Multispectral MRI contrast through cylindrical nanoshell agents

G. Zabow1,2, S. Dodd1, J. Moreland2, and A. Koretsky1
1NINDS, NIH, Bethesda, Maryland, United States, 2NIST, Boulder, Colorado, United States

Introduction

Recently it was shown that top-down microfabrication could be used to engineer precisely shaped magnetic microparticles that function as MRI contrast agents with tunable NMR spectral signatures [1]. The agents operated similarly to CEST / PARACEST agents [2,3], except with continuously tunable frequency shifts determined by control of the particle geometry, and with a magnetization-transfer signal acquisition scheme driven by diffusional-, rather than by chemical-exchange processes. The original demonstration was based on a design that, while well suited to conventional lithographic microprocessing [4], depended on complex double-disk magnetic microstructures. Non-conventional microprocessing, however, allows also for the possibility of creating cylindrical magnetic nanoshell structures [5]. Via elementary physical transformations, it can be shown that similar NMR tunability can be achieved through the use of such cylindrical nanoshells, which are in some ways simpler than double-disk structures in that they represent single, rather than complex, magnetic structures. Here NMR results from such cylindrical nanoshell agents are presented, with the work also being taken a step further by releasing these nanoshells from their fabrication substrate and demonstrating automatic magnetic self-alignment and signal acquisition from ensembles of such structures randomly distributed in an agarose gel.

Methods and Results

Hollow cylindrical nickel tubes with radii $R$ of 400 – 500 nm and wall thicknesses $t$ of 40 – 50 nm were fabricated via metal deposition, ion-milling and associated back-sputtering on a lithographically prepatterned substrate (Fig. 1). By including a sacrificial titanium layer between the microfabricated structures and the base substrate, a selective wet-etch combined with an ultrasonicating was able to remove the cylindrical nanoshells from the substrate. The nanoshells were then repeatedly washed in D.I. water and then either stored in clean D.I. water, or re-pipetted out onto a fresh substrate for scanning electron micrograph (SEM) imaging (Fig. 2), or transferred from the D.I. water and mixed into an agarose gel, which was then shaken to disperse the nanoshell particles. Agarose gels were transferred into the MRI magnet before they had cooled sufficiently to rigidly fix the nanoshells, thereby allowing the nanoshells to automatically align with the MRI $B_0$ field due to their built-in magnetic shape anisotropy. Once cooled, a series of magnetization-transfer signals were acquired at different offset frequencies. This yielded z-spectra showing distinct shifted NMR peaks indicating that the nanoshells had indeed self-aligned with the $B_0$ field inside the agar gel (Fig. 3a), and confirming that the cylindrical nanoshell structures are mechanically robust enough to undergo ultrasonicating and multiple washing and pipetting stages as would be required for any possible in-vivo studies. The origin of the observed NMR peak and the self-alignment of the shells were also confirmed by the disappearance of the NMR peak when rotating the agar sample (with rigidly fixed nanoshells) through 90° so that the nanoshells were deliberately misaligned with $B_0$ (Fig. 3b).

In summary, precisely dimensioned cylindrical nanoshells have been shown to provide another example of microfabricated, geometrically tunable, multispectral MRI agents, and one that appears robust enough for future testing in biological samples.

References