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Communication

Optimal electric fields for different sample shapes in high resolution NMR spectroscopy

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Abstract

For many applications, reducing sample resistance, rather than increasing probe Q or filling factor, is the only way to further improve the signal-to-noise ratio of cryogenically cooled NMR probes. In this paper, bounds are calculated for the minimum sample resistance that can be achieved for various sample geometries. The sample resistance of 100 mM NaCl in H_2O in 5 mm sample tubes was measured on a 600 MHz cold probe to be within 14% of the optimum value. The minimum sample resistance can however be lowered by altering the tube cross section. Rectangular tubes oriented with the long axis along the RF magnetic field are particularly favourable.

Keywords: NMR; Sensitivity; Electric field; Sample tube; Signal-to-noise ratio

1. Introduction

The signal-to-noise ratio in NMR may be written as [1–3]

$$\frac{S}{N} \propto \frac{M_0 B_1}{\sqrt{(T_a + T_s)P_s + (T_a + T_c)P_c}}, \quad (1)$$

where M_0 is the spin magnetization, P_c is the RF power absorbed by the coil during transmit at fixed RF magnetic field B_1, and P_s is the RF power absorbed by the sample. P_s is proportional to to sample resistance, R_s, and P_c is proportional to coil resistance, R_c. T_a is the noise temperature of the preamplifier, which is of the order 15 K for a cryogenic probe, T_s is the temperature of the sample, typically 298 K, and T_c is the temperature of the coil, typically 25 K. The relative importance of coil resistance, R_c, and sample resistance, R_s, is determined by the ratio α

$$\alpha = \frac{T_s + T_a}{T_c + T_a} \approx 8. \quad (2)$$

Most of the improvement in signal-to-noise ratio through better probe technology has focussed on reducing T_a, T_c, and P_c. Reducing P_c is equivalent to increasing the product $Q\eta$, where Q is the probe quality factor (without a sample), and η is the filling factor. The ratio P_s/P_c can be measured by comparing the Q of an empty probe to the Q of a probe tuned and matched with the sample present. In a Varian 600 MHz HCN cold probe P_s/P_c was measured to be 0.74 for 100 mM NaCl in H_2O in a 5 mm tube, which is often considered a moderately lossy sample. (In this case the empty probe Q was 1205 and the loaded probe Q was 694.) With the temperature factor $\alpha \approx 8$, the P_s term in Eq. (1) is about six times the size of the P_c term. P_s/P_c was measured to be 0.10 for D_2O, so that the P_s term in Eq. (1) is 0.8 times the P_c term even for this low loss sample. It is clear that further reduction in T_a, T_c, and P_c will bring diminishing or no return for many samples of practical interest unless P_s can also be reduced.

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While P_s has not been the primary focus in high resolution probe design in recent years, it has been of great importance in the imaging community, where it dominates over P_c due to the much greater sample size [4,5]. A general and elegant approach for calculating the limits to signal-to-noise ratio numerically in the imaging context is given in [6]. The point of this paper is to consider fundamental limits on the term P_s that can be calculated analytically for the sample geometries and RF magnetic fields that are relevant in the context of high resolution liquid state NMR.

The power dissipated in the sample, P_s, is given by

$$P_s = \frac{1}{2}\int \sigma E^2 \, dV. \tag{3}$$

Here the integral is over the volume of the sample, E is the peak RF electric field, and σ is the RF conductivity of the sample including dielectric loss. The problem addressed here is what electric field E minimizes P_s subject to the constraint that there exists the uniform RF magnetic field in the sample

$$\mathbf{B} = B_1 e^{i\omega_0 t}\hat{\mathbf{x}} \tag{4}$$

that is necessary for good quality NMR. (Here $\hat{\mathbf{x}}$ is a unit vector in the x direction.) How to actually design a coil to produce the optimal electric field is outside the scope of this paper. Rather, the intention is to discuss what coil performance is possible.

The concept that Eq. (4) applies throughout the volume of integration in Eq. (3) is an excellent approximation if the sample is physically constrained to be within the region of high homogeneity RF magnetic field. In high resolution NMR this can be accomplished through the use of susceptibility compensated plugs inserted into an NMR tube, or susceptibility compensated glass sample tubes and plungers such as manufactured by Shigemi. In situations where the sample extends axially out of the RF "window" of the coil it is assumed that the transition region where the RF magnetic field drops to zero is sufficiently abrupt that it can be neglected. This transition region then forms part of the boundary of the volume of integration in Eq. (3). Such an abrupt drop of magnetic RF field at the edges of the window represents an ideal coil for NMR since RF pulse widths are well defined and solvent suppression works well. In addition note that the uniform RF magnetic field in Eq. (4) is only possible when the wavelength and skin depth in the sample are sufficiently large compared to the sample size. For typical liquids NMR samples this is a good approximation. A final point about Eq. (4) is that it is assumed that a circularly polarized RF magnetic field is not produced, for example using a birdcage coil [7].

Substituting the magnetic field from Eq. (4) into Faraday's Law

$$\nabla \times \mathbf{E} = -i\omega_0 \mathbf{B} \tag{5}$$

and integrating, we obtain

$$\mathbf{E} = -iB_1\omega_0 e^{i\omega_0 t}(y\hat{\mathbf{z}} + \nabla\phi), \tag{6}$$

where ϕ is an arbitrary scalar function of space, and $\hat{\mathbf{z}}$ is a unit vector in the z direction. Within the homogeneous sample volume, the electric field must satisfy $\nabla.\mathbf{E} = 0$, from which we find ϕ must satisfy the Laplace equation $\nabla^2\phi = 0$.

The problem of finding the optimal electric field for NMR thus reduces to finding the harmonic function ϕ which minimizes the functional $P_s \propto \int (y\hat{\mathbf{z}} + \nabla\phi)^2 \, dV$. Following traditional practice in calculus of variations, consider the variation in P_s caused by a small variation in ϕ:

$$dP_s \propto \int (y\hat{\mathbf{z}} + \nabla\phi).\nabla\delta\phi \, dV, \tag{7}$$

$$\propto \oint (y\hat{\mathbf{z}} + \nabla\phi).\hat{\mathbf{n}}\delta\phi \, dS, \tag{8}$$

where $\hat{\mathbf{n}}$ is a unit vector normal to the surface bounding the sample volume. Setting the variation in P_s to zero for all $\delta\phi$, we find that the optimal electric field satisfies

$$(y\hat{\mathbf{z}} + \nabla\phi).\hat{\mathbf{n}} = 0. \tag{9}$$

The problem is restated as finding the solution, ϕ, to the Laplace equation, subject to the boundary condition given by Eq. (9). Once this solution is found the power may be conveniently calculated from the formula

$$P_s = \frac{1}{2}\sigma B_1^2\omega_0^2 \int (y\hat{\mathbf{z}} + \nabla\phi)^2 \, dV = \frac{1}{2}\sigma B_1^2\omega_0^2 \left[\int y^2 \, dV + \oint y\phi\hat{\mathbf{z}}.\hat{\mathbf{n}} \, dS\right]. \tag{10}$$

Consider cylindrical samples of length L, with circular cross section radius r_0, where the cylinder is coaxial with the static field and z axis, and the RF magnetic field is transverse to the cylinder along the x axis, and the origin of coordinates is at the center of the cylinder. The optimal electric field is given by Eq. (6) where the function ϕ which satisfies the boundary condition Eq. (9) may be found by standard methods [8]:

$$\phi = -\sum_{n=1,2,3..} \frac{2r_0^2 \sin\theta J_1(j'_{1,n}r/r_0)\sinh(j'_{1,n}z/r_0)}{j'_{1,n}(j'^2_{1,n} - 1)\cosh(j'_{1,n}L/2r_0)J_1(j'_{1,n})}, \tag{11}$$

where standard cylindrical polar coordinates have been used, J_1 is a cylindrical Bessel function and $j'_{1,n}$ is the nth zero of its derivative employing the conventions of [9]. The minimum dissipated power is

$$P_s = \frac{1}{8}\sigma B_1^2\omega_0^2\pi r_0^4 L\left[1 - \frac{16r_0}{L}\sum_{n=1,2,3..}\frac{\tanh(j'_{1,n}L/2r_0)}{j'^3_{1,n}(j'^2_{1,n} - 1)}\right]. \tag{12}$$

It is straightforward to calculate this optimal absorbed power for typical experimental parameters remembering that with proton NMR B_1 can be calculated from $B_1 = 2/(42.6\tau_{360})$, where τ_{360} is the time for a 360° pulse in microseconds and B_1 is the peak linearly polarized RF magnetic field in tesla. For a 5 mm NMR tube at 600 MHz with $L = 18$ mm, r_0 is 2.1 mm, and 100 mM NaCl in H_2O (with $\sigma \approx 1.1\ \mathrm{S\,m^{-1}}$ at 600 MHz at 298 K according to [10,11]), and with a 20 μs 360° pulse, the minimum possible dissipated power is found to be 10.2 W.

Measurements were made of the total power input at the base of the 600 MHz cold probe mentioned earlier. A 20 μs 360° pulse, with a sample of 100 mM NaCl in H_2O, in a 5 mm tube manufactured by Shigemi, with the window constrained to 18 mm, required 31.0 W. Network analyzer measurements indicate that 13% of this power is absorbed in various connectors in the probe before reaching the high Q probe circuit. Q measurements with and without the sample indicate that of the remaining power, 42.4% or 11.6 W is absorbed by the sample. This is only 14% more than the fundamental minimum imposed by Maxwell's equations. Inspection of Eq. (1) shows that even if a "perfect" (albeit non-quadrature drive) probe could be built such that both the sample resistance was reduced to the fundamental minimum and the coil resistance term, $(T_c + T_a)P_c$, was effectively zero (using for example superconducting coils at mK temperatures), the signal-to-noise ratio on 100 mM NaCl would only be improved by 15% over the existing probe used for measurement.

It is apparent that the signal-to-noise ratio bottle neck is the term P_s which is directly linked to the shape of the sample. Inspection of Eq. (12) shows that a simple approach is to reduce the size of the sample. The minimal P_s is an increasing function of L and r_0, becoming proportional to Lr_0^4 when $L \gg r_0$. Reducing r_0, for example by using 3 mm sample tubes, is a very effective way to reduce P_s and increase the signal-to-noise ratio, as long as M_0 remains fixed, i.e., the spin concentration must be increased. However, for many biological samples, the sample concentration, c, is already maximized to the highest practical level by the spectroscopist, in which case in Eq. (1) $M_0 = c\pi L r_0^2$. In this situation both M_0 and P_s decrease with decreasing r_0. The net effect is that signal-to-noise can be almost independent of r_0, when the P_s term dominates the P_c term in Eq. (1). However, as r_0 decreases, eventually the P_c term becomes important, and the signal-to-noise ratio drops off.

An alternative is to use samples of more general shape than cylinders with circular cross section. For samples of length L in the z direction, large compared to the width in the x and y directions, then the $\nabla\phi$ term in Eq. (6) is a relatively small end effect correction, and the electric field is approximately proportional to the y coordinate. It follows that a disproportionate amount of P_s is dissipated in the regions of the sample at large y. It is therefore rational to consider samples with large extent in the x direction, along $\mathbf{B}_1$, and small extent along y. For this reason, take cylindrical samples again of length L, but now with rectangular cross section, instead of the circular cross section considered initially. As with the circular case, the cylinder is coaxial with the static field and z axis, and the RF magnetic field is transverse to the cylinder along the x axis. The rectangle which forms the cross section of the cylinder is of width b in the x direction and a in the y direction. The origin of coordinates is at the center of the cylinder. The optimal electric field is given by Eq. (6) where the function ϕ which satisfies the boundary condition Eq. (9) may be found by standard methods [8]:

$$\phi = -\sum_{n=1,3,5..} \frac{4a^2}{n^3\pi^3} \frac{\sinh(n\pi z/a)}{\cosh(n\pi L/2a)} \cos(n\pi x/a). \tag{13}$$

The minimum dissipated power is now

$$P_s = \frac{1}{24}\sigma B_1^2 \omega_0^2 a^3 bL \left[1 - \frac{192a}{L\pi^5} \sum_{n=1,3,5..} \frac{\tanh(n\pi L/2a)}{n^5}\right]. \tag{14}$$

The above equation shows that the minimum P_s can be made arbitrarily small, even at fixed sample volume, Lab, by making b large and a small (see Fig. 1). In cases where $L \gg a$, then the minimum P_s is proportional to $a^3 b$. If the P_s term dominates the P_c term in Eq. (1) (such as for 100 mM NaCl in H_2O in 5 mm circular tubes) then at fixed spin concentration c, $M_0 = cLab$ and the signal-to-noise ratio from Eq. (1) is proportional to $\sqrt{b/a}$. This is a remarkable result, since it implies that at fixed concentration the maximum possible signal-to-noise increases by reducing the sample size, a, in the y direction—even though this means using less sample material.

In conclusion sample losses are now a fundamental limit to the signal-to-noise ratio in high resolution NMR, for many practical applications. These limits have been calculated for cylindrical samples with circular and rectangular cross section. The results indicate that rectangular sample tubes offer potentially unlimited advantages over circular tubes. While cryogenically cooled probes have been the main motivation for this work, the results derived here apply equally well to traditional room temperature probes. The sample effect is weaker in room temperature probes, but can still be significant.

It is worth noting that in EPR and ESR of lossy samples such a strategy has already been pursued, although the coil geometry is quite different [12]. An alternative approach is a birdcage type probe that produces circularly polarized RF magnetic field. This offers a potential signal-to-noise ratio improvement for lossy samples over current technology, but this is limited to a factor of $\sqrt{2}$.

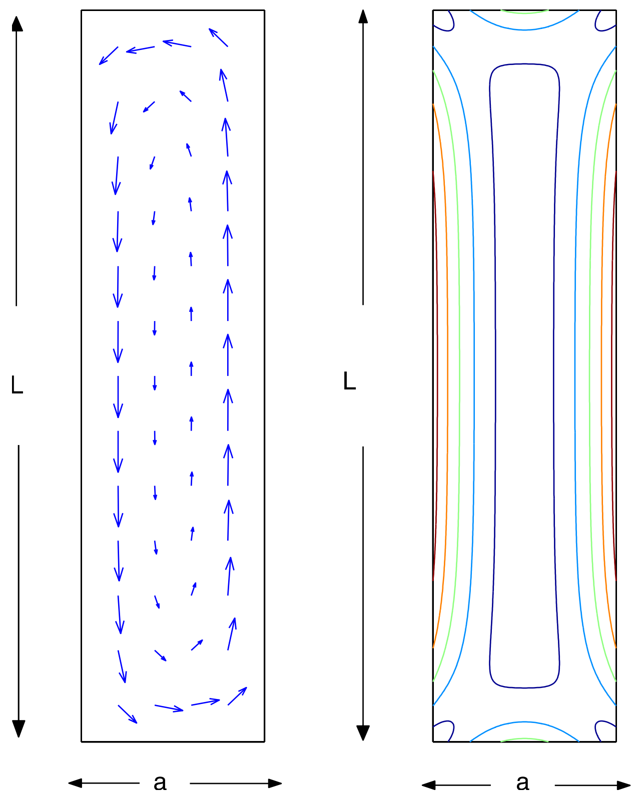

Fig. 1. Plots in the y–z plane of the optimal electric field and dissipated power in the case of a sample tube of length $L = 18$ in the z direction, and width $a = 4.2$ in the y direction. The tube has rectangular cross section so the fields are calculated from Eqs. (6) and (13). The left plot shows the electric field which is tangential to the edge of the sample volume. Away from the ends of the tube the field strength, denoted by the size of the arrow, is approximately proportional to the y coordinate. The right plot is a contour plot of dissipated power or E^2. The contour lines are at equally spaced levels of E^2 and clearly show the "hot" regions of high power dissipation at large positive and negative y coordinate.

This approach is now standard in MRI where changing the sample shape is not an option.

Finally, it may be of interest to consider the optimal electric field derived in this paper in light of Helmholtz's theorem. Helmholtz's theorem states that any vector field can be written as the sum of the curl of another vector field and the gradient of a separate scalar field $\mathbf{F} = \nabla \times \mathbf{G} + \nabla H$. The term ∇H is sometimes called the conservative part of the field $\mathbf{F}$ and has zero curl, and the term $\nabla \times \mathbf{G}$ is sometimes called the non-conservative part of the field $\mathbf{F}$ and has zero divergence. Because the electric field in this paper has a non-zero curl, and a zero divergence, it is clear that it can be written purely as the curl of some other vector field, and can be considered pure non-conservative. Unfortunately this choice is somewhat arbitrary.

While the Helmholtz decomposition can be shown to be unique for fields defined everywhere in space, the decomposition is not unique when the field is only defined for sub-regions of space such as the NMR sample space considered in this paper. The reason for this non-uniqueness is that for sub-regions of space there exist non-trivial fields with both zero divergence and zero curl which can be included in either term of the Helmholtz decomposition. An alternative Helmholtz decomposition of the electric field to pure non-conservative is of course given by Eq. (6), which makes the field look like both conservative and non-conservative terms are present.

To truly know how whether the electric field in the sample space contains a conservative part, knowledge of the geometry of the coil and circuit that make the field is required. Then the electric field is known everywhere in space, not just in the sample region.

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