The Limits of NMR Imaging

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Abstract

The limits of isotropic spatial resolution in NMR imaging are estimated starting from an explicit formula for S/N ratio. It is shown that the limit is essentially imposed by the sensitivity of the NMR experiment. The required acquisition time is of course also a factor, but since it increases with the 7th power of resolution, changing acquisition time from quite short to excessively long will cause only a relatively modest increase of the latter. For 1H NMR microscopy (samples of the order of 1cm in diameter), there is an "impossible" barrier of about 40 microns even at high fields (e.g., 300 MHz) for samples rich in hydrogen. On the other hand, there is no particularly sharp degradation of resolution when going to lower fields (e.g., 10 MHz), or hydrogen-poor samples, or some of the heteronuclei (e.g., 23Na). Consequently, NMR microscopy applications requiring isotropic voxel sizes of 100-500 microns have good chances of success even at surprisingly low fields/concentrations.

Keywords: MRI, NMR imaging, Sensitivity, Resolution

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● *MRI in Porous Media*

THE LIMITS OF NMR IMAGING

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The limits of isotropic spatial resolution in NMR imaging are estimated starting from an explicit formula for *S/N* ratios. It is shown that the limit is essentially imposed by the sensitivity of the NMR experiment. The required acquisition time is of course also a factor, but since it increases with the 7th power of resolution, changing acquisition time from quite short to excessively long will cause only a relatively modest increase of the latter. For ^{1}H NMR microscopy (samples of the order of 1 cm in diameter), there is an "impassable" barrier of about 40 microns even at high-fields (e.g., 300 MHz) for samples very rich in hydrogen. On the other hand, there is no particularly sharp degradation of resolution when going to lower fields (e.g., 10 MHz), or hydrogen-poor samples, or some of the heteronuclei (e.g., ^{23}Na). Consequently, NMR microscopy applications requiring isotropic voxel sizes of 100–500 microns have good chances of success even at surprisingly low fields/concentrations.

Keywords: **Imaging; Microscopy; Sensitivity; Resolution.**

INTRODUCTION

Spatial resolution in MRI is an important parameter for both *in vivo* imaging and *in vitro* NMR microscopy. Since imaging is currently done with different nuclei and at different field strengths, we need a generic procedure for estimating its limits. The principal barrier in NMR imaging is the signal to noise ratio *S/N* achievable within a reasonable time; virtually all other limitations are linked to the *S/N*. The problem therefore splits in two simpler tasks: Given basic technical parameters of a system, (a) calculate its *S/N* ratio, and (b) estimate the limit of interest (e.g., the spatial resolution achievable in a given time).

NMR SENSITIVITY

Many studies have been dedicated to the estimation of the *S/N* ratio.[1–11] The resulting formulae differ somewhat according to the adopted point of view. In particular, quantities like the coil quality factor Q, the matching impedance R, the equivalent coil and sample loss resistances, the coil geometric factors and the coil inductance form a set of interdependent parameters which can appear in many equivalent combinations. The formula used in this study for the *S/N* ratio at the beginning of an FID is (the derivation will be presented elsewhere):

$$S_{n0} = \sqrt{< S^2 >/< n^2 >} \quad (1)$$

where

$$< S^2 > = < e^2 > Q^2 M_f \quad (1a)$$

$$< e^2 > = (\mu_0 \eta \omega M_0 / D)^2 / 2$$

$$M_0 = N_{nuc} \, [I(I+1)\hbar^2 g^2 B_0]/(3kT_s).$$

$$< n^2 > = n_t^2 > + < n_{ei}^2 > \quad (1b)$$

$$< n_t^2 > = 2kT_c B_w R$$

$$< n_{ei}^2 > = v_{ei}^2 > \cdot B_w$$

The input quantities in Eq. (1) are:

N_{nuc}: number of nuclei inside the sample coil,
I : nuclear spin of the observed nuclei,
g : gyromagnetic ratio of the observed nuclei,
B_0 : magnetic field strength,
μ_0 : magnetic susceptibility of the vacuum,
ω : resonance frequency (equal to gB_0),
T_s : sample temperature,

Table 1. Field and spectral width dependence of the achievable resolution

F_0 MHz	1	10	100	300
Q	300	150	100	50
η	10	5	2	1
M_f	.95	.9	.5	.3
S_w = 1 Hz				
Very easy:	535	196	91	77
Easy:	380	142	66	56
Difficult:	280	103	47	40
Crazy:	200	74	34	29
S_w = 100 Hz				
Very easy:	1035	380	175	150
Easy:	745	275	127	107
Difficult:	535	196	91	77
Crazy:	385	142	66	56

Water protons, coil diameter 1.2 cm, sample diameter 1 cm. For other parameters, see text.

Q : coil quality factor (loaded),
M_f : coil matching factor,
D : coil diameter,
η : coil shape-efficiency factor,
R : coil assembly matching impedance,
T_c : coil enclosure temperature,
B_w: receiver bandwidth,
ν_{ei} : equivalent input noise of the preamp for 1 Hz bandwidth.

The intermediate, derived quantities are:

M_0 : nuclear equilibrium magnetization,
$< e^2 >$: rms of the induced electromotive force;
$< S^2 >$: rms of the signal signal at the preamplifier input,
$< n_{ei}^2 >$: rms of the equivalent input noise of the preamplifier,
$< n_t^2 >$: rms of the thermal noise at the preamplifier input,
$< n^2 >$: rms of the total noise perceived by the preamplifier.

While some of the input quantities are known with the utmost precision, several of them require further explanation. In particular, this regards Q, M_f, and η.

The quality factor Q of the coil is defined as the ratio between its impedance ωL (L being its inductance) and its equivalent loss resistance r, both intended for a loaded coil at the operating frequency. The inductance of a coil depends only upon its geometry and can be determined quite easily. The loss resistance, on the other hand, is much more difficult to estimate. It is a sum of two parts: the loss resistance r_L of the unloaded coil and the resistance r_s due to the losses within the sample. r_L depends upon the coil material, wire diameter, winding geometry, insulation material and operating frequency; phenomena such as skin effect are involved in its calculation. The sample losses r_s depend upon the sample volume and its absorption efficiency at the resonance frequency (dielectric and conductive losses). In general, r_s increases quite sharply with frequency.

Making an *a priori* estimate of Q is, therefore, a very difficult task. What we can do, however, is to list a few empirical rules. First of all, a well-constructed coil exhibits a substantially lower Q when loaded than empty. This indicates that sample losses r_s are dominant and r_L plays a minor role. In order to maximize Q, one should increase the inductance L as much as possible (e.g., by increasing the number of coil turns). However, this decreases rapidly the self-resonant frequency of the coil (given by its inductance and parasitive capacity) until the limit is reached where the latter becomes equal to the operating frequency. As a result, for any basic coil design, the maximum inductance achievable in practice decreases with frequency. This, combined with the rapid increase of r_s with frequency, leads to the empirical fact that Q factors of loaded optimized coils tend to decrease with frequency. Typical values expected for optimized devices are listed in Table 1.

The coil matching factor M_f is defined as $M_f = (R/\omega L)/Q$, where R is the matching impedance (usually 50 Ohm). Whenever a resonant LC circuit is matched to behave as an ohmic load of a given value, a compromise is made which involves a deviation from its free-running resonance frequency and the insertion of a suitable passive component. The resulting degradation in performance is expressed by M_f. The expected values of M_f tend to decrease from the maximum of 1 at low frequencies to a fraction of 1 at high frequencies (see Table 1).

It should be noted that Q and M_f appear in Eq. (1a), only in the product $Q^2 M_f$ which can also be expressed as R/r. If r is dominated by sample losses, this ratio is practically independent of the coil parameters. Quite different coils will therefore give comparable results when used in a matched circuit at the same operating frequency. The inherent variations in loaded Q are to a large extent offset by variations in M_f. The reason why we keep Q and M_f separate is that one can operate in the unmatched condition. This complicates the coupling between the coil and the preamplifier (fixed cable lengths, nonstandard specifications) but ensures effectively $M_f = 1$.

The shape-efficiency factor η is related to the geometry of the coil after scaling it to a unit diameter. The exact definition involves the magnetic flux Φ through the coil surface, due to a unit magnetic dipole located at the coil center. In our formula, η is defined as Φ/Φ_0, where Φ_0 is the same quantity for a perfectly flat (collapsed) two-turn coil. For any given coil geometry, η can be exactly calculated. Typical values are of the order of 0.7 for a Helmholtz coil, 1 for a bird-cage or a 3 to 5-turn solenoid, and proportionally more for many-turn solenoids. Due to the self-resonance limitations, the η factors for optimal coils tend to decrease with frequency from quite large values (hundreds in the kilohertz range) to about one (or even somewhat less) at high frequencies (see Table 1 for an educated guess).

Equation (1) can be easily modified for S/N estimates in high-resolution spectroscopy. Such a modified version has been tested against several dozen specifications given by two major manufacturers of spectrometers for a number of different nuclei, operating frequencies and sample diameters. A reasonable agreement has been found provided that the factors Q, M_f, and η follow the general pattern given in Table 1 and v_{ei} (the equivalent input noise of the preamplifiers) is of the order of 4–6 $nV/\sqrt{Hz}$. Comforted by this fact, let us proceed to the implications for NMR imaging.

INTERFERENCE

Both in NMR spectroscopy and NMR imaging we are faced with the situation where the FID contains a set of components with different frequencies. Since the interference between the individual components leads to a progressive destruction of the FID, we might have legitimate doubts whether the individual components can be recovered with the same signal to noise ratio as though each of them were the only one present.

It can be shown quite easily that both the initial FID amplitude (i.e., the integral of the absorption spectrum) and the total signal energy (integral of the power spectrum) are additive. Since the noise power is fixed, this garantees that the S/N ratio of the individual components, after having separated them by means of a suitable algorithm, is exactly the same as if each of them were the only one present. More specifically, in the case of NMR imaging, the S/N intensity for a single voxel, referred to a single pulse, equals the integral signal-to-noise ratio S_{n0} of the hypothetical FID corresponding to the same voxel if it were isolated.

It makes no difference whether to recover the image we have to use 1-, 2-, or 3-D Fourier transform or a projection reconstruction algorithm. If the complete algorithm forces us to use N_p pulses, then each component will come out with its signal-to-noise ratio enhanced by $\sqrt{N_p}$.

MRI RESOLUTION LIMITS

Let us now assume that the characteristic linear dimension of the sample is L (assume, e.g., that the sample is a cube). If linear resolution l_r is required, we have $N = L/l_r$ linear divisions, and therefore N^3 voxels, each with a volume of l_r^3.

To generate a 2-D image with the same resolution, we must find means to selectively excite a slice of thickness l_r and then apply the readout gradient; the procedure must be repeated N times for each scan. For a 3-D image, there is no need for selective excitation, but we must apply N^2 pulses for each scan.

Example: If L = 1 cm and l = .1 mm, we have N = 100, which means 10^6 voxels with a volume of 1 nanoliter each. In order to construct a 3-D map we must apply 10,000 pulses. In one such complete scan we recover our voxels with a signal-to-noise ratio corresponding to 100 times the S/N ratio of an isolated sample of 1 nanoliter.

Another factor to consider is the gradients to be applied. Suppose that the spectrum of the sample in the absence of a gradient has a width of S_w (Hz), due to any of the following phenomena:

- Transversal relaxation (natural line width).
- Magnetic field inhomogeneity.
- Chemical shifts spread.
- Magnetic susceptibility variations across the sample.

In all cases the final effect is a defocusing, since the spectral dispersion masquerades as a spacial dispersion. In order to recover an undistorted image, the applied gradients should cause a frequency dispersion from voxel to voxel at least as large as S_w. The gradient therefore should be at least

$$G_{min} = (2\pi S_w/g)/l_r \qquad (2)$$

The total spread of frequencies, and therefore the

Table 2. Dependence of the minimum number of pulses on the resolution

Resolution (microns)	Number of pulses needed for $S/N = 4$	Gradient (Gauss/cm)	Bandwidth (Hz)
30	74,993,591	23.488	100,000
40	10,010,436	17.616	75,000
50	2,099,341	14.093	60,000
60	585,888	11.744	50,000
70	199,153	10.066	42,857
80	78,207	8.808	37,500
90	34,291	7.829	33,333
100	16,402	7.046	30,000
110	8417	6.406	27,273
120	4578	5.872	25,000
130	2614	5.420	23,077
140	1556	5.033	21,429
150	960	4.698	20,000
160	611	4.404	18,750
170	400	4.145	17,647
180	268	3.915	16,667
190	184	3.709	15,789
200	129	3.523	15,000

The required number of grey levels per voxel is 4. Minimum gradient strength and receiver bandwidth are also listed, assuming $S_w = 3$ ppm. Water sample at 100 MHz, coil diameter 1.2 cm, $Q = 100$, $= 2$, $M_f = 0.5$, preamp $v_{ei} = 4\ \mathrm{nV}/\sqrt{Hz}.Q$, sample diameter 1.0 cm.

minimum receiver bandwidth, will then be

$$B_w = N\,S_w \tag{3}$$

Upon progressive increase of resolution, the increase of the required gradients and of the receiver bandwidth eventually leads to a technological limit independently of the acquisition time considerations.

The increasing receiver bandwidth contributes to the already sharp decrease of the single-voxel S/N ratio. In practice, a reduction of l_r by a factor of k decreases the S/N ratio by a factor of $k^{7/2}$ (k^3 due to the volume reduction and $k^{1/2}$ due to the bandwidth increase). If the image quality (S/N ratio per voxel) is to be maintained, this implies increasing the total number of pulses by the factor k^7 (7th power!). This dramatic increase in acquisition time eventually stops the quest for higher resolution.

One can carry the above consideration a step further. The factor of k in resolution will increase the number of pulses required for a complete 2-D sweep by k, while the number of pulses required for a 3-D scan will increase by k^2. Since, in order to obtain a given image quality, the number of pulses required by the S/N considerations increases as k^7, it is clear that at some (early) point the latter limit will become dominant and there will be no advantage (in terms of acquisition time) in acquiring 2-D images rather than the conceptually simpler 3-D images.

EXAMPLES AND CONCLUSIONS

Table 2 represents a "practical" example. The chosen parameters correspond to a water sample of modest size (1 cm) measured at room temperature at 100 MHz. The table should be inspected as follows: given a required resolution, what is the minimum number of pulses required to achieve a pre-defined number of grey levels (in our case 4). The 7th power dependence of the required number of pulses is nicely illustrated. So is the fact that — even for such a "strong" sample — it is hardly feasible to achieve a resolution better than 80 microns in a reasonable time. The difference between 2-D and 3-D acquisition times disappears below 100 microns.

Like Table 2, the results listed in Tables 1, 3, and 4 presume maximum proton density of pure water and image quality sufficient to assign 4 levels of grey to each cubical voxel. Rather than reporting the required number of pulses, however, the resolutions corresponding to 100, 1000, 10,000, and 100,000 pulses are listed and labelled as "very easy," "easy," "difficult," and "crazy," respectively.

Table 3. Field and spectral width dependence of the achievable resolution

F_0 MHz	1	10	100	300
Q	300	150	100	50
η	10	5	2	1
M_f	.95	.9	.5	.3
S_w = 100 Hz				
Very easy:	2750	1030	480	405
Easy:	2000	730	340	270
Difficult:	1440	530	240	210
Crazy:	1040	380	180	150
S_w = 10 kHz				
Very easy:	5350	1990	910	770
Easy:	3850	1430	660	560
Difficult:	2750	1030	480	405
Crazy:	2000	730	340	270

Water protons, coil diameter 12 cm, sample diameter 10 cm. For other parameters, see text.

Table 1 reports the resolution limits for a sample of 1 cm diameter at different field strengths and for two different spectral widths. The field dependence is quite interesting since intuitively one expets a qualitative jump in resolution when going from 10 MHz to 300 MHz; the actual result is not even a factor of 3! Even at 1 MHz one can reach a surprisingly high resolution of some 280 microns, corresponding to 3-D images with over 45,000 resolved voxels. Likewise, the spectral spread has a relatively modest impact: a bit less than a factor of 2 upon a 100-fold increase of S_w (7th root dependence). Once again we see that there is a kind of "wall" somewhere around 50 microns, even for quite special samples measured at 300 MHz.

Table 3 regards exactly the same conditions as Table 1, except for sample size (10 cm instead of 1) and one of the two assumed spectral widths. The general trends found in Table 1 are confirmed. Moreover, while the absolute resolution decreases with sample size (it can be shown that voxel size increases with the 3/7th power), the total number of voxels (relative resolution) increases (9/7th power).

In Table 4 we explore the impact of possible future improvements in the coil and preamplifier technology. The conditions assumed for the first column correspond exactly to those of Table 2. In the second column we assume a remarkable improvement in both the coil shape-efficiency factor (× 2.5) and the matching factor (× 2). The third column corresponds to an even more remarkable improvement in the preamp (× 40) and receiver (× 2) specifications. Finally, the last column reports the combined effect of all such improvements, which amounts roughly to a fator of 3. This indicates that significant progress due to advances in technology

Table 4. Effects of improvements in coil and/or detector

F_0 MHz	100	100	100	100
Q	100	200	100	200
η	2	5	2	5
M_f	.5	1	.5	1
v_{ei} (nV/Hz)	4	4	.1	.1
NF (dB)	1	1	.5	.5
Very easy:	205	118	120	68
Easy:	147	85	86	50
Difficult:	106	61	63	36
Crazy:	77	44	45	26

Water protons, coil diameter 1.2 cm, sample diameter 1 cm, S_w = 3 ppm. For other parameters, see text.

Table 5. Imaging of ^{23}Na at 1% w/w, assuming 20 Hz linewidth

F_0 MHz	.26	2.6	26	78
Q	300	300	200	120
η	30	10	5	3
M_f	.99	.95	.9	.6
Very easy:	> 5000	1875	695	525
Easy:	3655	1350	500	375
Difficult:	2630	970	360	270
Crazy:	1890	700	255	195

Coil diameter 1.2 cm, sample diameter 1 cm. The tolerable number of pulses is considered to be 10 times higher than for protons due to much shorter T_1. The field strengths correspond to 1, 10, 100, and 300 MHz for protons. Other parameters are the same as in the preceeding cases.

is possible. On the other hand, such progress will be quite slow — barring completely new approaches, revolutions are unlikely.

The 7th power between the required number of scans and the resolution has a pronounced levelling effect on achievable resolutions. Any variation in sensitivity is flattened when converted to voxel size. This makes it unlikely that resolutions below 40 microns can be achieved, even for watery samples at the highest fields. At the same time, however, it implies that less demanding resolutions can be reached at surprisingly low fields or at quite low concentrations. Likewise, imaging nuclei other than protons is by no means out of question.

Table 5 demonstrates the possibility of ^{23}Na microscopy of 1 cm samples at reasonably low concentrations (1%). The achievable resolution (~0.4 mm) appears to be quite appealing for a number of applications even at 26 MHz (field strength corresponding to 100 MHz for protons).

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