text); light and dark gray together indicate overall profile for R/L = 10.

the side of a cylindrical post. Naively, one might expect the sputtered coating to be much thicker at the base of the post than at its top, since points near the post's base are closer to the source of sputtered substrate atoms than are points higher up on the post. This is not the case, however, because the sputtered atom distribution is not isotropic. According to linear collision cascade theory [33, 34] sputter distributions are, to first order, proportional to  $\cos \theta$ , for  $\theta$  the angle between the sputtering direction and the substrate normal. Specifically, experiments [34, 35] have shown that sputter distributions vary from under-cosine, to cosine-like, to over-cosine as incident ion energies increase. Angular dependences are therefore generally approximated as proportional to  $\cos^{m} \theta$ , with values of *m* below or above unity representing under- or overcosine distributions, respectively. Returning to figure 3(a), suppose that a normally incident ion beam removes  $N_{\rm S}$ substrate atoms per unit area or, equivalently,  $N_{\rm S}r \, dr \, d\phi$ atoms from some representative differential substrate element P. At some distance d away from P, that substrate element yields an atom fluence per unit area of  $n_s(d) \cos^m \theta$ , with proportionality coefficient  $n_s(d) = (m+1)N_s r \, dr \, d\phi/(2\pi d^2)$ , determined by normalizing the integrated fluence through a hemispherical surface of radius d, centered on P, to the number of atoms emitted. Including the projection factor  $\cos\phi\sin\theta$  to account for the angle between the atom fluence and the cylinder surface normal, the number of atoms striking the cylinder per unit area at some representative point Q is then  $z^m(m + 1)N_S \cos \phi r^2 dr d\phi/(2\pi (r^2 + z^2)^{(m+3)/2})$ , where  $\cos \theta$ ,  $\sin \theta$ , and distance PQ, are expressed in terms of r and z. Integrating over that half of the substrate visible from point Q then gives the total number of atoms  $N_C$ , hitting the cylinder per unit area at height 0 < z < L as

$$N_{\rm C}(z) = N_{\rm S} \frac{z^m (m+1)}{\pi} \int_0^R \frac{r^2}{(r^2 + z^2)^{(m+3)/2}} \,\mathrm{d}r, \quad (2)$$

where R measures the effective substrate target size. In the limit  $R \rightarrow \infty$ , physically approximated by  $R \gg L$ , for all m > 0,  $N_{\rm C}$  reduces to  $N_{\rm S}\Gamma(m/2)/(2\pi^{1/2}\Gamma((m+1)/2))$ , where  $\Gamma$  represents the gamma function. That is,  $N_{\rm C}$  becomes independent of height, implying uniformly thick wall coatings. Moreover, thanks to the sputtering anisotropy, approximately uniform coatings result already for R only a few times larger than L. As examples, a cosine distribution gives  $N_{\rm C}(z) =$  $(N_{\rm S}/\pi)[\arctan(R/z) - (R/z + z/R)^{-1}]$ , implying a shell coating that, over the full cylinder length, deviates from its average thickness by no more than  $\pm 10\%$  once R/L exceeds about 7. Meanwhile, for a  $\cos^2 \theta$  distribution,  $N_{\rm C}(z) =$  $(N_{\rm S}/\pi)(1 + (z/R)^2)^{-3/2}$ , implying similar wall thickness uniformity already for  $R/L \ge 3$ . The sputtering anisotropy therefore facilitates efficient, parallel processing by allowing relatively closely packed arrays of structures on the processing substrate.

Note that for such arrays, partial shadowing effects from neighboring structures may introduce an angular dependence reflecting the lattice symmetry and precluding exact definition Fortunately, even for relatively closely spaced of R/L. structures, both the total fluence blocked by neighboring structures and the resulting angular dependence in that fluence are often negligibly small. Consider, for example, an array of cylinders of lattice constant a times the cylinder height. Assuming again  $t \ll L \approx 2\rho$ , the worst-case smallest spacing from the center of one shadowing cylinder to the closest points on the sidewall of its nearest neighbor is approximately (a - 0.5)L and the shadowing angle subtended is, accordingly,  $2 \arcsin(1/(2a - 1))$ . Since the projection factor  $\cos \phi$  integrates to  $\sin \phi$ , the sidewall coating fraction from a pie-shaped wedge of the substrate with this opening angle of 2  $\arcsin(1/(2a-1))$  is simply 1/(2a-1). Meanwhile, integrating  $N_{\rm C}(z)$  for all substrate points at radial distances greater than the nearest-neighbor distance gives the sidewall coating fraction from all points beyond the shadowing cylinder as  $(2/\pi) \operatorname{arccot}(a-0.5)$  and as  $1-1/[1+1/(a-0.5)^2]^{1/2}$  for  $\cos\theta$  and  $\cos^2\theta$  sputter distributions, respectively. Multiplied by the occluded angular fraction 1/(2a - 1) this approximates then the fractional coating loss due to the nearest-neighbor shadowing, which, for lattice spacings at least a few times L, can be asymptotically expanded to yield approximate scalings of  $1/\pi a^2$  and of  $1/4a^3$ , for  $\cos\theta$  and  $\cos^2\theta$  distributions, respectively. Total shadowing loss must include losses from all surrounding cylinders, but, given the rapid fall-off with distance a, next-to-nearest-neighbor contributions quickly become negligible and total loss remains small for any lattice spacings exceeding a few times the cylinder height. For example, for lattice constants as small as 3-4 (as they are in our experiments) shadowing corrections amount to only a small



**Figure 4.** Process flow diagram for cylindrical nanoshell fabrication. (a) Patterned cylindrical photoresist posts atop gold–titanium coated substrate, (b) angled copper evaporation, (c) magnetic material evaporation, (d) ion-milling removal of magnetic material and local resputtered coating of posts, (e) copper and photoresist removal, (f) release of hollow cylinders by selective gold wet-etch or ultrasound.

percentage. Moreover, given the lattice symmetry, resulting 180° rotational symmetry in any angular dependence of the cylinder wall thicknesses means that, in addition to the angular variation being small, its effect cancels out at least to first order in the resulting field homogeneity and has little effect on cylinder NMR linewidths.

While sputtering anisotropy allows relatively small lattice constants, structure spacing cannot be reduced indefinitely since as R/L shrinks further, maintaining wall thickness uniformity requires ever more peaked sputter distributions and ever higher ion beam energies. Not needing excessively high beam voltages renders externally coated arrays of cylindrical posts preferable to internally coated arrays of cylindrical holes; while such an inverse approach can produce ring-like structures [23], the limited sputter target area implies very low effective R/L values and substantial vertical variation in wall thickness for all but very short cylinders. Indeed the familiar redeposition of material ion-milled from within narrow channels, generally regarded as a deleterious, rather than as an exploitable, effect in microelectronics processing, is a geometrically similar problem with known non-uniform deposit thickness [36].

Returning to individual cylindrical posts, figure 3(b) shows example wall thickness variations based on equation (2) for various sputter distributions. Equation (2) also quantifies the absolute wall thickness. For example, simplifying for  $R \gg L$ , a cosine distribution (m = 1) gives  $N_C/N_S = 1/2$ . Assuming unit sticking probability, the shell wall thickness is therefore one half the thickness of the original layer ion-milled off the substrate. In this way, the nanometer-level height control common to planar thin-film layers translates into similar nanometer-level width control of thin, vertically oriented surfaces. Since the above analysis is not necessarily particular to a cylinder, it should be possible to similarly fabricate various other high-aspect-ratio structures; a caveat is that some alternative structure geometries may limit substrate visibility, implying locally differing limits to, and possible

couplings between, the above *R*- and  $\phi$ -integrals. Note also that equation (2) is strictly valid only for thin coatings ( $t \ll L$ ); for thicker coatings, the possibility of appreciable time-dependent modification to surface normals as substantial sidewall material accumulates, as well as the possibility of ion erosion of, and reflection from, that accumulated material cannot be ignored. While negligible for the high L/t aspect ratio thin-walled structures described here, general theory behind such secondary effects can be found elsewhere [36, 37].

Figure 4 sketches a sample fabrication process. Atop a sacrificial gold layer, cylindrical posts of radius  $\rho$  are patterned out of a photoresist layer of thickness L (figure 4(a)). To avoid resist exposure to the ion beam, and to aid structure release (described below), a thin sacrificial copper layer is evaporated obliquely at a  $45^{\circ}$  angle (figure 4(b)), coating the substrate everywhere except within the shadows cast by the cylindrical posts. This is followed by evaporation of the desired magnetic material (in our case nickel, evaporated at rates of 3-5 Å s<sup>-1</sup>) shown in figure 4(c). Subsequent removal of this magnetic layer from the substrate and the tops of the posts via argon ion beam milling (figure 4(d)) then leaves behind the redeposited sidewall coatings with thicknesses determined through controlling the thickness of the originally evaporated magnetic layer as per the above sputter redeposition analysis. A selective wet-etch of the underlying protective copper followed by an acetone resist removal then leaves the desired hollow cylinders (figure 4(e)), each attached to the substrate around just one half of their base, corresponding to their shadowed sides that received no copper coating previously. This keeps the hollow cylinders still attached to the substrate for further processing, if desired; meanwhile, with the cylinder-substrate connections thus pre-weakened, the shells can also be removed (figure 4(f)) via either a gentle ultrasound or a wet-etch of the underlying sacrificial layer (for example, by brief room-temperature submersion in Transene GE-8148<sup>3</sup>,

<sup>&</sup>lt;sup>3</sup> Commercial GE-8148 gold etchant was identified only to specify the experimental study and does not imply endorsement by NIST or NIH that it is necessarily the best available etchant for the purpose.



**Figure 5.** Scanning electron micrographs (SEM) of fabricated cylindrical nanoshells. (a) SEM showing partial wet-etch release of array of cylindrical nanoshells ( $\rho \approx 1 \mu m$ , shell thickness  $t \approx 75 nm$ ) from substrate. (b) SEM's of cylindrical nanoshells ( $\rho \approx 425 nm$ , shell thickness  $t \approx 40 nm$ ) that were ultrasounded off their substrate and subsequently pipetted out onto fresh substrates. Top image shows nanoshells pipetted out in the absence of any applied magnetic field. Bottom image shows same process but with background magnetic field applied illustrating automatic self-alignment of the cylindrical nanoshells with the applied field direction (black arrow).

a selective gold etchant that does not attack nickel, followed by washing in de-ionized water). Note that the copper layer is not essential but including it does ease the resist removal and provide the option of a subsequent water-based ultrasound release free of any metal etchants or solvents.

For the case of cylindrical posts, the magnetic material evaporation could also be performed at an oblique angle (as per the copper evaporation) provided that the substrate were continually rotated throughout the evaporation. However, while oblique evaporation can coat the post sidewalls, it will also coat the substrate, which will therefore still require subsequent ion-milling and be subject to similar sidewall redeposition. Only for evaporation at grazing angles to the substrate would the more complex rotated evaporation be substantially advantageous, but then the shadowing resulting from such high angles would limit the general applicability of the technique and the spatial density of structures that could be patterned. Note also that although coating the substrate could be avoided by instead obliquely shadow-evaporating [24] or sputtering [25] onto an inversely patterned array of cylindrical holes rather than posts, such geometries preclude uniformly thick wall coatings. Because of the circular cross-sections, line-of-sight penetration depths of evaporant material vary across each hole, resulting in cylindrical shells whose wall thicknesses taper down from top to bottom.

## 5. Results and discussion

Figure 5(a) shows a scanning electron micrograph (SEM) of a sample array of fabricated nickel nanoshells that have undergone a partial wet-etch release. The shells have wall thicknesses,  $t \approx 75$  nm, radii  $\rho \approx 1 \mu$ m, and close-to-optimal cylinder aspect ratio's  $L/2\rho \approx 1.2$ , implying wall height-to-thickness aspect ratios L/t, of around 30. Despite their thin walls, the cylindrical shells yield physically robust self-supporting structures that are undamaged during either wet-etch (figure 5(a)) or ultrasound release (figure 5(b)). Foregoing any wet-etch, nanoshells were ultrasounded off their substrate into a vial of water and then pipetted out onto fresh substrates

both in the absence, and in the presence, of an applied background magnetic field. Because of their high L/t aspect ratios, the structures' magnetic shape anisotropies ensure the necessary automatic alignment with the applied field direction (figure 5(b)).

Figures 6(a)-(d) show experimental z-spectra [38] acquired on an 11.7 T MRI scanner from four different arrays of cylindrical nanoshells submerged in water. Each frequency point in the z-spectra was acquired by first applying a train of off-resonant  $\pi/2$  pulses to saturate out the magnetization of protons with matching off-resonance precession frequencies, before an on-resonance pulse was used to excite and quantify the amount of remaining unshifted water. Showing the frequency-dependent saturated proton magnetization  $M_{\rm S}$ , as a fraction of the total proton magnetization  $M_0$ , the spectra record the magnetic fields to which the water molecules were exposed. In particular, the spectral peaks (appearing as absorption dips in the curves) measure the fraction of water that diffused through the cylindrical nanoshells' internal homogeneously shifted magnetic field regions. All nanoshells used had  $J_{\rm S} \approx 0.6$  T (nickel), structure aspect ratios  $L/2\rho \approx$ 1.2, and inter-particle array lattice spacings of 3-4 times the particle diameters; however, to test the theory presented in this paper they were fabricated with different overall sizes, wall thicknesses, and incident Ar<sup>+</sup> energies. The spectra in figures 6(a) and (b) are both from  $\rho \approx 1 \,\mu m$  cylindrical shells, both sputtered at incident ion energies of 300 eV, but with different wall thicknesses of  $t \approx 75$  nm and  $t \approx 150$  nm, respectively. By contrast, the spectra of figures 6(c) and (d)are from  $\rho \approx 425$ –450 nm shells, sputtered at 500 eV, with  $t \approx 40$  nm and  $t \approx 50$  nm, respectively. All frequency shifts fall within about 10% of the predictions of equation (1), and the narrowing linewidths of those shells sputtered with higher energy ions suggest the improving wall thickness uniformity predicted by equation (2). Further increasing  $Ar^+$  energy should further sharpen the resonances; meanwhile, the fact that these resonances are already easily resolved, speaks to the method's intrinsic high levels of uniformity in both sidewall thicknesses and overall structure geometries.



**Figure 6.** Spectral contrast. (a)–(d) H<sub>2</sub>O *z*-spectra showing frequency-dependent fractional proton magnetization saturation  $M_s/M_0$ , from water-submerged cylindrical nanoshells with radii  $\rho$ , and shell thicknesses *t*, of: (a)  $\rho \approx 1 \mu m$ ,  $t \approx 75$  nm; (b)  $\rho \approx 1 \mu m$ ,  $t \approx 150$  nm; (c)  $\rho \approx 425$  nm;  $t \approx 40$  nm; (d)  $\rho \approx 450$  nm;  $t \approx 50$  nm. All cylinder aspect ratios  $L/2\rho \approx 1.2$ . (e) Low and high magnification SEM's of array of cylindrical nanoshells ( $\rho \approx 450$  nm;  $t \approx 60$  nm) with all shell interiors, except for those comprising the 'MRI' lettering, blocked to 'turn off' their spectrally shifted signals. Also shown is an MRI (bottom left) of the array formed from the difference between two images: one collected after first saturating out proton magnetization around 1.25 MHz (corresponding to the measured nanoshell resonance); the other a background image acquired without any proton magnetization saturated out. Signal is visible only from those shells with open interiors that allow water to diffuse in and out.

Although all demonstrated nanoshells were made from nickel, an advantage of their physical, rather than chemical, deposition is that most other materials amenable to vapor deposition could be readily substituted and that multi-layered shells could be similarly fabricated. For example, ion-milling a pre-evaporated tri-layer gold–nickel–gold or titanium–nickel– titanium film would transform those planar tri-layer films into hollow magnetic cylinders coated in gold or titanium. Depending on the application, such non-magnetic coatings could serve as oxidation barriers, offer further mechanical strengthening, or provide surface coatings that are biologically inert (titanium) or that facilitate common bioconjugation protocols (gold).

Being analogous to a superposition of rotated doubledisk structures, the cylindrical shells naturally share many of those structures' advantages, including large, continuously tunable spectral ranges that do not depend on  $B_0$  for typical MRI scanners, and relatively low concentration requirements [16]. Additionally, like their double-disk counterparts, the cylindrical shells can function as local physiological probes. For example, if the cylindrical shells were blocked by some substance designed to break down under certain physiological conditions, then the shells could act as sensors with their spectral signals turned on or off depending on whether their internal regions were opened or closed to the surrounding water. This idea is suggested in figure 6(e) where, for demonstration purposes, photoresist was removed from only a controlled subset of the cylinders in the array, effectively turning those cylinders on, while the remaining cylinders, still blocked with photoresist, yielded no identifying spectral signal. A key difference between the cylindrical shells and the double-disk structures, however, is that with the disk spacing determined by separate posts, the double-disk resonances are potentially dynamically adjustable. On the other hand, the cylindrical shells' single-element construction is simpler and their synthesis more scalable in the nano-regime.

While the hollow cylinders' internal fields are relatively uniform, their external fields exhibit rapid spatial decays that manifest themselves as the frequency-broadened, but unshifted, background water signals seen in the experimental spectra of figures 6(a)–(d). This broadening is due to the shortened  $T_2^*$  due to the transverse magnetization dephasing



**Figure 7.**  $T_2^*$  contrast. Gradient-echo MRI (50  $\mu$ m isotropic resolution) showing hypointense  $T_2^*$  contrast (dark spots) surrounding locations of cylindrical nanoshells suspended in agarose imaging phantom.

caused by the particles' spatially varying external fields. Externally, therefore, the magnetic nanoshells function as  $T_2^*$ contrast agents. This is shown in the MRI of figure 7 that shows darkened spots, typical of the  $T_2^*$  contrast of regular superparamagnetic iron oxide (SPIO) nanoparticle contrast agents [7, 8, 39], but that now identify the spatial locations of cylindrical nanoshells that have been suspended in an agarose imaging phantom. This SPIO-like contrast is not surprising because at typical MRI spatial resolutions, which exceed nanostructure sizes by orders of magnitude, a hollow shell and a solid particle present similar dipolar field profiles, and contrast depends only on magnetic moment. With each cylindrical shell's material volume being equivalent to that of a solid sphere of diameter  $(12L\rho t)^{1/3}$ , comparison with similarly sized particulate agents [14] (that often contain only a small percentage of iron oxide) suggests that contrast from individual nanoshells is resolvable and that many of the dark spots in figure 7 are due to individual shells. Said another way, the hollow cylinders therefore double as both spatial and spectral MRI agents with their dipolar far-fields providing spatial contrast while their tailored internal, or near-fields, provide spectral contrast.

## 6. Summary

In conclusion, this work demonstrates that controlled local redeposition of back-sputtered material can provide a simple route to large-area parallel fabrication of monodisperse, self-supporting nanoscale structures. The technique's patterning accuracy affords new applications such as spectrally tunable MRI contrast agents that depend on precisely dimensioned resonance shifting cylindrical magnetic nanoshells. Simultaneously providing also  $T_2^*$  contrast, these multi-spectral nanoshell agents may provide an appealing complement to existing nanoparticle-based MRI agents.

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