

A Multiple-Probe Strategy for Ultra-High-Field Nuclear Magnetic Resonance Spectroscopy*

ERIC OLDFIELD

Department of Chemistry, University of Illinois at Urbana–Champaign, 505 South Mathews Avenue, Urbana, Illinois 61801

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During the past 40 years, the price of a commercial nuclear magnetic resonance spectrometer has been fairly predictable, $\sim \$1000/\text{MHz}$ being a good rule of thumb. For example, the earliest commercial instrument, the Varian HR-30, cost $\sim \$30,000$ for a 30 MHz instrument in 1952 (1), an HR-220 cost $\sim \$200,000$, and a Bruker HX-360 cost $\sim \$300,000$, and currently a 500 MHz spectrometer costs $\sim \$500,000$. However, in the past 2 or 3 years, spectrometer prices have escalated rapidly. A 600 MHz NMR costs $\sim \$1500/\text{MHz}$ and a 750 MHz $\sim \$4000/\text{MHz}$, and 1000 MHz spectrometers under construction have estimated costs of $> \$5000/\text{MHz}$ (2). The breakdown of the $\$1\text{K}/\text{MHz}$ “rule” comes almost exclusively from the magnet component of the spectrometer, since the main changes in console design, higher frequency synthesizers, mixers, and amplifiers, are not particularly expensive. These price trends are shown in Fig. 1 as a function of time. There is a simple exponential law behavior for state-of-the-art magnet and console price as a function of time, and in ~ 1990 , the two exponential law curves cross. This corresponds to $\sim \$500\text{K}$ costs for both magnet and console, for a 600 MHz spectrometer. However, as can also be seen from Fig. 1, beginning with 600 MHz spectrometers, a new type of exponential law behavior begins to be seen for magnet prices, which now overwhelmingly dominate the cost of complete ultra-high-field NMR spectrometers.

Now, in many NMR laboratories, there are a wide variety of experiments being carried out which benefit from high-field NMR. For example, solid-state studies of inorganic and geochemical systems are often faced with sensitivity problems since linewidths are broad, and high-field NMR helps, both because of basic sensitivity gains and because the linewidths (in ppm) of most nonintegral spin quadrupolar nuclei decrease quadratically with applied field strength (3, 4). In the biological area, the increased resolving power and sensitivity of ultra-high-field NMR are necessary for studying the structures of larger proteins in solution, while raw sensitivity is

required for investigating peptides and proteins in the semi-solid state (5). There are thus many different types of problem which require high-field NMR for a solution, and given the time pressures for access to such instruments, it is desirable to try to make the most effective use of a given magnet system.

The idea proposed here is simple and is that for many solid- or semisolid-state NMR applications *resolution* is not at a premium. For example, for most single-crystal, oriented sample or powder (static or spinning) applications, a static magnetic field inhomogeneity of ~ 1 ppm is quite adequate. It should thus be possible to incorporate several probes into a conventional high-resolution solenoid magnet and to observe signals from each probe, since the axial homogeneity is generally excellent over about 4 cm (typical solution NMR samples usually have an $\sim 3\text{--}3.5$ cm sample length). The reasons why this approach—outlined in Fig. 2A for a triple-probe design—should work are twofold. First, for solid- or semisolid-state samples, linewidths are typically large, so that ultra-high resolution is not necessary. Second, samples are

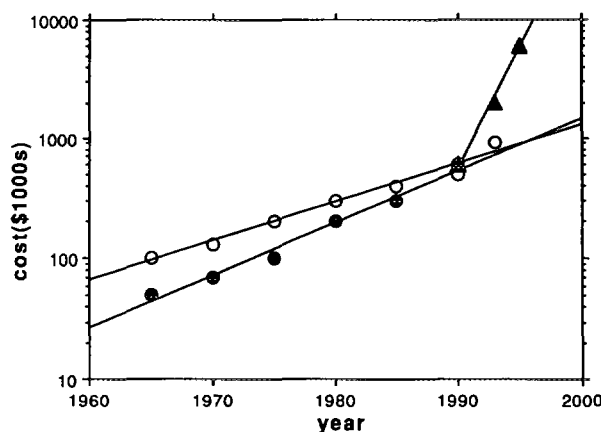


FIG. 1. Price trajectories for NMR spectrometers. \circ , console; \bullet , 60–600 MHz magnets; \blacktriangle , 600, 750, and 1000 MHz magnets. The price of state-of-the-art commercial NMR consoles and magnets obeys simple exponential laws with small exponents up to ~ 1990 (600 MHz). $R^2 > 0.98$ for all three data sets.

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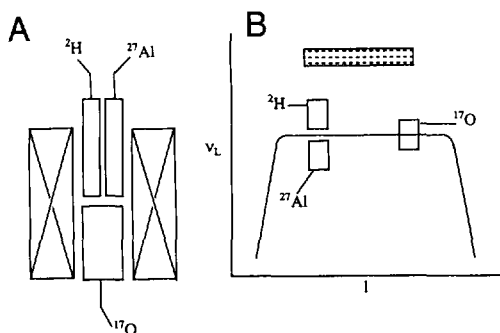


FIG. 2. Multiple-probe graphics. (A) Illustration of the triple-probe arrangement used in this Communication, showing the nuclei observed. (B) Schematic axial field plot showing the sample location in a conventional 5 mm \times 3.5 cm solution NMR probe (top) and three radial solenoid coil probes (bottom).

usually quite "thin," e.g., 5 mm cylindrical tubes placed horizontally, so that the amount of axial field inhomogeneity sampled is very small. This can be easily seen in the extreme case of the probe design reported by Bechinger and Opella (6), in which a lipid sample was sandwiched between a single pair of glass microscope cover slips, resulting in a total sandwich height of ≈ 1 mm (6). Clearly it should be possible to incorporate at least two such probe assemblies into an ultra-high-field magnet since, e.g., for ^2H NMR of membranes, field inhomogeneity at the 1 ppm level is unlikely to be a major cause of line broadening.

The idea is illustrated more graphically in Fig. 2B, which shows a schematic axial field plot (ν_L versus displacement along the central axis). In a conventional high-resolution solution NMR experiment, an ~ 3.5 cm long sample normally occupies most of the flat or homogeneous field region, shown at the top. In one embodiment of the proposed multiple-probe idea, two side-by-side 5 mm solenoid coils occupy the upper region of the magnet (Fig. 2A), while a third solenoid (or spinning) probe occupies the lower part of the homogeneous field (Figs. 2A and 2B). Of course, this basic idea is not completely new, since early high-resolution spectrometers like the Varian A-60 would typically have an "external" capillary for field-locking purposes—essentially a double-probe spectrometer—although the external lock sample would be fixed (e.g., C_6F_6 or H_2O).

To test whether the idea actually works in practice, three solenoid probes were constructed. The first one was tuned to ^{17}O at 11.7 T (67.77 MHz) and occupied the lower part of the magnet, and could in principle be a sample-spinning probe. The second and third probes had 5 mm solenoid coils separated by a Faraday shield and occupied the top part of the magnet. One was tuned to ^2H (76.74 MHz) while the other was tuned to ^{27}Al (130.27 MHz). All probes had Q values of ~ 100 (a value we typically use for solid-state work). Since the solenoids were separated by a Faraday shield, there was remarkably little cross talk between the two channels.

To test the operation of the three-probe spectrometer, we investigated the lineshapes of and interference between the three probes using $^2\text{H}_2\text{O}$, H_2^{17}O , and an aqueous solution of $^{27}\text{Al}(\text{NO}_3)_3$. After a modest amount of probe repositioning and coarse shimming (X , Y , Z^1 , Z^2) we obtained ~ 1 ppm linewidths for each nucleus (Fig. 3A)—certainly enough for many solid- or semisolid-state experiments. There was no appreciable difference in signal-to-noise ratio whether all three channels were pulsing or whether only a single channel was being used. In cases where there is cross talk, bandpass filters can be employed. Thus, the three-probe spectrometer appears to satisfy our requirement of having all three spectrometers operating simultaneously from a single magnet, and the solids requirement of an ~ 1 ppm static linewidth can be met. Further examples of this approach to multinuclear NMR are shown in Figs. 3B–3D: ^2H NMR of $[^2\text{H}_5]\text{pyridine}$ in a thermotropic mesophase, ^{27}Al NMR of a spectrally edited ZSM-5/ $\gamma\text{-Al}_2\text{O}_3$ mixture, and ^{17}O NMR of H_2^{17}O in a magnetically oriented lyotropic mesophase, all acquired with all three channels operational.

The results shown are of interest since they may help solve an important problem in NMR spectroscopy—how to make best use of an expensive, ultra-high-field NMR magnet resource. In reviewing the literature, it is clear that conventional high-resolution NMR magnets are typically used for most types of NMR experiment—whether it be on a solid-, a liquid-, or a gas-phase sample. However, a conventional high-resolution magnet is often not necessary for solid-state NMR. In the past, when the cost of a commercial console was much greater than that of the magnet, the strategy I have outlined

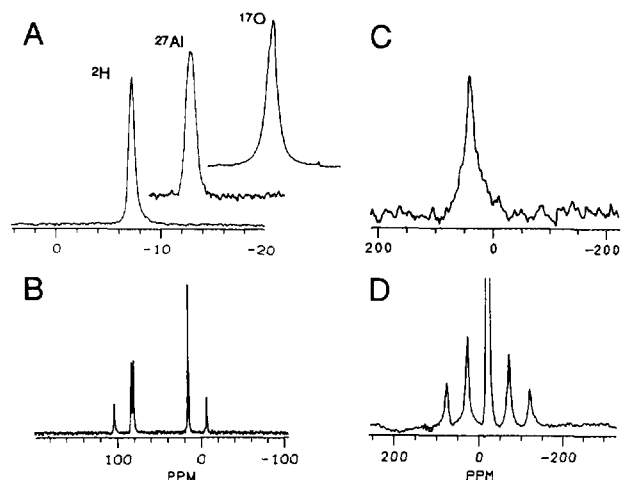


FIG. 3. Spectra obtained from a triple-probe spectrometer. (A) $^2\text{H}_2\text{O}$, H_2^{17}O , and $[\text{Al}(\text{H}_2\text{O})_6]^{3+}$ resonances showing ~ 1 ppm linewidths. Data were obtained during the same time period. (B) The 76.74 MHz ^2H spin-echo NMR spectrum of $[\text{H}_5]\text{pyridine}$ in *p*-methoxybenzylidene-*n*-butyl aniline (MBBA). (C) The 130.27 MHz ^{27}Al selective-excitation spin-echo NMR spectrum of $\text{NH}_4\text{-ZSM-5}/\gamma\text{-Al}_2\text{O}_3$ with editing of the alumina signals. (D) The 67.77 MHz ^{17}O NMR spectrum of H_2^{17}O in a magnetically ordered lyotropic mesophase.

above would be less effective. However, as shown in Fig. 1, the crossover point when magnet and console costs are equivalent has now been reached, making the multiprobe approach more attractive. The alternative solution, of using a second lower-resolution spectrometer for solids work, is also a possibility, but funding, e.g., *two* 750 MHz spectrometers, one low resolution and one high resolution, has drawbacks in terms of overall costs. This would apply even more so to the ~ 1 GHz systems currently under development, which are likely to serve both the solid- and the liquid-state NMR communities (2). Multiple-probe operation for solid and semisolid operation should help solve these problems

and may even be applicable to liquid-state experiments as well.

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