

## Portable, low-cost NMR with laser-lathe lithography produced microcoils

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### Abstract

Nuclear Magnetic Resonance (NMR) is unsurpassed in its ability to non-destructively probe chemical identity. Portable, low-cost NMR sensors would enable on-site identification of potentially hazardous substances, as well as the study of samples in a variety of industrial applications. Recent developments in RF microcoil construction (i.e. coils much smaller than the standard 5 mm NMR RF coils), have dramatically increased NMR sensitivity and decreased the limits-of-detection (LOD). We are using advances in laser pantographic microfabrication techniques, unique to LLNL, to produce RF microcoils for field deployable, high sensitivity NMR-based detectors. This same fabrication technique can be used to produce imaging coils for MRI as well as for standard hardware shimming or “ex-situ” shimming of field inhomogeneities typically associated with inexpensive magnets.

This paper describes a portable NMR system based on the use of a 2 kg hand-held permanent magnet, laser-fabricated microcoils, and a compact spectrometer. The main limitations for such a system are the low resolution and sensitivity associated with the low field values and quality of small permanent magnets, as well as the lack of large amounts of sample of interest in most cases. The focus of the paper is on the setting up of this system, initial results, sensitivity measurements, discussion of the limitations and future plans.

The results, even though preliminary, are promising and provide the foundation for developing a portable, inexpensive NMR system for chemical analysis. Such a system will be ideal for chemical identification of trace substances on site.

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**Keywords:** Microcoils; Portable NMR; Table-top NMR; Permanent magnets; Ex situ NMR; Chemical analysis; In the field chemical analysis

### 1. Introduction

The need for portable chemical analysis of suspect analytes in the field, including signatures from production of chemical and biological weapon agents, drugs, explosives, toxins, and poisons is well established. Demand for portable analysis equipment is growing in the defense and intelligence communities and, as a result, a number of field deployable analytical methods are being developed, including mass spectrometric- and infrared-based systems. Still, unambiguous identification of

suspect reagents can be difficult because of the dilute concentrations of suspect analytes as well as the typically large background signals from complex mixtures. The unambiguous assignment of molecular signatures to scheduled compounds can be compromised in mass spectrometry by derivitization steps or unexpected chemistry in the high temperatures present in gas chromatographic columns. Nuclear Magnetic Resonance (NMR), however, offers a non-destructive, reagentless analytical method for the identification of suspect analytes. NMR is one of the more important techniques for quantitative analysis [1–3], in no small part because it provides the inherently quantitative spectrum with unique structural information encoded in the chemical shifts and coupling constants

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Unfortunately, commercial systems are not well suited for portable NMR platforms due to the inherent lack of sensitivity of standard NMR receiver coils and the bulky size of the associated superconducting magnet. During recent years several groups are developing. Portable NMR systems offer several advantages over conventional NMR, such as scanning in the field, access to immovable, arbitrary-sized objects, lower cost, and increased robustness. Existing unilateral sensors are now being used routinely to perform NMR imaging and relaxation measurements. Despite the strongly inhomogeneous fields, devices such as the NMR MOUSE [4–9], and other unilateral or inside-out sensors [10–16] are being used for applications ranging from materials (e.g. mechanical properties of polymers, fat content of dairy products) and tissue evaluation [17–25] to flow measurements [26,27], art preservation [28,29] and oil well logging [30,31]. However, the spatial inhomogeneity of the static magnetic field has precluded the use of such devices for high-resolution spectroscopy.

During the past few years ex-situ methodologies have been developed to obtain high-resolution NMR spectra in the presence of field inhomogeneities, typical of MOUSE-type instruments [32,33], ex-situ shimming [34] and hardware shimming [35] have been used to acquire high-resolution spectra in single-sided systems. The open-sided field geometry, as well as the inherently low static field of such systems, result in a decreased sensitivity relative to laboratory NMR systems.

Microcoils are now used to increase the sensitivity of NMR spectra for mass limited samples [36–42] because the reduced RF coil diameter leads to an increase in the sensitivity of the coil itself [36,37,41,43]. Thus, for mass limited samples, one can obtain a significant increase in signal-to-noise (SNR). Olson et al. [37] have even reported limits of detection to the order of pico-moles. Others use planar microcoils that are made in two-dimensions for NMR experiments, [64] but these systems still lack sensitivity because flat coils are inherently less sensitive than RF coils surrounding the sample. Most solenoidal microcoils are hand-wound with insulated copper wire around a capillary [37,43–47].

Numerous groups have demonstrated effective results with hand-wound microcoils, as shown in some of the cited references in the present paper. However, the goal of our research is to go beyond the current state-of-the art (i.e. wire-wound microcoils) and advance the limits of NMR technologies. Even though hand-wound microcoils have reproducible results, the geometry precision and design flexibility of such coils is limited by human factors. Lithography, the basis of the integrated circuits manufacturing industry, has demonstrated unparallel precision in the construction of electronic devices. We expect these techniques, when developed for three-dimensional geometries, to be far more precise than manually produced microcoils. Rogers

et al. [39,40] were the first to employ micro-fabrication techniques (based on a wet-resist transfer method) to manufacture RF coils with variable design parameters. This technique uses photolithographic fabrication of an elastomeric stamp with a series of evenly spaced raised lines. This stamp is then coated with resist or ink, which is transferred to a titanium–silver coated capillary tube by rolling it across a wet line at a specific angle. This process yields RF microcoils that show an increase in SNR in a standard NMR experiment.

We have reported previously on the fabrication of complex design RF microcoils by a 3-dimensional laser direct-write lithographic technique [48]. This technique is used on a variety of micro-devices, including micro-catheters and electrical contacts to diamond anvil cells [49]. We have used this strategy to produce microcoils on the order of 100  $\mu\text{m}$  in diameter. While the properties of our coils are very similar to those described by Sillerud et al. via the focused ion beam lathe for microcoil fabrication [50], we have the ability to control to a larger extent the fabrication process and therefore are able to achieve more desirable characteristics (e.g. thicker deposition corresponds to lower direct current resistance), as well as complex shapes. Our fabrication process and electrical characterization of these microcoils are discussed elsewhere [48,51].

As described in Ref. [52], a portable NMR system based on microcoil technology has numerous advantages. First, the sensitivity of the system increases as the sample volume decreases (a conventional system using a 5 mm diameter RF coil can detect  $10^{17}$  spins while 100  $\mu\text{m}$  coils can detect  $10^{12}$  spins [44]). Second, the power needed to efficiently excite nuclei decreases by orders of magnitude, reducing the need for large RF amplifiers [53]. Third, the need for the large regions of field homogeneity produced by superconducting magnets is eliminated due to the drastic decrease in sample volume, thus permitting the use of small permanent magnets (NdFeB and SmCo magnets can produce fields of 2 T in a 1 kg package). At 2 T, the proton Larmor Frequency is 85 MHz, which is quite acceptable for the identification of low molecular weight compounds, considering that 90 MHz was the frequency of the standard laboratory-size NMR in the 1980s.

The small portable, permanent magnets, such as Halbach- and barrel-based, U-shaped, and dipoles, are unfortunately characterized by complex magnetic field profiles requiring field compensation via pole shaping, magnetic shims or shim coils. Their small size further requires a large amount of RF circuitry to be fit in a restricted space. The design and construction of such coils is ill-suited to typical construction methods, but becomes feasible with LLNLs unique microfabrication methods [48]. In a similar fashion, this lithography method affords the integrated design and manufacturing of combined receiver, shim, and gradient coils, as well as flow and multiplex capabilities in a compact package. These advantages of LLNL lithographic fabrication allow the production of microcoils for portable, high resolution, high sensitivity NMR.

## 2. Setup of a portable system

The goal of our research is to produce a compact, inexpensive NMR system for on-site chemical analysis of compounds, as previously reported [52]. For such a system to materialize, there are several parameters that need to be optimized; including the RF probe characteristics, the magnet, and the spectrometer. There are several companies now producing inexpensive spectrometers for frequencies applicable to permanent magnet based sensors.

The spectrometer we used for the experiments reported in this paper is a custom made spectrometer from Tecmag Inc, which has a frequency range of 0.002–100 MHz. The technical specifications are available from the manufacturer [54]. Briefly, the instrument includes an RF pulse programmer, digital receiver, waveform generators for shim control and imaging, and signal-averaging capabilities. The system is controlled via a laptop computer with NTNMR software for instrument control and data processing. Already commercially available systems, such as the Tecmag LapNMR or Magritek Kea [54,55], can perform the tasks necessary for our experiments. In addition, other groups are starting to produce inexpensive, home-made or custom-built controllers for NMR experiments [56,57].

Advances in portable, inexpensive permanent magnet design and construction are making promising steps towards the development of low-cost devices for use in portable, and on-site sensing and analysis of suspect samples. Permanent magnet design optimization and construction is now a task undertaken by several groups and companies. Despite the general focus in this area, a commercial permanent magnet with high field homogeneity has not yet been produced; however, this is an on-going field. For this study, we have employed a magnet with a Halbach [58] design based upon an eight element internal dipolar flux [59] and a resulting 2 T permanent field. The magnet was pur-

chased off-the-shelf from Magnetic Solutions Ltd., and weighs less than 2 kg. It has 9 cm diameter, 7 cm height and easily fits into the palm of a hand. Alternatives to Halbach designs for field optimization have been described in various references [59–63].

A picture of the first generation microcoil NMR table-top system is shown in Fig. 1. A compact Tecmag spectrometer, a small permanent magnet, and an RF probe with laser-lathe lithographically produced microcoils were used. A picture of the Halbach magnet and RF probe with a 360  $\mu\text{m}$  outer diameter microcoil on a translation stage, which is used to map out the magnetic field of the Halbach magnet, is shown in Fig. 2. The RF microcoil has an inductance of 76 nH and direct current resistance of 1.8  $\Omega$ . The probe is made from a transmission line probe design and achieved a forward to reflected power of 20-to-1. The measured  $Q$  factor of the probe is 28.15, while the calculated  $Q$

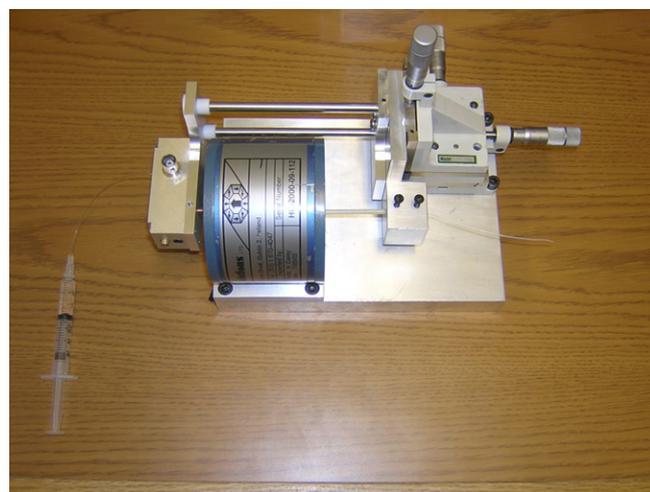


Fig. 2. A picture of the Halbach magnet and RF probe with a 360  $\mu\text{m}$  microcoil on a translation stage, which is used to map out the magnetic field of the Halbach magnet.

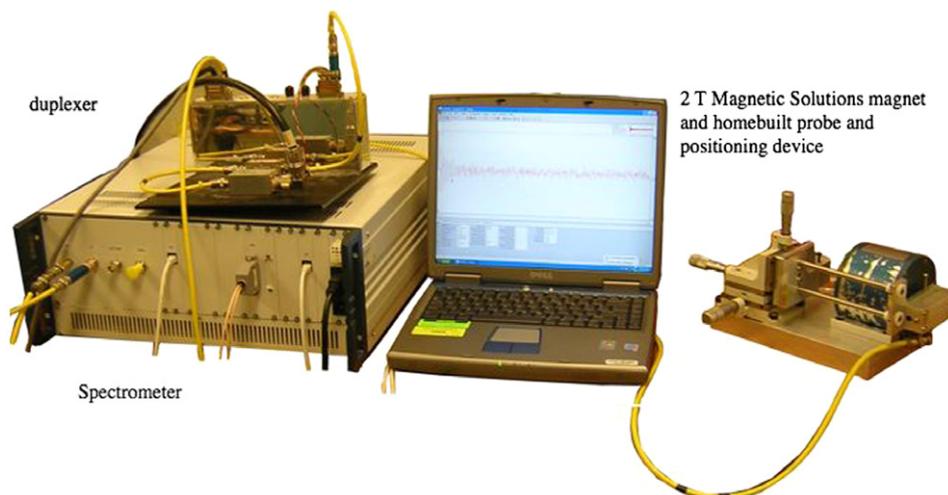


Fig. 1. Picture of our table-top laser-lathe lithographically microcoil NMR setup, which consists of a Tecmag spectrometer for control, a small Halbach magnet, and an RF probe with a 360  $\mu\text{m}$  microcoils.

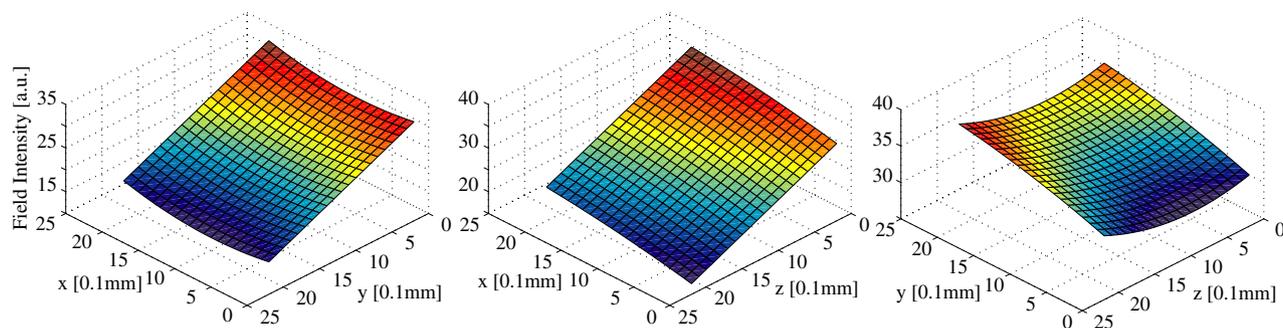


Fig. 3. 2D surface plots of the static field in the Halbach magnet.

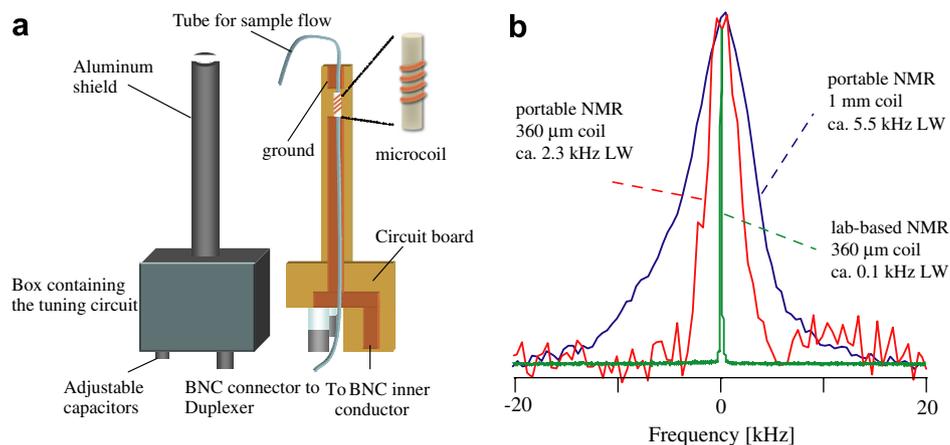


Fig. 4. (a) A Schematic of our first generation microcoil probe made on a circuit board. (b) NMR spectra taken from a homebuilt probe with a 360  $\mu\text{m}$  RF microcoil for our 500 MHz system, a homebuilt probe made from a circuit board with a 1 mm and 360  $\mu\text{m}$  RF microcoil for our portable 2 T Halbach magnet.

factor of the coil (from  $Q = \omega L/R$ ) is 22. The magnet is fixed and the position of the probe can be adjusted manually.  $^1\text{H}$  NMR spectra were taken at 0.1 mm increments in all three directions ( $x, y, z$ ). The linewidths of the  $^1\text{H}$  NMR spectra were subsequently evaluated. The resulting field map (Fig. 3) and the 3D offset from the central frequency (83.69 MHz) as a function of 3D space is shown to have a linear dependence on the  $x$  direction, and linear and quadratic dependence in  $y$  and  $z$ ,  $y$  being the direction of the field. The 3D fit is given by<sup>1</sup>:

$$\gamma\Delta B_0(x, y, z) = 25.5 - 0.7646x + 0.0866y + 0.2636z + 0.0191y^2 - 0.0051z^2 \quad (1)$$

The spatial dependence of the field was not symmetric along the direction of the field,  $y$ , which is contrary to what we expected from the magnet design. This could be due to manufacturing inconsistencies of the permanent blocks used for the construction of the magnet.

We have used the LLNL laser-lathe lithography system to fabricate microcoils with 1 mm, 360  $\mu\text{m}$ , and 100  $\mu\text{m}$

outer diameters. Our first RF microcoil probe was made with a circuit board. A schematic of the probe is shown in Fig. 4a.<sup>2</sup> Since the bore of the 2 T magnet is 0.8 cm in diameter, the circuit board RF microcoil probe fit very tightly in the magnet. Using this probe it was not feasible to obtain field maps of the magnet and to search for the region of maximum homogeneity. Fig. 4b compares spectra from our first generation, circuit board RF microcoil probe with a 1 mm and 360  $\mu\text{m}$  RF coil with a lab-based 500 MHz Bruker Advance instrument with a 360  $\mu\text{m}$  RF coil surrounding a sample of water. The resolution of the lab-based 360  $\mu\text{m}$  probe is 0.1 ppm in the 500 MHz superconducting magnet. Originally, the resolution of the portable RF microcoil on a circuit board probe was approximately 64.4 ppm with a 1 mm microcoil and approximately 27 ppm with a 360  $\mu\text{m}$  microcoil.

Our current RF microcoil probe uses a 360  $\mu\text{m}$  coil and is based on a transmission line design [2]. Our RF microcoil probe is extremely compact and is 0.2 cm in diameter, a

<sup>1</sup> The unit of space is in increments in translation stage (1/25 inches) and the offset units in kHz (offset from the central frequency that was chosen, 83.69 MHz).

<sup>2</sup> The RF microcoil is separated from the tuning circuit by a coaxial cable of 2 inches length, something not atypical for homebuilt probes. The addition of this transmission line corresponds to addition of 5 pF capacitance in parallel. This is something that was taken into consideration in the circuit calculations.

Table 1  
Portable, low-cost NMR

Power (W)	Voltage (V)	90° pulse width ( $\mu\text{s}$ )
319	126	0.21
151	87	0.34
29	38	0.70
5	16	2.80
0.02	1	6.29

Power consumption of the portable NMR microcoil system is shown above.

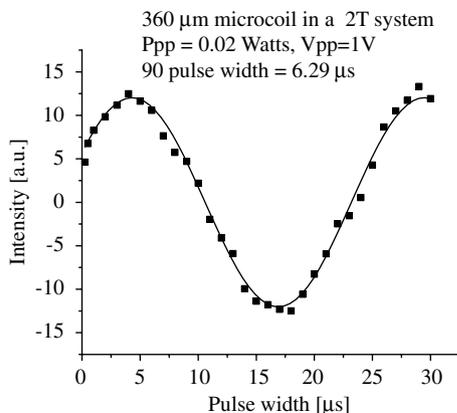


Fig. 5. Nutation curve of the portable RF probe with 360  $\mu\text{m}$  OD microcoil for 0.02 W of power.

fraction of the bore of the magnet. The behavior of the RF probe was evaluated at various power values, as summarized in Table 1. The 90° pulse widths range from 0.21  $\mu\text{s}$  with 391 W of power to 6.3  $\mu\text{s}$  for 0.02 W of power. A typical nutation curve for our current RF microcoil probe in the handheld 2 T magnet is shown in Fig. 5. These measurements demonstrate the robust characteristics of the microcoils; they are able to withstand high RF powers, yet are also capable of commercial probe 90° pulse times with only 20 mW of power.

### 3. Preliminary results

An NMR spectrum was taken with a single pulse-observe experiment in the most homogeneous region of the field (i.e. the sweet spot) after the field profiles were mapped, as described in the previous section. This region is not in the geometrical center of the magnet, but offset by 3 mm along the  $y$ -axis. A fluorinated compound, Fluorinert (FC-43), was used to demonstrate a spectral resolution of 17 ppm, while in separate experiments signal was obtained for proton and phosphorous by retuning of the probe. Fig. 6 shows the Fourier transform of the acquired  $^{19}\text{F}$  NMR signal from the sweet spot using a 360  $\mu\text{m}$  microcoil with an inner diameter of 320  $\mu\text{m}$ . The fluorine spectrum clearly shows two resolved peaks, where the amount of liquid inside the 360  $\mu\text{m}$  microcoil was approximately 80 nL. This data was taken at a field of frequency of

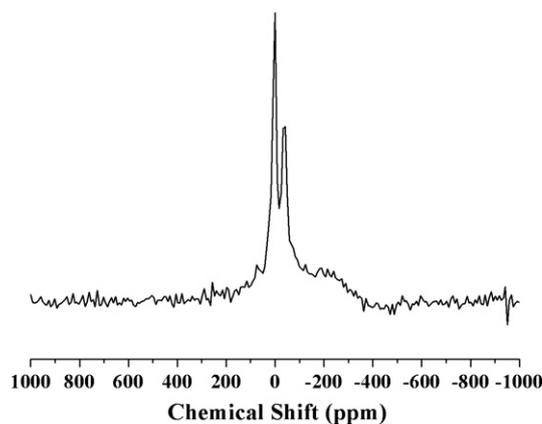


Fig. 6.  $^{19}\text{F}$  spectrum in the optimal sweet spot of the magnet. The resolution is 17 ppm.

78.89 MHz, with 64 averages, a 1 s delay time, and a pulse width of 0.35  $\mu\text{s}$ . Thus, the total time of acquisition was ca. 30 min. The signal-to-noise ratio (SNR) (in the Fourier Transfer Mode) was 32, much lower by comparison to that reported by Sillerud et al. for a single scan [50].

The low SNR is mainly related to the much lower resolution in our magnet by comparison to the larger NEO-MAX magnet which was used by Sillerud et al.<sup>3</sup>; however our magnet is portable. Additionally the low SNR is attributed to grounding problems between the magnet and the probe and other noise factors inherent to the large-opening Magnetic Solutions magnet.<sup>4</sup> Optimization of the RF microcoil geometry and characteristics, according to the findings reported in [51], and probe design, as well as testing of a variety of magnets is underway.

### 4. Microcoil sensitivity analysis

The NMR sensitivity, as reflected by the SNR, is dependent on the nuclear precession frequency, the sample volume, concentration, and natural abundance of the nuclei in question, the magnitude of the RF field induced for a current unit, as well as the noise [53,38]. Because of the latter dependence, the RF coil and probe circuitry properties are important parameters to be optimized in designing a robust NMR system. To compensate for the volume reduction in NMR measurements of small samples, high RF strengths are desirable, especially when use of higher static fields is not feasible. Pre-concentration of the sample and high filling factors are also desirable. The noise in the SNR calculation represents conductive, magnetic and dielectric losses due to the sample and surroundings, how-

<sup>3</sup> The resolution in the 30 cm cube 1 T NEOMAX magnet is 0.056 ppm. For the equivalent resolution we have estimated an SNR of 1200 for a single scan, which is larger than the SNR reported by Sillerud et al., i.e. 137.

<sup>4</sup> The gap in this magnet is 1 cm. The problem is more apparent in a 1 T magnet by Magnetic Solutions with a 2 cm opening that we have tested. These results are not included here.

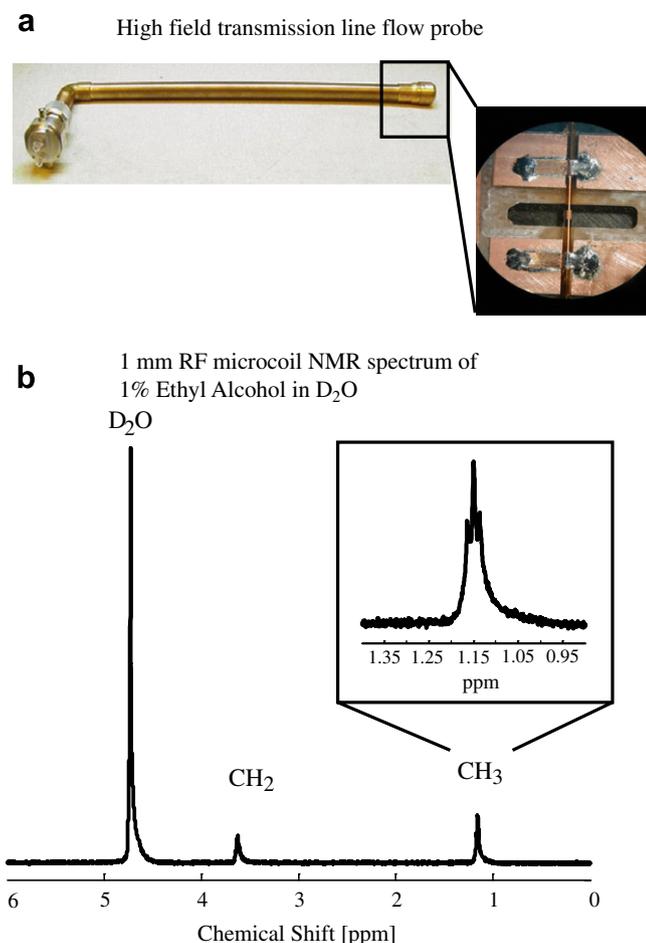


Fig. 7. Double resonance, transmission line flow probe for 500 MHz NMR spectrometer. The photo on the right is a close up image of the end of the probe, including the flow system, RF connection, and fine tuning capacitor.

ever it is primarily dependent on the resistance of the coil for microcoils.<sup>5</sup> The microcoil resistance in turn depends on the coil diameter, surface of the wire, inter-winding spacing, thus fine control of the properties of the microcoil is advantageous. We have shown that we can fabricate coils of various thicknesses, winding, number of turns, pitch, and therefore have the ability to control the inductance and resistance of the coil, and detailed evaluations of the laser-lathe lithography based fabricated coils is presented elsewhere [51].

Of course the SNR increases with the number of acquisitions and therefore the total acquisition time ( $t_{\text{acq}}$ ). Thus, to measure the NMR sensitivity ( $S$ ) with a particular RF coil, one must take into account the sample concentration ( $C$ ) or mass and the total experiment time. Also, a number of interest is the limit of detection (nLOD), i.e. the approx-

imate concentration or mass of a sample needed to obtain a desired SNR:

$$S_C = \frac{SNR}{C \cdot t_{\text{acq}}^{1/2}} \quad \text{and} \quad \text{nLOD}_C = \frac{3}{S_C} \quad (2)$$

The performance of NMR probes and RF microcoils under different analytical situations can be compared with these above criteria [44].

To test the sensitivity of two laser-lathe microcoils (diameters of 1 mm and 360  $\mu\text{m}$ ), a  $^1\text{H}$  transmission line probe for an 11.5 T (500 MHz) Bruker magnet was built. Photos of the transmission line flow probe are shown in Fig. 7. For  $^1\text{H}$  NMR sensitivity on LLNLs RF microcoils, we used a 1% ethyl alcohol solution in  $\text{D}_2\text{O}$ . The molarity of the solution was 165 mM. The 1 mm coil was constructed with an outer diameter of 1 mm, an inner diameter of 0.7 mm, 25 turns, 3 mm length, and 3  $\mu\text{m}$  thick copper. The 360  $\mu\text{m}$  was constructed with an outer diameter of 360  $\mu\text{m}$ , an inner diameter of 320  $\mu\text{m}$ , 25 turns, 1 mm length, and copper thickness of 10  $\mu\text{m}$ . In Table 2 the  $S_C$ ,  $S_M$ ,<sup>6</sup>  $\text{nLOD}_C$ , and  $\text{nLOD}_M$  for LLNLs laser-lathe RF microcoils of two different diameters, 1 mm and 360  $\mu\text{m}$ , are compared with previously reported NMR RF coils, including a Varian 5 mm, Nalorac SMIDG, and a hand wound microcoil of diameter 850  $\mu\text{m}$  [44]. In order to fairly compare the limits of detection of our microcoils to those of the coils reported in Ref. [44] as they would be expected at a 2 T (85.1 MHz) field, we have extrapolated, assuming the same order of homogeneity as the 500 and 600 MHz systems, according to  $B_0^{7/4}$ . While the  $S_C$  is smaller for the LLNL microcoils, the  $S_M$  is higher and the  $\text{LOD}_M$  is also dramatically improved, showing that portable NMR is indeed a real possibility for small sample sizes.

## 5. Gradient and shim coil fabrication

The laser-lathe system has produced coils of various geometries, and we used this technique to build coils for conventional shimming or for the application of shim pulses as described in reference [33]. A set of gradient coils was designed and built for the initial tests. This was a modified Maxwell pair producing a gradient in the  $y$ -direction (Fig. 8A), which is the direction of the main field. The coils were placed so that they surround the microcoil probe (Fig. 8B). Fig. 8C shows a schematic of the gradient coil and the simulated field produced by the coil in the center of the gradient along the coil length for an  $xy$  slice, as indicated in the schematic. The field produced by the gradient coils has a linear dependence along  $y$  over the sample region and is constant along the  $x$  and  $z$  directions ( $z$  is not shown). The coil resistance was 1.5  $\Omega$  and for the initial tests a Techron LVC 2016 linear amplifier was used to drive current through the coil.

<sup>5</sup> As stated in Ref. [38] as the size of the sample and coil decrease, the noise from the sample becomes negligible by comparison to that of the coil, thus the coil resistance is the dominant noise source in microcoil systems.

<sup>6</sup> The  $S_M$  and  $\text{nLOD}_M$  can be obtained from the same equations as  $S_C$  and  $\text{nLOD}_C$  by substituting the concentration with moles of sample.

Table 2

Data for LLNLs 1 mm RF microcoil, LLNLs 360  $\mu\text{m}$  RF microcoil, and HW 850  $\mu\text{m}$  microcoil were collected with a 500 MHz spectrometer

Figure of merit (units: C in mM, V in $\mu\text{L}$ , $t_{\text{acq}}$ in s)	Varian 5 mm (600 MHz)	Nalorac SMIDG (600 MHz)	HW microcoil 850 $\mu\text{m}$ (500 MHz)	LLNL's microcoil 1 mm (500 MHz)	LLNL's microcoil 360 $\mu\text{m}$ (500 MHz)
$t_{\text{acq}}$	4.1	4.1	4.1	10	10
Volume	222	38.3	0.62	1.15	0.08
C	2.26	21.8	— <sup>a</sup>	165	165
SNR	136	193	— <sup>a</sup>	452.35	15.82
$S_C$ (@85.1 MHz)	0.98	0.14	0.03	0.009	$3.16 \times 10^{-4}$
$S_M$ (@85.1 MHz)	4.39	10.49	50.15	98.50	489.47
$n\text{LOD}_C$ (@85.1 MHz)	3.05	21.05	97.6	332.59	9512
$n\text{LOD}_M$ (@85.1 MHz)	671	292.9	61.01	31.04	6.21

Data for Varian 5 mm and Nalorac SMIDG were collected with a 600 MHz spectrometer. Varian 5 mm, Nalorac SMIDG, and HW microcoil 850  $\mu\text{m}$  were done elsewhere [44]. Data for all coils were normalized to 85.1 MHz, according to  $B_0^{7/4}$ .

<sup>a</sup> These values were not reported in the original reference.

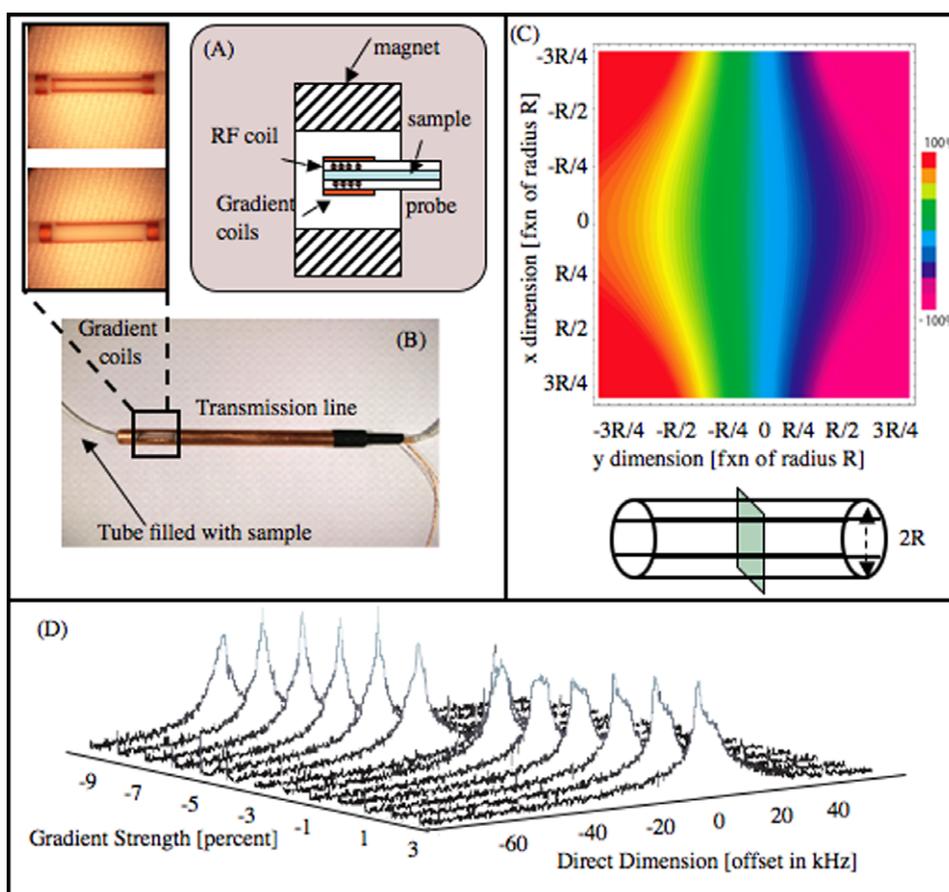


Fig. 8. (A) Photographs of the Gradient coils and schematic of the probe and magnet. (B) Photograph of the assembled probehead (RF and gradient coils, sample tube). (C) The simulated field produced by the gradient coils is assumed to be linear along the  $y$  direction and constant on  $x$  and  $z$ . Here an  $xy$  slice of the  $y$  component is shown. The field strength is in arbitrary units as a percentage of the total field produced by the coil. The position of the slice is shown in the schematic of the coil to the right. (D) Applying different gradient strengths, we see changes in the lineshape. The results here show that for an offset from the sweet spot we actually are shimming the field as indicated by the fact that we have a better lineshape in the presence of the gradient. Here the gradient strengths are shown as percentages, with 10% corresponding to 200 mV or 0.13 A of current.

An applied current of 0.1 A was enough to completely spoil the signal, corresponding to a value of 8% of the amplifier capabilities. Changing the gradient strength results in changes in the spectrum lineshape (Fig. 8D). When the sample was offset from the “sweet spot”, the gradients acted as shims, with a resulting improvement

in linewidth from 200 to 20 ppm. Application of shim currents while the sample is at the sweet spot did not yield any linewidth improvements, therefore higher order shims or shim pulse corrections are necessary. This work is currently under investigation and will be the subject of a subsequent publication.

## 6. Conclusions

The sustainability of a portable NMR system for chemical analysis of samples in the field is within reach. However, critical developments remain necessary: smaller control system electronics, lower power requirements, sensitivity and resolution enhancements. RF transmitter and receiver components in single boards have been developed from several companies<sup>7</sup> and advances in wireless communications have the potential of assisting in further miniaturization of the control electronics. For our initial system we used an off-the-shelf Halbach magnet. Permanent magnet manufacturing companies,<sup>8</sup> however, are making progress and several approaches toward smaller, higher field strength and quality systems seem to offer promising alternatives.

The use of microcoils to study small amounts of samples is well established. We have previously presented a microcoil fabrication scheme [48]. We have studied the properties of the microcoils as a function of winding spacing, width, and thickness of the loops, allowing for choice of most desirable characteristics, i.e. maximum quality factor and minimum resistance give higher SNR, though that work is outside the scope of this publication and is published separately [51]. For a 360  $\mu\text{m}$  outer diameter coil of 76 nH inductance and 1.8  $\Omega$  resistance, we built an RF probe and accomplished modest resolution using only 0.02 W of RF power, which gave a 90° pulse width of 6.7  $\mu\text{s}$ . While using higher homogeneity permanent magnets is an option we are hoping to have, to improve the resolution and sensitivity we next plan to use smaller microcoils in both length and diameter.

We have shown that the lithographic microcoil fabrication process can produce complex three dimensional shapes and we have produced field gradient and field shim coils to improve the field quality of the permanent magnet. While these coils are clearly effective at creating significant field perturbations with small amounts of current, the quadratic and higher order spatial dependence of the Halbach-type or other portable systems will require higher order shim coils. It is also feasible to use the present coils for effective shimming based on the series of ex-situ methodologies developed in the Pines lab [57], where by special pulse sequences (e.g. combinations of frequency and amplitude modulated RF pulses and amplitude modulated gradients) are used to impart spatially dependent phase corrections. Higher homogeneity will also improve the sensitivity of our experiments. In addition standard NMR approaches for sensitivity enhancement, as well as sample pre-concentration and combination with higher sensitivity detection schemes is an area we are currently undertaking.

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## References

- [1] R.R. Ernst, G. Bodenhausen, A. Wokaun, Principle of Nuclear Magnetic Resonance in One and Two-Dimensions, Clarendon, Oxford, New York, 1987.
- [2] E. Fukushima, S.B.W. Roeder, Experimental Pulse NMR: A Nuts and Bolts Approach, Addison-Wesley, New York, 1981.
- [3] P.T. Callaghan, Principles of Nuclear Magnetic Resonance Microscopy, Oxford, New York, 1991.
- [4] G. Eidmann, R. Savelsberg, P. Blümer, B. Blümich, The NMR MOUSE, a mobile universal surface explorer, J. Magn. Reson. A. 122 (1996) 104.
- [5] B. Blümich, P. Blümli, G. Eidmann, A. Guthausen, R. Haken, U. Schmitz, K. Saito, G. Zimmer, Concepts Magn. Reson. 16 (1998) 479.
- [6] P.J. Prado, B. Blümich, U. Schmitz, One-dimensional imaging with a palm-size probe, J. Magn. Reson. 144 (2000) 200.
- [7] G. Guthausen, A. Guthausen, F. Balibanu, R. Eymael, K. Hailu, U. Schmitz, B. Blümich, Soft-matter analysis by the NMR-MOUSE, Macromol. Mater. Eng. 276 (2000) 25.
- [8] F. Balibanu, K. Hailu, R. Eymael, D.E. Demco, B. Blümich, Nuclear magnetic resonance in inhomogeneous magnetic fields, J. Magn. Reson. 145 (2000) 246.
- [9] F. Casanova, B. Blümich, Two-dimensional imaging with a single-sided NMR probe, J. Magn. Reson. 163 (2003) 38.
- [10] W.E. Kenyon, J.J. Howard, A. Sezinger, C. Straley, A. Matteson, K. Horkowitz, R. Ehrlich, Pore size distribution and NMR in microporous cherty sand-stones, Transactions of the SPWLA 30th annual Logging Symposium, Denver, Colorado, USA, 1989.
- [11] D.P. Murphy, Advances in MWD and formation evaluation for 1995, World Oil 216 (1995) 39.
- [12] R. Freedman, C.E. Morriss, Processing data from an NMR logging tool, Presented at the 70th SPE Annual Technical Conference and Exhibition, Dallas, Texas, USA, 1995.
- [13] P.J. McDonald, B. Newling, Stray field magnetic resonance imaging, Rep. Prog. Phys. 61 (1998) 441.
- [14] M.J.D. Mallett, M.R. Halse, J.H. Strange, Stray field imaging by magnetic field sweep, J. Magn. Reson. 132 (1998) 172.
- [15] E. Fukushima, J. Jackson, The NMR News Lett. 490 (1999) 40.
- [16] P.T. Callaghan, R. Dykstra, C.D. Eccles, T. Haskell, J.D. Seymour, A nuclear magnetic resonance study of Antarctic sea ice brine diffusivity, Cold Reg. Sci. Technol. 29 (1999) 181.
- [17] A. Guthausen, G. Zimmer, P. Blümer, B. Blümich, Analysis of polymer materials by surface NMR via the MOUSE, J. Magn. Reson. 130 (1997) 1.
- [18] R. Haken, B. Blümich, Anisotropy in Tendon investigated *in Vivo* by a portable NMR scanner, the NMR-MOUSE, J. Magn. Reson. 144 (2000) 195.
- [19] W. Kuhn, M. Klein, A. Wiesmath, D.E. Demco, B. Blümich, J. Kelm, P.W. Gold, The NMR MOUSE: quality control of elastomers, Magn. Reson. Imag. 19 (2001) 497.
- [20] S. Anferova, V. Anferov, D.G. Rata, B. Blümich, J. Arnold, C. Clauser, P. Blümli, H. Raich, A mobile NMR device for measurements of porosity and pore size distributions of drilled core samples, Concepts Magn. Res. B 23 (2004) 26.

<sup>7</sup> e.g. Tecmag Inc., Quantum Magnetics/GE Security, Magritek, Topspin.

<sup>8</sup> e.g. Aster Enterprises, NEOMAX.

- [21] G. Zimmer, A. Guthausen, B. Blümich, Characterization of crosslink density in technical elastomers by the NMR-MOUSE, *Solid State Nucl. Mag.* 12 (1998) 183.
- [22] M. Todica, R. Fecete, B. Blümich, Selective NMR excitation in strongly inhomogeneous magnetic fields, *J. Magn. Reson.* 164 (2003) 220.
- [23] A. Guthausen, G. Zimmer, P. Blümer, B. Blümich, Analysis of polymer materials by surface NMR via the NMR MOUSE, *J. Magn. Reson.* 130 (1998) 1.
- [24] H.T. Pedersen, S. Ablett, D.R. Martin, M.J.D. Mallet, S.B. Engelsen, Application of the NMR-MOUSE to food emulsions, *J. Magn. Reson.* 165 (2003) 49.
- [25] N.O. Goga, A. Pirnau, L. Szabo, R. Smeets, D. Riediger, O. Cozar, B. Blümich, Mobile NMR: applications to materials and biomedicine, *J. Optoelectron. Adv. M.* 8 (2006) 1430.
- [26] F. Casanova, J. Perlo, B. Blümich, Velocity distributions remotely measured with a single-sided NMR sensor, *J. Magn. Reson.* 171 (2004) 124.
- [27] J. Perlo, F. Casanova, B. Blümich, Velocity imaging by ex-situ NMR, *J. Magn. Reson.* 173 (2) (2005) 254.
- [28] B. Blümich, S. Anferova, S. Sharma, A.L. Segre, C. Federici, Degradation of historical paper: nondestructive analysis by the NMR-MOUSE, *Magn. Reson. Imag.* 161 (2003) 204.
- [29] N. Proietti, D. Capitani, E. Pedemonte, B. Blümich, A.L. Segre, Monitoring degradation in paper. Part II: Non-invasive analysis by unilateral NMR, *J. Magn. Reson.* 170 (2004) 113.
- [30] R.L. Kleinberg, Well logging, *Encyclopedia of NMR* 105 (1996) 4960.
- [31] R.L. Kleinberg, NMR Well Logging at Schlumberger, *Concepts Magn. Res.* 13 (6) (2001) 396.
- [32] C.A. Meriles, D. Sakellariou, H. Heise, A.J. Moule, A. Pines, Approach to high-resolution ex situ NMR spectroscopy, *Science* 293 (2001) 8.
- [33] D. Topgaard, R.W. Martin, D. Sakellariou, C. Meriles, A. Pines, “Shim Pulses” for NMR spectroscopy and imaging, *Proc. Natl. Acad. Sci. USA* 101 (51) (2004) 17576.
- [34] J. Perlo, V. Demas, F. Casanova, C. Meriles, J. Reimer, A. Pines, B. Blümich, High-resolution NMR spectroscopy with a portable single-sided sensor, *Science* 308 (2005) 1279.
- [35] J. Perlo, F. Casanova, B. Blümich, Ex situ NMR spectroscopy in highly homogeneous fields:  $^1\text{H}$  spectroscopy, *Science* 315 (2007) 1110.
- [36] N. Wu, L. Webb, T.L. Peck, J. Sweedler, Online NMR detection of amino-acids and peptides in Microbe-LC, *Anal. Chem.* 67 (18) (1995) 3101.
- [37] D.L. Olson, T.L. Peck, A.G. Webb, R. Magin, J.V. Sweedler, High resolution microcoil H-1 NMR for mass-limited, nanoliter-volume samples, *Science* 270 (1995) 1967.
- [38] T.L. Peck, R.L. Magen, P.C. Lauterbur, Design and analysis of microcoils for NMR microscopy, *J. Magn. Reson. B* 108 (1995) 114.
- [39] J.A. Rogers, R.J. Jackman, G.M. Whitesides, D.L. Olson, J.V. Sweedler, Using microcontact printing to fabricate microcoils on capillaries for high resolution proton nuclear magnetic resonance on nanoliter volumes, *Appl. Phys. Lett.* 70 (18) (1997) 2464.
- [40] J.A. Rogers, R.J. Jackman, G.M. Whitesides, Constructing single- and multiple-helical microcoil and characterizing their performance as components of microinductors and microelectromagnets, *J. Microelectromech. S.* 6 (3) (1997) 184.
- [41] R. Subramanian, A.G. Webb, Design of solenoidal microcoils for high-resolution C-13 NMR spectroscopy, *Anal. Chem.* 70 (13) (1998) 2454.
- [42] R. Subramanian, M.M. Lam, A.G. Webb, RF microcoil design for practical NMR of mass-limited samples, *J. Magn. Reson.* 33 (1998) 1967.
- [43] A.G. Webb, Radiofrequency microcoils in magnetic resonance, *Prog. Magn. Reson.* 31 (1997) 1.
- [44] M.E. Lacey, R. Subramanian, D.L. Olson, A.G. Webb, J.V. Sweedler, High-resolution NMR spectroscopy of sample volumes from 1 nL to 10  $\mu\text{L}$ , *Chem. Rev.* 99 (1999) 3133.
- [45] D.A. Seeber, J.H. Hoftiezer, W.B. Daniel, M.A. Rutgers, C.H. Pennington, Triaxial magnetic field gradient system for microcoil magnetic resonance imaging, *Rev. Sci. Instrum.* 71 (2000) 4263.
- [46] K.R. Minard, R.A. Wind, Solenoidal microcoil design. Part I: Optimizing RF homogeneity and coil dimensions, *Concepts Magn. Reson. B* 13 (2001) 128.
- [47] K.R. Minard, R.A. Wind, Solenoidal microcoil design. Part II: Optimizing winding parameters for maximum signal-to-noise performance, *Concepts Magn. Reson. B* 13 (2001) 190.
- [48] V. Malba, R. Maxwell, L.B. Evans, A.F. Bernhardt, M. Cosman, K. Yan, Laser-lathe lithography—a novel method for manufacturing nuclear magnetic resonance microcoils, *Biomed. Microdevices* 5 (2003) 21.
- [49] D.D. Jackson, C. Aracne-Ruddle, V. Malba, S.T. Weir, S.A. Catledge, Y.K. Vohra, Magnetic susceptibility measurements at high pressure using designer diamond anvils, *Rev. Sci. Instrum.* 74 (2003) 2467.
- [50] L.O. Sillerud, A.F. McDowell, N.L. Adolphi, R.E. Serda, D.P. Adams, M.J. Vasile, T. Alan,  $^1\text{H}$  NMR Detection of superparamagnetic nanoparticles at 1 T using a microcoil and novel tuning circuit, *J. Magn. Reson.* 181 (2006) 181.
- [51] V. Demas, J.L. Herberg, R.S. Maxwell, A.F. Bernhardt, V. Malba, S. Yerkes, R.C. Moreno, Electronic characterizations of lithographically patterned microcoils for high sensitivity NMR, in preparation.
- [52] V. Demas, Ex situ NMR: single sided and portable magnetic resonance sensors, PhD Thesis, UC, Berkeley (2006).
- [53] D.L. Hoult, R.E. Richards, Signal-to-noise ratio of nuclear magnetic resonance experiment, *J. Magn. Reson.* 24 (1976) 71.
- [54] Technology for magnetic resonance company website retrieved April 4, 2007, <<http://tecmag.com/>>.
- [55] Portable NMR, Magritek company website, Retrieved April 4, 2007, <<http://www.magritek.com/portable.html>>.
- [56] P. Prado, A. Bussandri, V. Demas, J. Franck, A. Pines, A portable system for ex-situ NMR, in preparation.
- [57] Mobile Ex-Situ Project in Pines Lab website, Retrieved April 4, 2007, <<http://waugh.cchem.berkeley.edu/research/index.php?rescat=8>>.
- [58] K. Halbach, Physical and optical properties of rare earth cobalt magnets, *Nucl. Instrum. Methods* 187 (1981) 109.
- [59] H. Raich, P. Blümli, Design and construction of a dipolar Halbach array with a homogeneous field from identical bar magnets: NMR Mandhalas, *Concepts Magn. Reson. B* 23 (1) (2004) 16.
- [60] G. Moresi, R. Magin, Miniature permanent magnet for table-top NMR, *Concepts Magn. Reson. B* 19 (1) (2003) 35.
- [61] A.E. Marble, I.V. Mastikhin, B.G. Colpitts, et al., A constant gradient unilateral magnet for near-surface MRI profiling, *J. Magn. Reson.* 183 (2) (2006) 228.
- [62] J. Paulsen, L. Bouchard, J. Franck, V. Demas, Least squares magnetic-field decomposition for optimal NMR magnet design, *IEEE* (2007), submitted for publication.
- [63] Aster Enterprises Inc., MRI and NMR Permanent Magnets Retrieved April 4, 2007, <<http://asterenterprises.com/MRI.htmlwau>>.
- [64] A.G. Goloshevsky, J.H. Walton, M.V. Shutov, J.S. de Ropp, S.D. Collins, M.J. McCarthy, Development of low field nuclear magnetic resonance microcoils, *Rev. Sci. Instrum.* 76 (2005), 24101-1.