MAGNETIC RESONANCE MICROSYSTEMS FOR LIFE SCIENCE APPLICATIONS

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ABSTRACT

Nuclear magnetic (MR) resonance spectroscopy and imaging technique are powerful methods available for determining molecular structures and non-invasive 3D imaging. In the effort of developing a nanoMRI microsystem, we have designed, fabricated, assembled and did preliminary characterization of the nanoMRI probe. A multilayer high aspect ratio metal process has been developed for this project. NanoMRI probes are designed through multi-physics finite element 3D analysis, integrated using the high aspect ratio process, assembled, and the RF coils are matched and tuned to a 500MHz system. Due to the large magnetic field gradients and fast switching gradient coils, the high mass-sensitivity and additional orthogonal RF signal channels, special MR pulse sequencies [5] can be developed for imaging and molecular structural analysis.

Keywords: RF Microsystem, MRI, NMR

INTRODUCTION

Nuclear magnetic (MR) resonance spectroscopy and imaging technique are powerful methods available for determining molecular structures and non-invasive 3D imaging. The MR spectroscopy has relatively recently been used to measure distance between specific nuclei in complicated structures and used to reconstruct the biological macromolecular 3D conformation or the enzyme-substrate complex. The imaging is achieved by spatially coding (with gradient coils) the precessing frequencies/phases of nuclear magnetic moments of the sample under a bias magnetic field (typically 0.5 Tesla to 10's of Tesla) and using RF coils to excite/detect these in a certain sequence. The 3D image is reconstructed after signal processing in a processor. In medical diagnosis, a resolution of a few millimeters is typically adequate; however, if the subject under study is an organ of a small animal, then an NMR microscopy is required. MRI's current resolution is limited to the few millimeters resolution for the medical imaging MRI, or to a few micrometers for the NMR microscopy or micro MRI imaging. General availability of high resolution at low cost is desired.

MAGNETIC RESONANCE MICROSYSTEM

Matching MRI field components to comparable size is desirable when the size of the subject under imaging is small such as a cluster of living cells or a single cell at room temperature. Through the reciprocal theorem in electromagnetic theory, it's known that scaling of RF sensors will increase the mass sensitivity inverse to the scaling factor [1]-[3], since magnetic fields generated by a fixed current source scale inversely with the size. This also makes the magnetic field gradients scale with the inverse 2^{nd} power of the size. The "NanoMRI",

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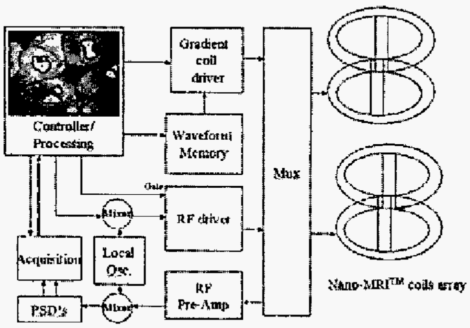
as compared to conventional MRI in Table 1, is an on-going research project, and Figure 1 shows the schematic of an example MRI array system under development for high-content screening.



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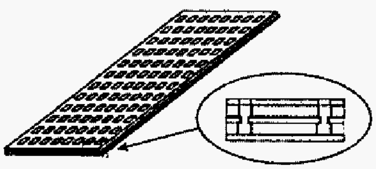

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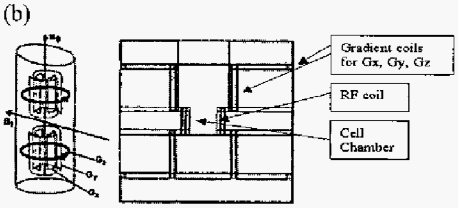


(c)

Figure 1 (a) The schematic of a nanoMRI system, with the imaging coil array shown in 96-well format, and (c). the cross section of each gradient and RF coil set embedded in a dielectric material surrounding a cell chamber.

Systems	Current	Size	Field Gradient	Resolution
MacroMRI	100A	~m	10 mT/m	1mm
MicroMRI	40A	10cm	1 T/m	10μm
NanoMRI	<1A	100μm	600T/m	~1μm

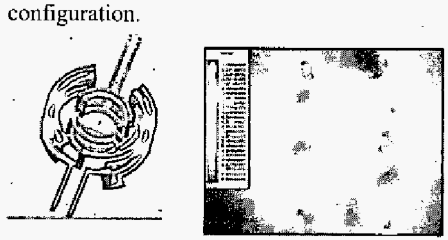
Table 1 Magnetic Resonance System Comparison

Strong magnetic field gradients are required for high resolution. The signal in the MRI imaging from various spatial locations of the sample is encoded as the precession frequency shifts as the result of the magnetic field gradient. For a minimum resolvable frequency variation $\omega-\omega_0$, larger magnetic field gradient Gx means better spatial resolution.

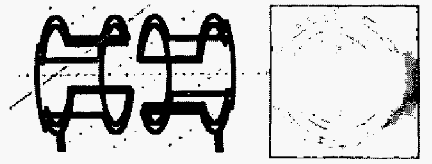
A further requirement on the field gradients comes from the diffusion. Since diffusion happens during the MRI imaging, high resolution requires small sampling time. Since the sampling time Ts needs to be long enough to resolve the minimum frequency variation associated with the minimum spatial resolution, a high resolution MRI system requires a high magnetic field gradient. Miniaturization enables drastic increase in field gradients.

Design Analysis & Microfabrication

There are many possibilities and trade-offs of RF and gradient coil designs. For the sub-mm RF coil, resistive noise of the coil dominates [4] the SNR. These are analyzed using 3D thermal, mechanical and electromagnetic field finite element analysis. Figure 2(a) shows a cross section of the field distribution of a 2-channel copper micro saddle-coil antenna under a 500MHz RF excitation using Ansoft HFSS & 2(b) shows a gradient coils using Golay configuration.



(a)



(b)

Fig 2. (a) A pair of RF saddle coils for quadrature detection. (b) Gradient coils using Golay configuration which canceled out terms to fifth harmonics.

The susceptibility variation in the materials (copper, air & fluid etc.) near the sample can lead to localized distortions of the static magnetic field in the sample region. This is an important factor in the NMR spectroscopy where sample is placed within a glass tube and placed within the coil, leaving an air gap between the copper coil and glass tube. The susceptibility of copper and water are similar, but the susceptibility of glass and air are more different from those of copper & water. Typically, a matching fluid such as FC-43 is used. Since our device will be used in a micro-fluidic cell array type of platform with copper coils imbedded in a dielectric material (measured in a SQUID magnetometer to have similar diamagnetic susceptibility), no glass tube container (and air gap) is included so no separate perfluorinated compensation fluid is required to overcome the signal void caused by susceptibility mismatch.

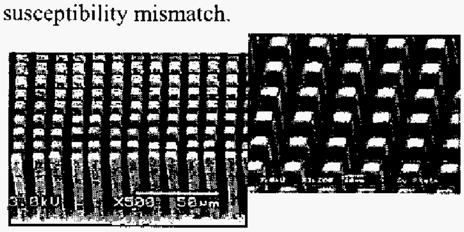


Fig. 3. (a) polymer studs and (b) copper studs.

A multilayer, high-aspect ratio copper process is developed for constructing the 3D RF helical coil and saddle coil structures 50 μm tall with 5-10 μm line width. Figure 3(b) shows an array of 50-μm-tall copper studs.

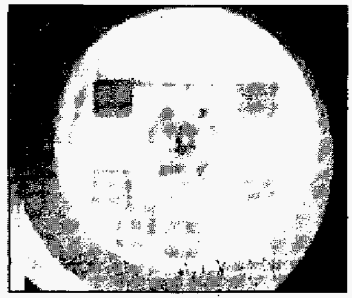


Fig. 4. A microfabricated RF transceiver w. three orthogonal coil sets.

Figure 4 shows a microfabricated saddle-coil device with three sets of orthogonal RF coils. Potentially, it can be used for molecular structure analysis with multidimensional NMR spectroscopy.

Packaged Probe Subsystem Assembly

A Bruker 500MHz (B_0=11.7T) spectrometer is used to characterize the RF coil. The matching and tuning network needs to be adjusted from the outside. Figure 5 shows the top portion of a home-made probe with the two-channel microfabricated RF coils and their matching and tuning network tunable from outside.

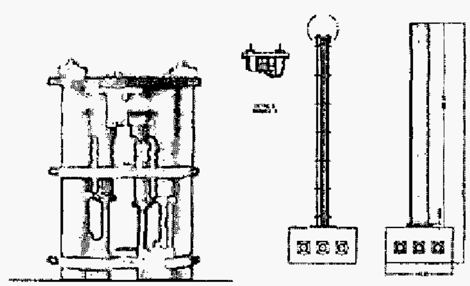


Fig. 5 A home-made probe with microfabricated RF coils tunable from outside.

CHARACTERIZATION

The probe is tuned to 500MHz and matched to

50Ω impedance. Figure 7 shows the corresponding S_{11} and Smith chart measured with a network analyzer. The center analytical chamber is loaded with sample as shown in Fig. 7. Fig. 8 shows a typical spectrum of sucrose using D_2O as the solvent. The gradient system is underdevelopment at the preparation time of this manuscript.

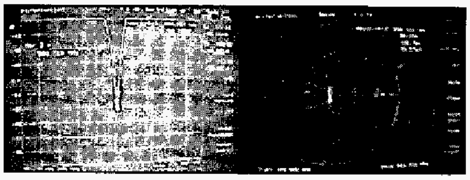


Fig. 6. The RF is tuned at 500MHz and matched to 50Ω.

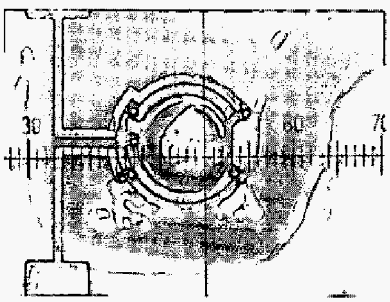


Fig. 7. A microfabricated RF saddle coil loaded with sample.

Fig. 8. The chemical shift of sucrose in D_2O.

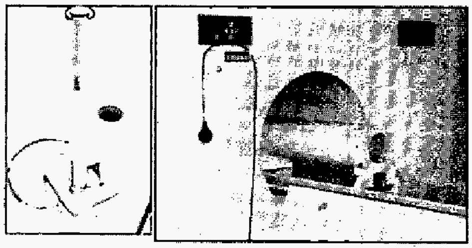


Fig. 9 The nanoMRI probe and the probe adaptation insert of an MRI system.

SUMMARY

We have designed, fabricated, assembled and did preliminary characterization of the nanoMRI probe. A multilayer high aspect ratio metal process has been developed for this project. NanoMRI probes are designed through multi-physics finite element 3D analysis, integrated using the high aspect ratio process, assembled, and the RF coils are matched and tuned to a Bruker 500MHz system. In the near future, biomolecules and biological cells will be injected into microwells of the nanoMRI probe for study. Due to the large magnetic field gradients and fast switching gradient coils, the high mass-sensitivity and additional orthogonal RF signal channels, special MR pulse sequencies [5] can be developed for imaging and molecular structural analysis. We'll report the results in later publications.

Acknowledgements

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