Microfabricated magnetic structures for multi-spectral contrast

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Introduction

Magnetic resonance imaging (MRI) benefits from numerous types of image-enhancing contrast agents. However, be they relaxivity-based gadolinium-chelates, image dephasing superparamagnetic iron oxide particles(1), off-resonant chemically exchanging macromolecules(2), or even agents based on different nuclei such as encapsulated liquid perfluorocarbons(3), they are generally all produced through some form of chemical synthesis. Here we consider instead the potential of photolithographically-defined microfabrication for constructing purposely designed contrast agents. We find that microfabrication's more direct engineering control can yield contrast agents with both increased functionality and sensitivity. In particular we discuss how it is possible to engineer magnetic microstructures that generate discrete, and user-definable, Larmor frequency shifts enabling multi-spectral off-resonance contrast. We further show how these structures can enable a form of off-resonant saturation imaging contrast via diffusional water exchange that can boost traditional MRI sensitivity.

Results and discussion

As an example, Figure 1 shows an angled scanning electron micrograph (SEM) of an array of such microfabricated structures – each just 3 micrometers across – that each consist of two magnetizable 50 nm-thick nickel plates separated by three external non-magnetic epoxy-based posts. The structures are microfabricated through a series of metal evaporation and electrochemical depositions, followed by photolithographically-defined ion-milling, selective wet-etching, and support post patterning. When magnetized by the applied B_0 field, the relatively homogeneous magnetic fields of this structure frequency-shift water contained inside creating a distinct spectral peak. With the precise k-space position of this peak determined by microstructure geometry, it is possible to tune the frequency shift by controlling the structure's microfabrication process parameters. In this way multiple different frequency shifts can be generated, enabling multiplexed multi-spectral MRI. Depending on their size, the structures can be directly spectrally detected in the free induction decay following a broadband (hard) $\pi/2$ pulse; and/or they can be indirectly detected via self-diffusion-driven magnetic exchange between water inside the structure (that is pre-saturated by a series of off-resonant $\pi/2$ pulses) and unsaturated water outside the structure. In this way the structures' off-resonance signals are not unlike those of PARACEST agents(2), except that here, because the structures can be ferro- or superparamagnetic, their shifts can be much larger, in turn enabling much faster exchange rates, and much higher sensitivity. Indeed, their ferromagnetic nature results in full magnetic saturation of the structures in even low fields, giving field-independent frequency shifts and enabling imaging across a range of field strengths. Figure 2 shows an example of z-spectra from similar such structures when placed in water (data from three different field strengths: 11.7T, 7.0T, and 4.7T) showing an off-resonance frequency-shifted signal that is independent of MRI field. (The plot is the integral of the fid from bulk water when preceded by off-resonance $\pi/2$ pulses at different frequencies). It is noted that sensitivity of the diffusion based experiment does however improve with field strength due to increasing T1's of the surrounding water.

In summary, micro-engineering appears an attractive alternative to traditional chemical synthesis for MRI agent fabrication with increased functionality and sensitivity.

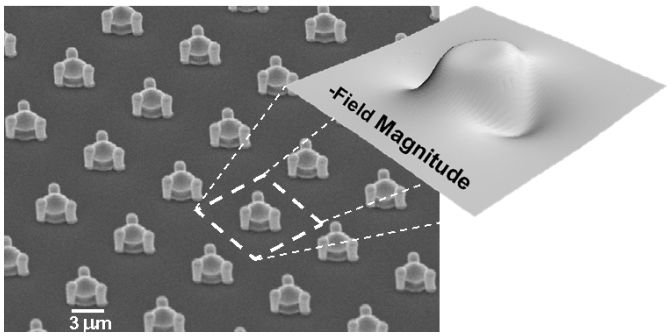

Figure 1. Scanning electron micrograph of an array of microfabricated magnetic structures for off-resonance MRI contrast. Inset shows homogeneous field shift profile over a mid-plane through one of the structures.

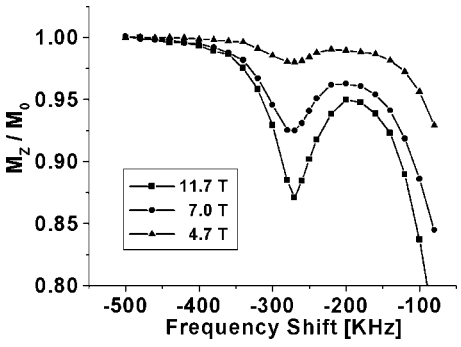

Figure 2. Sample z-spectra showing structure's MRI-field-independent frequency shift.

References:

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