lengths of the maximum and minimum diameters through the center of gravity of the opaque area, and the location of the lowest and most lateral points of the area. From these measurements, the rates and accelerations are computed from differences between the values measured in successive frames.

The FIDAC instrument and the FIDACSYS programming system are thus opening up new fields of investigation in the area of quantitative analysis of pictorial data. While the variety of applications to which the system may eventually be put cannot possibly be predicted now, it is evident that this tool may well bring numerous problems now occupying the minds of biomedical research scientists within reach of a solution (*10*).


**References and Notes**

1. R. S. Ledley, *Science* **130**, 1225 (1959).
2. When the specimen is seen at a magnification of 1000, the field has a diameter of about 50 μ. Thus 750 points across the field give about 750/50 = 15 points per micron on the specimen, or 3 points per 0.2 μ, where 0.2 μ is the optical resolution of a microscope at 1000 power.
3. The fact that FIDAC is on-line with the computer, with no intermediate magnetic-tape recording, means that pictorial data on film can be used; a single 100-foot roll of 16-mm film, which fits in a 3½-inch diameter can, contains 4000 frames and will record over 4 million bits of information; this would require over 50 conventional magnetic-digital tape reels, making a stack over 4 feet high.
4. We used the IBM 7094 computer equipped with a direct data channel.
5. The computer used has a memory cycle time of about 2 μsec and the core memory has 32,768 words of 36 bits each.
6. For example, the IBM 360 series computers can have up to five times the high-speed core memory and more than twice the speed of the computer presently used.
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11. A large team of biologists, physicians, engineers, and programmers are contributing to this work: F. Ruddle, Yale University; B. Migeon, The Johns Hopkins University; E. Ramon-Moliner, Laval University; G. L. Rasmussen, National Institutes of Health; E. Freis and G. Shugoll, Mount Alto Veterans Administration Hospital; and L. S. Rotolo, J. B. Wilson, J. Jacobsen, T. Golab, M. Ginsberg, and G. Cheng, National Biomedical Research Foundation. I am grateful to Drs. Robert E. Cooke and H. Van der Loos for their kind encouragement. The Goddard Space Flight Center also assisted this work. The work is supported, in part, by NIH grants GM 10789, GM 10797, and NB 04472 to the National Biomedical Research Foundation, and in part by a legacy of Loula D. Lasker, New York City.


# Nuclear Magnetic Resonance Spectroscopy in Superconducting Magnetic Fields


F. A. Nelson and H. E. Weaver


The availability of superconducting wire which can carry current of many amperes in a very high magnetic field has made fields in excess of 50 kilogauss practical. The exploitation of these magnetic fields for high-resolution magnetic resonance spectroscopy provides exciting prospects for extending the range and sensitivity of this type of analytical instrumentation. The benefits include increase in chemical shift, with resultant simplification of the spectra of large molecules; greater resolution of broad resonance lines; increased Knight shift in metals; and an increase in signal-to-noise ratio.

Ever since the initial commercial development of nuclear magnetic resonance spectroscopy as an analytical technique in the early 1950's, considerable effort has been directed toward increasing the sensitivity and resolution of the type of spectrometer used in this method. This has resulted in the availability, over the last decade, of spectrometers operating at an ever-increasing resonance frequency, beginning with 30 megacycles per second (corresponding to a field intensity of 7050 gauss) with continual improvement in sensitivity, stability, and resolution. The attainment of these latter characteristics has required very high quality iron-core electromagnets and associated electronic stabilization circuits. It is now apparent that a field strength of 23.5 kilogauss (or 100 Mcy/sec, for protons) is the practical upper limit for such iron magnets. While it is too early to make accurate predictions of practical upper limits for field strength attainable with superconducting magnets, 100 kilogauss may be mentioned as a practical limit with some degree of confidence.

Since the original discovery in 1911 by K. Onnes that certain metals lose all measurable trace of electrical resistance at temperatures near absolute zero, it has been the dream of scientists to use those materials in the form of wire-wound solenoids to generate very high magnetic fields without continual expenditure of large amounts of electrical energy and the associated need for exorbitant amounts of coolant. These early attempts were frustrated by an unexpected incompatibility between the state of zero resistance and a certain maximum intensity of an applied magnetic field. It was quickly established that the magnetic field above which resistivity was restored was a field of only a few hundred gauss. This effect received more attention in the 1930's, when Meissner and Ochsenfeld established the interesting fact that a superconductor, when cooled below its transition temperature, spontaneously expelled a magnetic field from its interior, so long as the intensity of the applied field was below the critical value for the material. In other words, a superconducting metal, when cooled below its characteristic transition temperature, not only lost all measurable resistivity but assumed the magnetic susceptibility of a perfect (or very nearly perfect) diamagnet. This abrupt change in magnetic susceptibility with decreasing temperature, occurring simultaneously with


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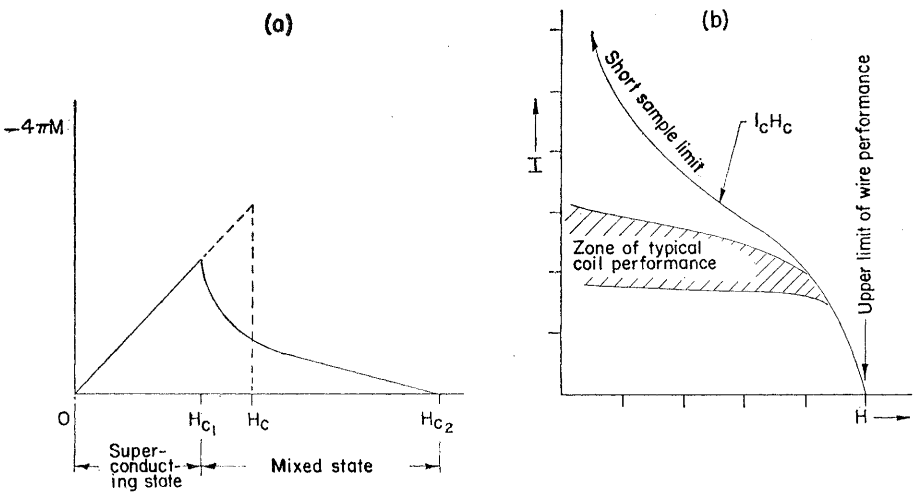


Fig. 1. (*a*) Magnetism of ideal superconductors with magnetic field applied transversely to current direction. The dotted line shows the abrupt field penetration at critical field, $H_c$, of an ideal type I material. The solid curve represents type II material which has a starting flux penetration at $H_{c1}$ and complete penetration at $H_{c2}$. (*b*) Effect of a transverse magnetic field applied to the superconducting wires upon the maximum current the wires can carry. The upper curve is performance of a short sample of wire. The wire in large solenoids has a lower critical current in the range of the hatched area. The product $I_cH_c$ is important in magnet performance.

the loss of electrical resistance, is the basis today for the characterization of so-called soft (so designated from their mechanical properties) or type I superconductors. Mercury and lead are examples of type I superconductors.

For years after the detailed experimental observation of this magnetic effect, which carries the name of the Meissner effect, very little was done toward employing subsequently discovered materials in solenoid construction. About 3 to 4 years ago, however, a few solenoids were constructed by Lincoln Laboratories from niobium wire, to be used in a maser. These were operated successfully, but at magnetic field intensities of only a few thousand gauss. It was not until the discovery (at Bell Telephone Laboratories and at Atomics International) of the very high field tolerance of the intermetallic compound of $Nb_3Sn$ and of NbZr alloy that an intensive investigation of the suitability of superconducting materials for solenoids was re-established. Briefly stated, it has been ascertained that these niobium-based materials are essentially different from superconductors of the type I class in several important aspects: the transition temperatures are significantly higher (18°K for $Nb_3Sn$), the magnetic susceptibility relative to the applied field is markedly different, and the mechanical properties are those of a refractory material. As a consequence of the mechanical properties of these niobium-based materials, their fabrication frequently requires rather subtle metallurgical techniques. That some of these more tractable materials are now commercially available in wire (or tape) form in lengths of several kilometers is a tribute to the success of present-day industrial research.

One of the important practical distinctions between this latest group of superconductors and the earlier forms is that the penetration of an applied magnetic field into the material is not necessarily simultaneous with the appearance of resistance. Materials exhibiting this magnetic behavior have been classed as type II superconductors, wherein essentially two critical fields are experimentally evident: $H_{c1}$, the field at which the magnetic flux begins to penetrate, and $H_{c2}$, the field at which electrical resistance first appears (see Fig. 1*a*). In the type II superconductor, $H_{c2}$ is significantly greater than $H_{c1}$; this relationship clearly has practical significance for high-field application. According to one theoretical model, the type II material at fields higher than $H_{c1}$ tends to break up into small domains (this breakup is often referred to as the onset of the mixed state) instead of favoring a single domain and, accordingly, total flux exclusion of the diamagnetic type II. Furthermore, with the type II material a current driven from an external source can flow without detectable resistance until the pressure of the applied (or self-generated) fieła causes the domains to vanish. Simultaneously with this event resistance will be restored over a significant fraction of the material, and a transition to the "normal" state occurs.

It is this tendency (associated with the energy of surface formation) of the type II superconductor to form many superconducting domains within a matrix of material in the normal state which allows smooth penetration of the magnetic flux lines until $H_{c2}$ is exceeded. It is just this property of flux penetration, becoming more complete as the magnetic field exceeds $H_{c1}$ by larger and larger amounts, that permits application, in a thick solenoid consisting of many thousands of turns of small-diameter wire, of a strictly classical mathematical analysis of the distribution of a magnetic field.

The generally accepted theoretical basis for understanding the behavior of type II superconductors was proposed by the physicists Ginzburg, Landau, and Abrikosov (*1*), who presented a mathematical model which postulated the existence of, and formulated a relationship between, the upper critical field, $H_{c2}$, and a thermodynamical critical field, $H_c$, in terms of a parameter $\kappa$. $H_c$ is the thermodynamic critical field as defined by the relation

$$\frac{H_c^2}{8\pi} = F_n - F_s,$$

where $F_n$ and $F_s$ are the Gibbs free energy of the normal and superconducting state, respectively. The relationship between $H_{c2}$ and $H_c$ is established by the expression

$$H_{c_2} = 2^{\frac{1}{2}}\,\kappa H_c$$

(see *2*). The parameter $\kappa$ is related to measurable characteristics of the material in the normal state. The foregoing relation allows one to make theoretical estimates of magnetic behavior of materials, and these estimates can be compared with experimental results, though considerable care must be exercised in sample preparation. For carefully prepared experiments the agreement with theory has been rather good.

Despite the rather impressive theoretical successes to date, no satisfactory general procedure has been derived which would allow unequivocal prediction of the occurrence of the superconducting transition in metals and alloys, though certain salient features stand out from the wealth of accumulated experimental evidence. The practical engineering problem of finding a suitable material and converting this material into a useful solenoid for reliable production of a high magnetic field still has a largely empirical solution. For example, to be of practical interest a material must have the ability to carry high current densities up to a field very close to $H_{c2}$. It is in the achievement of this characteristic that metallurgical legerdemain has excelled.

## Solenoidal Fields

The foregoing remarks have been concerned with rather ideal examples of the two classes of superconductors. These examples are ideal in the thermodynamic sense of showing nearly perfect reversibility of behavior with variation of an applied magnetic field. The materials used in high-field solenoids deviate rather drastically from the ideal case and exhibit considerable magnetic hysteresis with variation of the applied magnetic field (*3*). The useful niobium-based compounds or alloys have a high concentration of lattice defects. Wires made of niobium alloyed with zirconium and titanium are purposely cold-drawn to insure saturation of lattice defects. This mechanical treatment appears to be one of the important factors necessary for increasing the current density at high fields. Associated with these defects, current loops or "vortex" currents induced by the magnetic field are stabilized within the wires, and the behavior of such a wire when a magnetic field is applied will then depend upon its magnetic history. These vortex currents can trap flux and give rise to an induced paramagnetism when there is a decrease in the intensity of the applied field. Thus, in large solenoids a fairly large remanent magnetic field can be measured even though the driven, or "transport," current has been reduced to zero. The peak value of this remanent field may be several hundred gauss, depending on the intensity of the field to which the solenoid was last energized. This flux trapping reminds one of the characteristics of iron-cored magnets. When this phenomenon was reported (*4*) it was thought that the irregular distribution of flux trapping, which was completely unpredictable in a coil that had been driven normal, would preclude the use of superconducting solenoids for the production of highly homogeneous magnetic fields. As was revealed by experiments conducted at laboratories of Varian Associates, homogeneous fields could be achieved irrespective of the magnetic and thermal history of the solenoid at the relatively high field values needed for nuclear magnetic resonance spectroscopy. In fact, in a solenoid constructed for high-resolution proton spectroscopy, field homogeneities of a few parts per million over a distance of 2 centimeters along the axis have been achieved. By employing the well-established techniques of spinning the sample tube and using additional gradient-canceling coils, the homegeneity over the sample has been extended to a few parts in $10^9$, or resolution of better than 1 cycle per second with resonance frequency of 200 Mcy/sec for protons.

To complete the qualitative discussion of the characteristics of this type II defect-saturated superconductor, the phenomenon of "training" should be mentioned. When solenoids of reasonable size were wound and tested, it was discovered that wire which, in short lengths, had excellent $I_cH_c$ performance ($I_c$ and $H_c$ are critical current and critical field intensity, respectively) quenched —that is, went normal—at disappointingly low currents, frequently well below the $I_cH_c$ curve for the short lengths, when wound in longer lengths in a solenoid (see Fig. 1*b*). Wire wound in a solenoid appeared to be current-limited in fields well below the upper critical field for the material. In many cases reenergizing the solenoids after initial quenching raised the critical current significantly, so that after one or more such cycles the solenoid performance closely approximated that for the short sample. Such improvement in solenoid performance is known as "training"—that is, increasing the maximum operating current by successive quenching steps. Once a solenoid has been "trained" its performance is stabilized and much less sensitive to changes in the value of the driven current. Improvement is realized in this way after a series of superconducting-to-normal excursions, even though in the interior of the coil temperatures have risen well above the critical temperature of 11°K for NbZr. This temperature rise is especially noticeable in large-inductance solenoids. It is reasonable to expect that lengths of wire wound in a solenoid and buried in the interior, with very poor thermal conduction to the helium bath, will get warm as the field-current changes. Measurements have shown that, while the field is increasing or decreasing, the temperature in the interior of a coil rises. Some of this temperature rise is due to joule heating from flux penetration in normal metal surfaces; this part can be minimized through control of the rate of change in the applied current. Another experimentally substantiated cause of heating is collapse of the vortex currents in the superconductor. If a sufficient number of these vortex currents collapse abruptly under the magnetic pressure at a given current level, then a section of the wire can experience too great a rise in temperature and can go "normal," providing an internal lossy mechanism for continual dissipation of the magnetic energy ($\frac{1}{2}LI^2$, where $L$ is inductance and $I$ is current) of the whole solenoid. As a consequence, this normal section propagates rapidly (at a rate of several meters per second) along the wire and, to a lesser extent, across the insulated boundaries of the wire. This process is very rapid, and the field collapses within a fraction of a second, with resulting

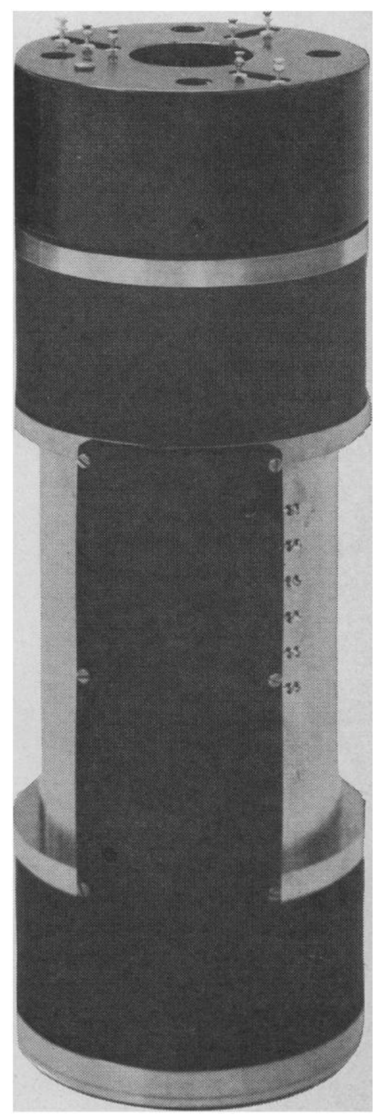

Fig. 2. Photograph of the solenoid, with end-correcting coils, after removal from its dewar enclosure. The end-correcting coils are at top and bottom; the main winding is hidden from view.

sudden conversion of the magnetic energy into heat. The heat, however, is dissipated into the helium bath comparatively slowly, over a period of several minutes, ultimately vaporizing a corresponding amount of liquid helium. Therefore, an explosion does not occur, despite the final conversion into heat of large amounts of energy ($10^3$ to $10^5$ joules) stored in the solenoidal field.

Much improvement in the performance of solenoids has been realized through the use of wire (or tape) coated with copper (coatings up to 0.02 mm thick) or some other high-conductivity metal. The action of the normal metal is twofold: (i) it serves as a tightly coupled secondary which can handle the current in the event a portion of the superconductor primary goes normal; (ii) it serves both as a source of heat capacity and as a good thermal conductor along the wire. As a consequence, training in a given solenoid can be minimized and often avoided altogether through conservative current design. Furthermore, solenoids wound with metal-clad wire (or tape) and insulated with some organic insulation of high dielectric constant are very rarely damaged during the superconducting-to-normal transitions. Finally, if the solenoid is insulated for high voltage, a substantial amount of the magnetic energy can be dumped into an external load of high resistance and nearly constant voltage (about 5 kv), with resultant conservation of liquid helium.

## Coil Design

Now that magnetic fields well in excess of 50 kilogauss are realizable with commercially available wire, it becomes of interest to investigate the possibility not just of producing a high field but of making this high field homogeneous through manipulation of the current distribution in a solenoid. At various intervals during the past 30 years or so different schemes of coil arrangement for producing homogeneous or shaped fields have been proposed. Perhaps the best known are the Helmholtz two-coil and the Maxwell three-coil axially symmetric systems, on which later schemes are based. Recently Garrett (5) has introduced a unified mathematical approach for calculating field distributions, which is designed to exploit the capabilities of modern high-speed digital computers. His analysis is particularly suitable for axially symmetrical coil configurations and is useful in the practical task of designing thick solenoids for applications requiring a homogeneous field. The approach is that of altering the cross section of a right circular solenoid made up of many turns, each carrying the same total current, in such a way that there are more ampere turns near the ends of the coil than near the center. In this way, remarkably good homogeneities are theoretically possible; in fact, for one type of solenoid, described later, a field homogeneity of 1 part in $10^7$ over an axial distance of 1 centimeter is theoretically possible. Such homogeneities cannot easily be achieved in practice because the attempt makes unrealistic demands upon construction techniques. However, field homogeneities in the range of 1 part per million can be achieved through careful construction, and the field homogeneity can be further improved by as much as two orders of magnitude through the use of auxiliary current shim coils.

## Solenoid for Proton Resonance

To determine the feasibility of constructing superconducting solenoids for use in high-resolution nuclear magnetic resonance spectroscopy, one such solenoid was constructed at Varian Associates for proton resonance at 200 Mcy/sec. The $H^1$ nucleus requires a field intensity of 47 kilogauss to establish magnetic resonance at 200 Mcy/sec, and, to be really useful, it requires a field homogeneity and time stability of the order of a few parts in $10^9$. A solenoid which has met these basic requirements is shown in Fig. 2. The solenoid proper has an overall length of about 35.7 centimeters, an inner diameter (at helium temperature) of 4.25 centimeters, and an outer diameter of 12.7 centimeters, and it weighs about 13.2 kilograms. The inner diameter is such that, together with its associated sample-isolation dewar, the solenoid provides a through-access, at room temperature, of about 2.6 centimeters. This solenoid was first shown in operation at a meeting of the New York American Physical Society in January 1964; it was shown again, together with an experimental nuclear magnetic resonance spectrometer operating at 200 Mcy/sec, in Pittsburgh in March 1964. As a figure of merit for resolution and time stability of the higher field, the spin-coupled quartet of the $CH_2$ functional group in the acidified ethyl alcohol molecule is used. Figure 3 shows this proton-proton spin coupling, at 200 Mcy/sec. The distance between peaks is 7 cycles; it is independent of the intensity of the applied magnetic field. For this result to be achieved, it should be remembered, the solenoid must provide a basic homogeneity in the range of 1 part per million, in order that the residual gradients may be relatively easily handled by supplementary gradient-canceling coils and through spinning of the sample tube by means of an air turbine. Large transverse gradients would, for example, require unduly high spinning rates, with consequent vortexing of the liquid sample. This would generate "spinning side bands" of considerable intensity, and these would complicate the interpretation of a complex spectrum by introducing unwanted spectral "ghosts."

One possible configuration for a fully compensated solenoid with the correction coils on the outside of the main winding is known as an outside-notch sixth-order solenoid. The term *sixth order* indicates the degree to which a solenoidal field has been "flattened" through the action of the compensating coils. The higher the order, the flatter or more homogeneous the field. This terminology is of mathematical origin and stems from the fact that the field may be expanded about the geometric center in terms of a power series involving Legendre polynomials, where the coefficients of these polynomials contain an expression for the $N$th-order derivative of the appropriate algebraic expression for the field as evaluated at the origin. The series expansion of the components of an axially symmetric field, with the origin at a plane of symmetry, may be written as follows:

$$B_\phi = 0$$

$$B_z(r,\theta) = B_z(0,0)\ [1 + \varepsilon_2(r/a_1)^2P_2(u) + \varepsilon_4(r/a_1)^4P_4(u) + \ldots]$$

$$B_\rho(r,\theta) = B_z(0,0)\ [\varepsilon_2(r/a_1)^2P_2'(u) + \varepsilon_4(r/a_1)^4P_4'(u) + \ldots]$$

where the field components are written in cylindrical coordinates ($\rho$, $\phi$, $z$) but as a function of $r$ and $\theta$, or spherical coordinates, where $u = \cos\theta$. The term $\varepsilon_i$ denotes the corresponding derivatives of the expression for the field as evaluated at the origin, and $P_i'$ denotes the derivative of the polynomial

$P_i$. The field at the origin of a right-circular solenoid is given by

$$B_z(0,0) = G(\nu)^{1/2} a_1 I/A$$

where

$$G = \frac{\sqrt{2\pi}}{5}\left(\frac{\beta}{\alpha^2 - 1}\right)^{1/2} \ln\left[\frac{\alpha + (\alpha^2 + \beta^2)^{1/2}}{1 + (1 + \beta^2)^{1/2}}\right]$$

and

$$\nu = 2\pi(\alpha^2 - 1)\beta$$

with

$$\alpha = \frac{2a_2}{2a_1} = \frac{\text{outside diameter}}{\text{inside diameter}}$$

$$\beta = \frac{2b}{2a_1} = \frac{\text{length}}{\text{inside diameter}}$$

and $A$ = total cross-sectional area required by each conductor, including the copper jacket and the dielectric insulation.

The design problem for generating a homogeneous solenoidal field consists of altering the cross section of a solenoid in the manner illustrated in Fig. 4. Under these conditions one or more of the $\varepsilon_i$ error coefficients can be made to vanish. For a system of three axial coils all carrying the same current it is theoretically possible to cancel $\varepsilon_2$ and $\varepsilon_4$ exactly, leaving only a net contribution to $\varepsilon_6$ and the higher-order terms. This is the origin of the "sixth-order" terminology. If less than the maximum attainable homogeneity is demanded, it is often possible to cancel only the $\varepsilon_2$ error term, leaving $\varepsilon_4$ as the first significant error term. By definition such a system of coils is called a fourth-order geometry. In this way, with a computer-oriented program, it is possible to treat a range of homogeneity requirements with various coil geometries designed to cancel a given set of error terms, as dictated by the needs of the problem. High-resolution nuclear magnetic resonance spectroscopy is perhaps the most demanding application, for it does not allow a compromise on homogeneity. In order for the technique to be useful for many applications, resolution better than 1 cy/sec is needed, irrespective of the field value. Therefore, the problem of satisfying these homogeneity and stability requirements becomes more severe with increase in field intensity.

## Spectrometer Instrumentation

The probe, which is located in the field of the magnet and which contains the sample under investigation, is the most critical component in the nuclear magnetic resonance detection system. An assembly of small coils in the probe bathes the sample in a radio frequency field and picks up the induced voltage due to resonating nuclei in the sample. A transmitter or radio frequency generator is coupled to one set of coils for excitation of the nuclei, while a receiver amplifier is coupled to the pickup coil. (Sometimes one coil is used for both functions, in a divider or bridge circuit.) If either the field of the magnet or the frequency of the transmitter is slowly varied, the absorption of the nuclear magnetic resonance can be sensed as a change in output from the receiver; this output is then detected and presented on an oscilloscope or recorder.

The small strength of the nuclear magnetic resonance signal with respect to the irradiation signal (from the transmitter) requires a careful probe balance if the receiver amplifiers are not to be overloaded. This delicate balance can make the operational problem of achieving mechanical and electrical stability of the probe an extremely difficult one. A technique in which the magnetic field is modulated by a sine wave sweep can produce an output signal from the receiver detector in the form of an alternating-current carrier which can be amplified and demodulated to give, as an output signal, either the derivative of, or a direct representation of, the original nuclear magnetic resonance signal. The derivative output has been used in wide-line nuclear magnetic resonance work for many years, and during the past few years instrumentation for high-resolution nuclear magnetic resonance spectroscopy has been almost completely converted to field-modulation systems which reproduce the absorption line shape.

The magnets used for nuclear magnetic resonance studies are always large compared with the field volume occupied by the sample. This is necessary because of the requirements for field homogeneity. In either an iron-core or an air-core magnet there usually is a relatively large volume of field whose intensity varies by less than 10 percent, but in high-resolution nuclear magnetic resonance studies all of the field at the useful part of the sample volume should be of essentially the same value, within a range of 1 part in $10^7$ to 1 part in $10^9$. Even with the best iron or coil geometries, the volume of field with

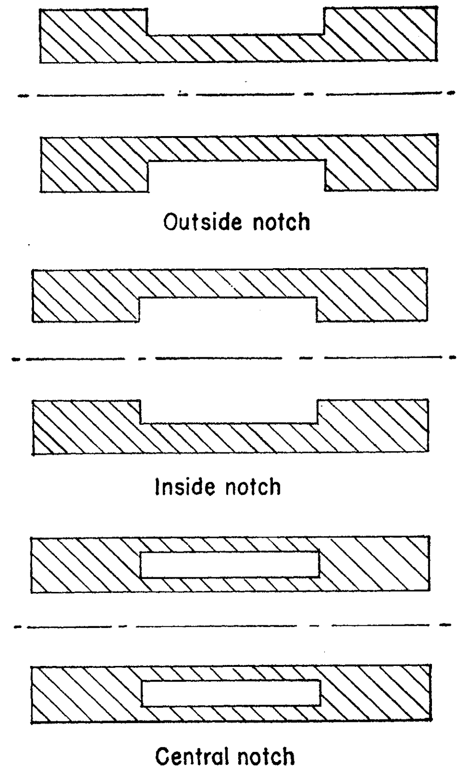


Fig. 4. Three examples of compensation for axially symmetrical solenoids with isotropic current distribution. For practical reasons either the outside or the inside notch is usually employed.

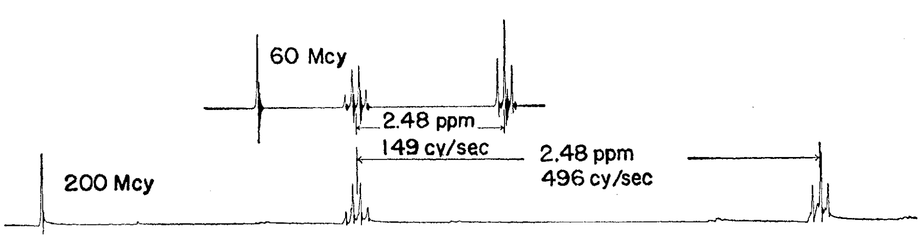


Fig. 3. Two spectra of acidified ethanol showing (left to right) lines for the OH, $CH_2$, and $CH_3$ protons. The bottom spectrum, at 200 Mcy/sec (47 kilogauss), has greater chemical shifts than the top spectrum, at 60 Mcy/sec (14.1 kilogauss). The proton spin couplings produce 7-cy/sec splittings which give the multiplets, which are independent of field magnitude.

this homogeneity is a small percentage of the volume of field available.

The higher the field homogeneity is, the more important the stability, with time, of the field intensity becomes. To realize the benefits of high homogeneity, it is necessary to scan very slowly across narrow absorption lines. The recording of these lines is badly distorted if there are random changes in either the radio frequency source or the field intensity. In the case of electromagnets, power supplies can be built which reduce these unwanted changes to about 1 part in $10^6$. Special flux-stabilizing systems can reduce these shifts by another factor of 10 to 100, but it is difficult to prevent drifting even though the environmental temperature is held extremely stable.

One method used with high-resolution spectrometers, called a field-frequency system, allows the field and the frequency to vary by small amounts but keeps their ratio exact by means of a second nuclear magnetic resonance. If a separate sample is used for control purposes, the field difference between the samples can be scanned. If a common sample is used, a separate irradiation radio frequency field at a second frequency is used, together with one line of the spectrum, for purposes of field-frequency control, and the difference between this frequency and the normal irradiation frequency is varied for scanning the remainder of the spectrum. Such systems are quite complex, but the improved performance of such an instrument makes the complexity worth while. Systems which use a field-frequency ratio control have sufficient stability to permit the use of an X-Y recorder with calibrated chart paper (marked off in field parts per million or frequency units). Use of an X-Y recorder with calibrated paper is clearly more difficult if the field intensity and radio frequency have to be separately controlled.

As might be expected, the incorporation of a superconducting magnet in a nuclear magnetic resonance spectrometer introduces some new problems of design. Some of these are mechanical and some are operational, but many are electrical problems such as could be expected with any fundamental change in the magnet system. The normal magnet used in a nuclear magnetic resonance spectrometer has large iron pole pieces with a horizonal axis, and there is relatively easy access from above for changing samples (see Fig. 5). It is possible to make a split-coil superconducting magnet with a horizontal field and radial access, but with this geometry the structure would have to be very large to give sufficient coil separation for access at room temperature. It is thus much more efficient to produce a field in a solenoid with access along the axis. The smaller size and greater rigidity of the solenoid are also important factors. Accordingly, in the majority of superconducting magnets with very homogeneous fields, coil combinations which provide axial access have been used.

Mounting of these coils in cylindrical dewars with their axes vertical facilitates cooling of the coil by immersion in liquid helium. The nuclear magetic resonance probe can be installed in an inner dewar which is inserted into the solenoid from the top, or, if the experiment is to be performed at 4°K, no isolation of the probe is required. The most satisfactory arrangement for operation at variable temperature or room temperature is a dewar with built-in vacuum-jacketed inner wall with as large a hole as possible going through from top to bottom of the dewar. This arrangement gives a magnetic field in the vertical direction, with the most homogeneous part of the magnetic field in the center of the hole, possibly 20 or 30 centimeters from the bottom of the dewar, and with access from the top or bottom. The probe can then be at or near room temperature and can be easily removed, and its position can be precisely adjusted. Sample changing is somewhat difficult inside such a dewar, because the distance to the nuclear magnetic resonance probe from the upper portion of the dewar is normally a large fraction of a meter. Removing the probe in order to exchange samples has been found more practical than lowering the sample from the top. Development of a system for varying the temperature of the sample, with its associated insulated piping, will, however, require some unusual arrangements of probe assembly.

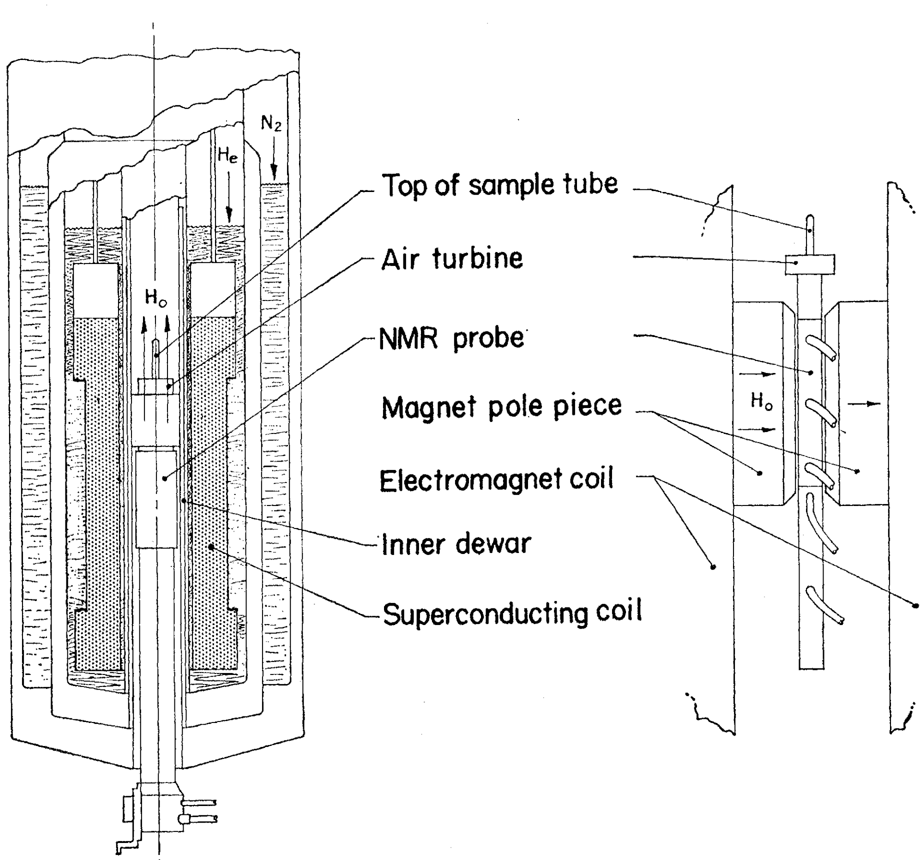


Fig. 5. Position and shape of the nuclear magnetic resonance sensing probe in the 47-kilogauss superconducting magnet and dewar, compared with the position and shape of a conventional probe in the gap of the usual iron core magnet. Because of limited accessibility, the probe is removed from the superconducting solenoid for exchange of samples.

Sample spinning is important in high-resolution work because if the nuclei are moved rapidly they resonate at the frequency corresponding to the average intensity of the field through which they move. Small transverse gradients can be effectively eliminated by rotation of the sample tubes. To get effective averaging of the resonances, the spinning rate has to be proportional to the gradient across the sample. This technique, standard in all high-resolution nuclear magnetic resonance instrumentation, is also used with the superconducting magnets. It should be noted that if the percentage of transverse gradient is the same for two magnets, the magnet with the higher field has the larger gradient, and therefore a spinning rate proportional to the field value is required. Very high spinning rates are not practical, and consequently the higher field should have greater relative homogeneity.

The shape of the sample also dictates the possible form of the radio frequency coils in the probe. Normally, the pickup coil for the receiver is wound about the long sample tube, so that the coil and the tube have the same axis. In order that a nuclear magnetic resonance signal may be induced, the axis of this coil must be perpendicular to the direction of the main magnetic field $H_0$. With such a geometry in a superconducting solenoid, a spinning sample tube would have to rotate with its spinning axis perpendicular to the axis of the dewar. Since this mounting is not very practical because of difficulty in changing samples, the tube has been generally mounted along the field axis. Spinning parallel to the field axis requires a transverse-pickup-coil design, so that the coil may detect the signal vector which precesses about $H_0$. This requirement makes it more difficult to get good coupling to the sample. In those applications of nuclear magnetic resonance spectroscopy where ultrahigh homogeneity of the magnetic field is not required, more efficient coil geometries can be employed, with better coupling or filling factors.

Thermal and instrumental noise are ultimately a problem when the amount of sample is restricted. In wide-line nuclear magnetic resonance spectroscopy, noise is the most important consideration, and in high-resolution instrumentation it is secondary only to the problem of insuring adequate field homogeneity. The superconducting magnet provides an advantage here, for at a given temperature the net polarization of nuclei is proportional to the field intensity. The frequency increases in proportion to increase in field intensity, and the pickup of voltage in a given

Table 1. Characteristics of some of the isotopes important in the nuclear magnetic resonance technique.

| Isotope | Frequency for field intensity of 47 kilogauss (Mcy/sec) | Natural abundance (%) | Sensitivity relative to equal proton spins at same field (%) |
|---|---|---|---|
| $H^1$ | 200 | 99.98 | 100.0 |
| $H^2$ | 30.7 | 0.015 | 9.6 |
| $Li^7$ | 77.7 | 92.57 | 29.4 |
| $B^{11}$ | 64.2 | 81.17 | 16.5 |
| $C^{13}$ | 50.3 | 1.108 | 1.6 |
| $N^{14}$ | 14.5 | 99.64 | 0.1 |
| $O^{17}$ | 27.1 | 0.037 | 2.9 |
| $F^{19}$ | 188 | 100 | 83.4 |
| $Na^{23}$ | 52.9 | 100 | 9.3 |
| $P^{31}$ | 80.9 | 100 | 6.6 |

receiver coil is proportional to this frequency, $\omega$. These two effects combine to give a signal amplitude proportional to the square of the field intensity or frequency. However, this factor of $(H_0)^2$ or $\omega^2$ is not, unfortunately, fully realizable, because the thermal noise in the same coil also increases as $\omega^{1/2}$. Therefore the highest possible rate of increase in signal-to-noise ratio would be a rate proportional to $\omega^{3/2}$. However, coil losses and lead inductance are usually larger at a higher frequency, and in practice the net increase in signal-to-noise ratio for a given isotope is more nearly proportional to $\omega$, which is a linear function of the field intensity. The higher fields of a superconducting magnet should, nonetheless, permit a significant increase in signal relative to noise.

The technique of superimposing a small-amplitude oscillating field upon the main field is also desirable in the nuclear magnetic resonance system with a superconducting magnet. This superposition is not detrimental to the performance of the solenoid, for the coils whose field modulates the main field, $H_0$, are located close about the sample probe. Their return flux is inside the magnet, and therefore the rapidly changing field does not penetrate the superconducting solenoid. An important additional problem arises from the fact that, with the higher field intensities attainable with a superconducting magnet, the spectrum extends over a greater frequency range, and therefore, in order not to have an overlapping of the spectrum by its own modulation side bands, the frequency of the modulating field must be raised a corresponding amount. Also, in order to keep the index of modulation a constant, the amplitude of the modulating field must be kept proportional to the modulating frequency. This has not been, to date, a problem in work with protons, but it may now present serious engineering problems in work with nuclei such as $F^{19}$, whose spectra are usually spread out by more than an order of magnitude relative to $H^1$ spectra. When the high-modulation currents in the modulating coils react with the high field intensity from the magnet, large mechanical forces are produced in and about the probe assembly. This means that the high modulation frequency, with its increased current (for a constant index of modulation), will result in a significant increase in the forces acting on the probe and in power dissipation in the coils. Excessive power dissipation would give rise to temperature instabilities in the probe assembly. The vibrational forces are not great enough to damage the probe assembly, but they produce a coherent effect at the modulation frequency which is amplified along with the nuclear magnetic resonance signal. This effect results in a degradation of the instrument performance.

The techniques for producing a homogeneous magnetic field with a superconducting magnet and with an iron-core magnet are different. In the latter case, the shape and material used in fabrication of the iron pole pieces are the most important factors; in the case of a superconducting magnet the field homogeneity depends solely upon the spatial distribution of the current. The external field gradients have a much greater effect upon field shape in an air-core magnet than in the gap of an iron magnet. As noted earlier, to be useful for nuclear magnetic resonance spectroscopy, the superconducting magnet must have the same absolute homogeneity at its higher field intensities that the iron magnets have at their lower field intensities. This requirement leads to a further problem in the design of the probe, because a distortion of the magnetic field by the different magnetic susceptibilities of the sample and the probe parts is proportional to the strengh of $H_0$. These are not limiting problems, but they do require that more careful attention be given to the construction of the instrument at these higher operating field intensities. Some of the gradients in the magnetic field can be removed by means of shim coils built into the magnet assembly; such

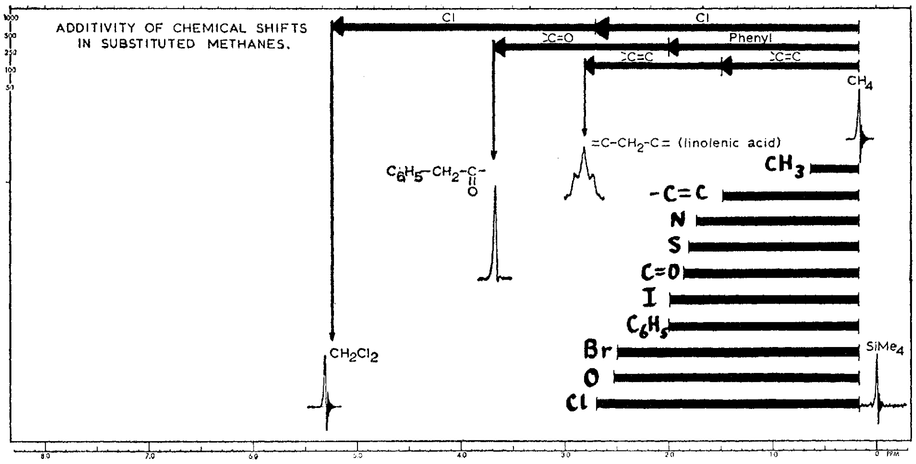


Fig. 6. Proton chemical shifts as affected by some neighboring groups, and how these effects add.

coils are frequently built into the gap of an iron magnet, but the geometry of these coils is necessarily quite different in a solenoidal magnet. Essentially, what is done is this: a set of shim coils is provided which superimposes a small field with large gradient upon the field provided by the main magnet, which is a large field with small gradient. The currents in the shim coils are adjusted to cancel the residual gradients of the solenoidal field. This adjustment can be made with little or no change in the average value of the field, $H_0$, at the sample.

Often it is a great advantage to study nuclear magnetic resonance spectra at two different magnetic field intensities in order to see which lines are groups with fixed line spacing and which lines have separations dependent upon field value. The superconducting magnet can be designed with special compensation features, so that the field intensity can be shifted from one magnitude to another without lessening the degree of homogeneity of the field. Future refinements in these systems should make it possible to change field intensity by a factor of at least 2 in a few minutes.

As mentioned above, the stability of the magnetic field is very important in nuclear magnetic resonance studies. The superconducting magnet has a further advantage here. When the superconducting coils are short-circuited by a superconducting switch, this is described as operation of the solenoid in the persistent mode. Under this condition the current stability is not affected by any instability of power supply—in fact, the power supply is turned off during normal operation. The temperature of the coil in the persistent mode is not affected by any external source, and no heat is generated inside the coil as long as the solenoid is operated in the persistent mode. There are, however, some observable instabilities in a superconducting magnetic field. The linear gradients of external origin can penetrate the magnet without changing the field intensity at the center of the coil. Thus, the solenoid will not shield effectively against such field distributions, since there is no net change in the total flux. Furthermore, some of the higher-order nonlinear gradients do change the central field intensity, but, despite these effects, very good stability has been obtained with unshielded magnet structures. A stability of 1 part in $10^8$ can be achieved, provided external fields and the effect of ferromagnetic objects are controlled. Shielding of the magnet with a permeable medium is a natural solution to both problems, because it restricts the extent of the large fringe field of the solenoid. However, it is quite possible to lose the inherent stability of the superconducting solenoid by using a poorly designed shield. Use of a superconducting shield is also an interesting possibility in connection with this problem.

## Applications

As mentioned earlier, the increased intensity of magnetic field, with the correspondingly higher resonance frequency, results in a theoretical increase proportional to $\omega^{3/2}$ in signal-to-noise ratio in the pickup coil, but normally at the relatively high proton frequencies an increase proportional only to $\omega$ can be realized. At low frequencies, however, where the radio frequency losses are not as great and the interconnecting leads are responsible for only a small percentage of the total resistance and inductance of the pickup coil, it is possible to get an increase closer to the theoretical enhancement of $\omega^{3/2}$. This marked increase has generated renewed interest in nuclei with small gyromagnetic ratios and low isotopic abundance. For the specific case of high-resolution nuclear magnetic resonance spectroscopy, the most important of the nuclei resonating at lower frequencies is $C^{13}$ (1.07 kcy $sec^{-1}$ $gauss^{-1}$). The $C^{13}$ nuclear magnetic resonances are very sharp, but the low natural abundance of $C^{13}$ and the correspondingly weak signals have kept it from becoming very important in spectroscopy. A method of semirapid passage (*6*) with high radio frequency excitation is a useful technique for increasing the signal-to-noise ratio, but it results in a considerable loss of resolution. One possible way to circumvent the problem of poor signal is to incorporate enriched $C^{13}$ into the samples, but this is time-consuming and often expensive. The low natural abundance of $C^{13}$ (only about 1 percent of the total carbon) has one important advantage: there is only one chance in a hundred that a neighboring carbon atom is $C^{13}$. (The abundant $C^{12}$ atoms do not have a magnetic moment and cannot be observed by nuclear magnetic resonance spectroscopy.) If the sample is enriched, many combinations of carbon-carbon spin couplings give rise to a spectrum whose character is dependent on this enrichment, and this often leads to an undesirable complication in the analysis. When higher fields of greater sensitivity are achieved it should become practical to perform standard high-resolution spectroscopic analysis on naturally occurring $C^{13}$ with natural line widths. The uncomplicated and detailed information thus obtained about spin coupling of the rare $C^{13}$ nucleus to the abundant protons would provide important correlating evidence for comparison with findings for the proton spectrum of the same molecule. This would clearly facilitate structural determination of many organic systems. In addition, the semirapid passage technique will also be improved, both because of increased sensitivity and because the spectrum will be further spread out by the higher magnetic field while the individual lines will not be broadened by this technique beyond the broadening at lower fields.

The chemical shift which is caused by the shielding effects of the electrons in the molecule is proportional to field intensity, while the splitting due to spin couplings between nuclei is, to the first order, field-independent (see Fig. 6). Therefore, if atoms of a molecule are located in two positions with almost the same magnetic shielding, they may yield overlapping lines. If each group is further split by spin couplings of neighbors, the spectrum can be highly structured and nearly impossible to analyze. The higher field intensity helps to further separate the slight chemical nonequivalence, facilitating interpretation. This means that the nuclear magnetic resonance technique can be more effectively applied to the study of larger and more complex molecules, such as steroids and alkaloids. The spectra of some of the petroleum products which have many similar groups would also be improved. The chemist synthesizing natural products and complex new molecules will find many instances where the higher-field nuclear magnetic resonance technique is the most rapid method of analysis.

The effect observed when the technique is used for analyzing metals is an example of the interaction between the magnetic moment of the nucleus and the magnetic field-dependent polarization of the conduction electrons. As a consequence of this interaction, the field at the resonating nucleus differs very slightly (up to a few percentage points) from the applied field, and the nuclear magnetic resonance signal is said to be "shifted" from its corresponding resonance in a diamagnetic compound. This effect is called the Knight shift, after its discoverer, W. D. Knight (7). In a solid, when motional averaging is essentially absent, both field-dependent and field-independent magnetic interactions can arise. Hence, in a noncubic environment, analysis of the competing field-dependent and field-independent interactions (magnetic dipole-dipole interactions) can be significantly aided by performance of these experiments in both high and low magnetic fields. Most metals and nonferrous alloys of interest contain nuclei with magnetic isotopes of low gyromagnetic ratio or low abundance, or both. Hence, the expected enhancement in the signal-to-noise ratio at the higher field values, together with the larger Knight shift, should result in an even greater range of application of this important technique.

There is another class of isotopes—those which possess a magnetic moment but which do not normally have very narrow spectral lines even in liquids. The resonances from isotopes of this class are broadened because of an interaction of the nuclear quadrupole moment (an index which measures the lack of spherical electric-charge distribution in the nucleus) and the electrical field gradient at the nucleus; $B^{11}$, $Na^{23}$, and $N^{14}$ are typical examples of nuclei with moderate quadrupole line broadening. Their resonances may produce a good signal-to-noise ratio, but the broad lines often mask, at ordinary magnetic fields, shifts due to magnetic interactions. The increase in field intensity spreads the moderately broad lines further apart and can give structural information about the molecule which could not be obtained before higher fields became available (Fig. 7). Studies of other isotopes with significant quadrupole broadening, such as $O^{17}$ (see also Table 1), will also benefit, because of increase in chemical shifts between resonances of atoms within a molecule.

The semisolid substances are another class of materials whose analysis will be benefited by the high field intensity available with superconducting magnets. These materials include mixtures of liquids and solids and the polymers. If a solid can be dissolved in a solvent, the tumbling and diffusion average out the effects (magnetic couplings) of neighboring molecules, but in the solid state this averaging is usually not complete and the random distribution of local magnetic fields produced by the interaction with thousands of neighboring magnetic moments broadens the nuclear magnetic resonance line. A liquid within the solid may diffuse and thereby yield partial averaging, or a polymer may have loose ends which have some freedom to move. A material of this class usually yields a spectrum which is strongly temperature-dependent and frequently consists of a narrow component superimposed upon a broad one. Such properties as completeness of polymerization, degree of crystallinity (at a given temperature), and tacticity have been measured by the nuclear magnetic resonance method. The higher field intensity, which increases the field anomalies within the molecular structure, should make it easier to analyze these difficult problems.

Because, with this technique, signal-to-noise ratio is increased, it is natural to consider the possible applications of superconducting-magnet nuclear magnetic resonance systems to biological problems. The increased chemical shifts are also helpful here, since biochemicals are often large molecules containing many functional groups of nearly equal magnetic shielding. These nearly equivalent groups produce essentially superimposed spectral lines at lower operating field intensities, and such mol-

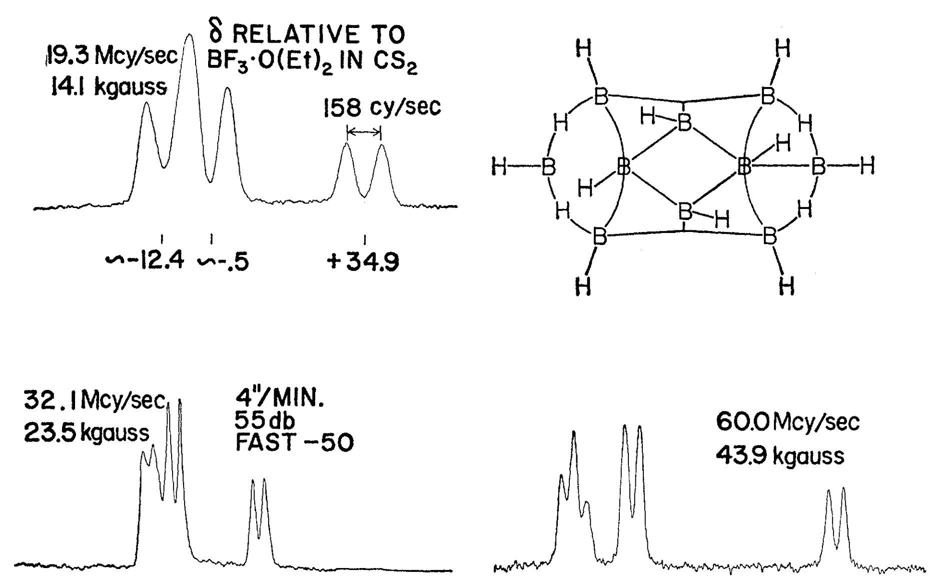


Fig. 7. The $B^{11}$ nuclear magnetic resonance spectrum of decaborane at 60 Mcy/sec (43.9 kilogauss) compared with that at lower field intensities (14.1 and 23.5 kilogauss). The naturally broad lines will be resolved into four doublets with further increase in field intensity. The doublets with their fixed spacings are due to spin couplings between $H^1$ and $B^{11}$ atoms.

ecules often do not diffuse or tumble rapidly enough for complete line narrowing. A significant increase in signal-to-noise ratio should increase the accuracy of nuclear magnetic resonance relaxation studies in complex systems. Despite the present limitations, the technique is already becoming very useful as one of the structure-determining tools in the biochemical field, and it should become even more useful when the higher resolution and the increase in signal-to-noise ratio anticipated with these new high-field magnets have been realized.

### Operational Problems

In this discussion of the performance characteristics of a high-resolution nuclear magnetic resonance spectrometer with a superconducting magnet, little has been said about the operational problems—for example, the necessity of cooling the solenoid to liquid helium temperature and maintaining this temperature with an adequate supply of liquid helium and liquid nitrogen. While the procurement of cryogenic liquids may present no major problem for some research laboratories located in or near major industrial areas, these liquids are not in general supply. The shortage of liquid helium is even more acute in countries outside the United States which do not have their own source of the gas. Moreover, not every industrial laboratory has personnel who are familiar with the properties of liquid helium and trained in handling it. Some experienced person has to be on hand every day to see that adequate supplies of the liquids are maintained.

These factors may delay general acceptance of this type of instrument. However, the problem of maintaining the necessary low temperatures will be lessened to a large degree when dependable closed-cycle refrigeration becomes generally available. Ideally, such a refrigerator would supply all the liquid helium and probably all the liquid nitrogen needed, and it would operate continuously for weeks with very little attention or care.

### Summary and Conclusion

The first high-resolution nuclear magnetic resonance spectrometer operated at 30 Mcy/sec (7.05 kilogauss). The magnets constituted the only major obstacle to raising the frequency, but by continuous development over 10 years this frequency for proton resonance was increased to 100 Mcy/sec (23.4 kilogauss). Now, in one step, a system has been made to operate at twice this frequency and field intensity. It is not expected that superconducting magnets will generally replace iron magnets, but it is interesting to note that very few laboratories use the 30- and 40-Mcy/sec proton systems today.

Notwithstanding the cost and operating problems of the superconducting magnet system for the nuclear magnetic resonance spectrometer, the fact that this is the only practical means of developing both a stable and a high-intensity field puts it in a class by itself. For this reason, even though the maintenance of spectrometers with superconducting magnets requires rather specialized skills, this type of instrumentation will clearly have an important role in advancing scientific knowledge, by making possible analyses which have not been possible with presently available instruments.

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8. We gratefully acknowldge the contributions of our colleagues and supporting staff, which aided materially in the successful development of the instrumentation discussed in this article.


# News and Comment

## The Election: Partisan Activity of Scientists Unlikely to Sow Discord in Scientific Community

The formation of groups of scientists in the camp of each presidential candidate (*Science*, 21 August, 25 September) has raised some concern about the possible divisiveness that may ensue in the scientific community from these ventures into national politics. It is just such concern that has caused some well-known scientists to decline invitations to become involved with either party in the campaign. And fear of divisiveness may well have played a part in the establishment this week of the latest scientific group to grow out of the presidential campaign. This is the 1964 Scientists Committee for Information, a ten-member body chaired by Edward L. Tatum, a Nobel laureate and geneticist at the Rockefeller Institute. The committee, which describes itself as "non-partisan"—though it is a safe assumption that most, if not all, its members favor Johnson—intends to stay above the fray and offer "impartial and accurate information" on scientific issues that may arise in the campaign. Tatum and other members insist that the committee originates from nothing more than a feeling that a politically neutral group of scientists might be useful for illuminating scientific-political issues, but implicit in the committee's existence is the feeling that science may be encouraging dangerous divisions within its own ranks by getting mixed up in partisan politics.

It is difficult, however, to see in what way partisan political preferences might be related to the internal affairs of the scientific community. That lots of scientists don't like each other can easily