

containing a number of rare-earth atoms like praseodymium-ammonium-nitrate), and start by cooling it down with liquid helium to one or two degrees absolute in a strong magnetic field. Then the factor $\mu B/kT$ is larger than 1—say more like 2 or 3. Most of the spins are lined up, and the magnetization is nearly saturated. Let's say, to make it easy, that the field is very powerful and the temperature is very low, so that nearly all the atoms are lined up. Then you isolate the salt thermally (say, by removing the liquid helium and leaving a good vacuum) and turn off the magnetic field. The temperature of the salt goes way down.

Now if you were to turn off the field *suddenly*, the jiggling and shaking of the atoms in the crystal lattice would gradually knock all the spins out of alignment. Some of them would be up and some down. But if there is no field (and disregarding the interactions between the atomic magnets, which will make only a slight error), it takes no energy to turn over the atomic magnets. They could randomize their spins without any energy change and, therefore, without any temperature change.

Suppose, however, that while the atomic magnets are being flipped over by the thermal motion there is still some magnetic field present. Then it requires some work to flip them over opposite to the field—they *must do work against the field*. This takes energy from the thermal motions and lowers the temperature. So if the strong magnetic field is not removed too rapidly, the temperature of the salt will decrease—it is cooled by the demagnetization. From the quantum-mechanical view, when the field is strong all the atoms are in the lowest state, because the odds against any being in the upper state are impossibly big. But as the field is lowered, it gets more and more likely that thermal fluctuations will knock an atom into the upper state. When that happens, the atom absorbs the energy $\Delta U = \mu_0 B$. So if the field is turned off slowly, the magnetic transitions can take energy out of the thermal vibrations of the crystal, cooling it off. It is possible in this way to go from a temperature of a few degrees absolute down to a temperature of a few thousandths of a degree.

Would you like to make something even colder than that? It turns out that Nature has provided a way. We have already mentioned that there are also magnetic moments for the atomic nuclei. Our formulas for paramagnetism work just as well for nuclei, except that the moments of nuclei are roughly a *thousand times smaller*. [They are of the order of magnitude of $q\hbar/2m_p$, where m_p is the *proton* mass, so they are smaller by the ratio of the masses of the electron and proton.] With such magnetic moments, even at a temperature of 2°K, the factor $\mu B/kT$ is only a few parts in a thousand. But if we use the paramagnetic demagnetization process to get down to a temperature of a few thousandths of a degree, $\mu B/kT$ becomes a number near 1—at these low temperatures we can begin to saturate the nuclear moments. That is good luck, because we can then use the adiabatic demagnetization of the *nuclear* magnetism to reach still lower temperatures. Thus it is possible to do two stages of magnetic cooling. First we use adiabatic demagnetization of paramagnetic ions to reach a few thousandths of a degree. Then we use the cold paramagnetic salt to cool some material which has a strong nuclear magnetism. Finally, when we remove the magnetic field from this material, its temperature will go down to within a *millionth* of a degree of absolute zero—if we have done everything very carefully.

35-6 Nuclear magnetic resonance

We have said that atomic paramagnetism is very small and that nuclear magnetism is even a thousand times smaller. Yet it is relatively easy to observe the nuclear magnetism by the phenomenon of "nuclear magnetic resonance." Suppose we take a substance like water, in which all of the electron spins are exactly balanced so that their net magnetic moment is zero. The molecules will still have a very, very tiny magnetic moment due to the nuclear magnetic moment of the hydrogen nuclei. Suppose we put a small sample of water in a magnetic field B . Since the protons (of the hydrogen) have a spin of 1/2, they will have two possible energy states. If the water is in thermal equilibrium, there will be slightly more

protons in the lower energy states—with their moments directed parallel to the field. There is a small net magnetic moment per unit volume. Since the proton moment is only about one-thousandth of an atomic moment, the magnetization which goes as μ^2 —using Eq. (35.22)—is only about one-millionth as strong as typical atomic paramagnetism. (That's why we have to pick a material with no atomic magnetism.) If you work it out, the difference between the number of protons with spin up and with spin down is only one part in 10^8 , so the effect is indeed very small! It can still be observed, however, in the following way.

Suppose we surround the water sample with a small coil that produces a small horizontal oscillating magnetic field. If this field oscillates at the frequency ω_p , it will induce transitions between the two energy states—just as we described for the Rabi experiment in Section 35-3. When a proton flips from an upper energy state to a lower one, it will give up the energy $\mu_z B$ which, as we have seen, is equal to $\hbar\omega_p$. If it flips from the lower energy state to the upper one, it will *absorb* the energy $\hbar\omega_p$ from the coil. Since there are slightly more protons in the lower state than in the upper one, there will be a net *absorption* of energy from the coil. Although the effect is very small, the slight energy absorption can be seen with a sensitive electronic amplifier.

Just as in the Rabi molecular-beam experiment, the energy absorption will be seen only when the oscillating field is in resonance, that is, when

$$\omega = \omega_p = g \left(\frac{q_e}{2m_p} \right) B.$$

It is often more convenient to search for the resonance by varying B while keeping ω fixed. The energy absorption will evidently appear when

$$B = \frac{2m_p}{g q_e} \omega.$$

A typical nuclear magnetic resonance apparatus is shown in Fig. 35-8. A high-frequency oscillator drives a small coil placed between the poles of a large electromagnet. Two small auxiliary coils around the pole tips are driven with a 60-cycle current so that the magnetic field is “wobbled” about its average value by a very small amount. As an example, say that the main current of the magnet is set to give a field of 5000 gauss, and the auxiliary coils produce a variation of ≈ 1 gauss about this value. If the oscillator is set at 21.2 megacycles per second, it will then be at the proton resonance each time the field sweeps through 5000 gauss [using Eq. (34.13) with $g = 5.58$ for the proton].

The circuit of the oscillator is arranged to give an additional output signal proportional to any *change* in the power being absorbed from the oscillator. This signal is fed to the vertical deflection amplifier of an oscilloscope. The horizontal sweep of the oscilloscope is triggered once during each cycle of the field-wobbling frequency. (More usually, the horizontal deflection is made to follow in proportion to the wobbling field.)

Before the water sample is placed inside the high-frequency coil, the power drawn from the oscillator is some value. (It doesn't change with the magnetic field.) When a small bottle of water is placed in the coil, however, a signal appears on the oscilloscope, as shown in the figure. We see a picture of the power being absorbed by the flipping over of the protons!

In practice, it is difficult to know how to set the main magnet to exactly 5000 gauss. What one does is to adjust the main magnet current until the resonance signal appears on the oscilloscope. It turns out that this is now the most convenient way to make an accurate measurement of the strength of a magnetic field. Of course, at some time *someone* had to measure accurately the magnetic field and frequency to determine the g -value of the proton. But now that this has been done, a proton resonance apparatus like that of the figure can be used as a “proton resonance magnetometer.”

We should say a word about the shape of the signal. If we were to wobble the magnetic field very slowly, we would expect to see a normal resonance curve. The energy absorption would read a maximum when ω_p arrived exactly at the

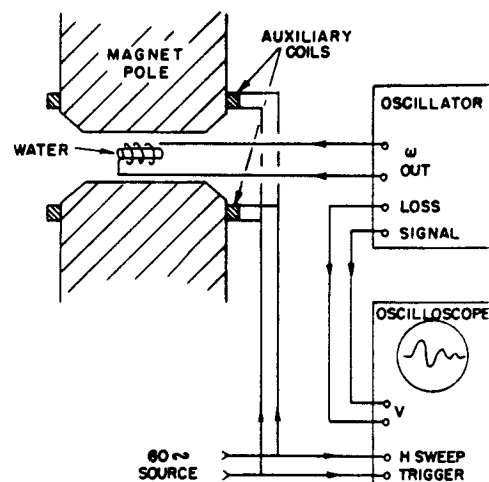


Fig. 35-8. A nuclear magnetic resonance apparatus.

oscillator frequency. There would be some absorption at nearby frequencies because all the protons are not in exactly the same field—and different fields mean slightly different resonant frequencies.

One might wonder, incidentally, whether at the resonance frequency we should see any signal at all. Shouldn't we expect the high-frequency field to equalize the populations of the two states—so that there should be no signal except when the water is first put in? Not exactly, because although we are *trying* to equalize the two populations, the thermal motions on their part are trying to keep the proper ratios for the temperature T . If we sit at the resonance, the power being absorbed by the nuclei is just what is being lost to the thermal motions. There is, however, relatively little “thermal contact” between the proton magnetic moments and the atomic motions. The protons are relatively isolated down in the center of the electron distributions. So in pure water, the resonance signal is, in fact, usually too small to be seen. To increase the absorption, it is necessary to increase the “thermal contact.” This is usually done by adding a little iron oxide to the water. The iron atoms are like small magnets; as they jiggle around in their thermal dance, they make tiny jiggling magnetic fields at the protons. These varying fields “couple” the proton magnets to the atomic vibrations and tend to establish thermal equilibrium. It is through this “coupling” that protons in the higher energy states can lose their energy so that they are again capable of absorbing energy from the oscillator.

In practice the output signal of a nuclear resonance apparatus does not look like a normal resonance curve. It is usually a more complicated signal with oscillations—like the one drawn in the figure. Such signal shapes appear because of the changing fields. The explanation should be given in terms of quantum mechanics, but it can be shown that in such experiments the classical ideas of precessing moments always give the correct answer. Classically, we would say that when we arrive at resonance we start driving a lot of the precessing nuclear magnets synchronously. In so doing, we make them precess *together*. These nuclear magnets, all rotating together, will set up an induced emf in the oscillator coil at the frequency ω_p . But because the magnetic field is increasing with time, the precession frequency is increasing also, and the induced voltage is soon at a frequency a little higher than the oscillator frequency. As the induced emf goes alternately in phase and out of phase with the oscillator, the “absorbed” power goes alternately positive and negative. So on the oscilloscope we see the beat note between the proton frequency and the oscillator frequency. Because the proton frequencies are not all identical (different protons are in slightly different fields) and also possibly because of the disturbance from the iron oxide in the water, the freely precessing moments soon get out of phase, and the beat signal disappears.

These phenomena of magnetic resonance have been put to use in many ways as tools for finding out new things about matter—especially in chemistry and nuclear physics. It goes without saying that the numerical values of the magnetic moments of nuclei tell us something about their structure. In chemistry, much has been learned from the structure (or shape) of the resonances. Because of magnetic fields produced by nearby nuclei, the exact position of a nuclear resonance is shifted somewhat, depending on the environment in which any particular nucleus finds itself. Measuring these shifts helps determine which atoms are near which other ones and helps to elucidate the details of the structure of molecules. Equally important is the electron spin resonance of free radicals. Although not present to any very large extent in equilibrium, such radicals are often intermediate states of chemical reactions. A measurement of an electron spin resonance is a delicate test for the presence of free radicals and is often the key to understanding the mechanism of certain chemical reactions.

MAGNETIC RESONANCE

Atomic nuclei and electrons, which spin on their axes like tops, can be tipped over by magnetic fields. The technique furnishes much information about complex molecules and chemical reactions

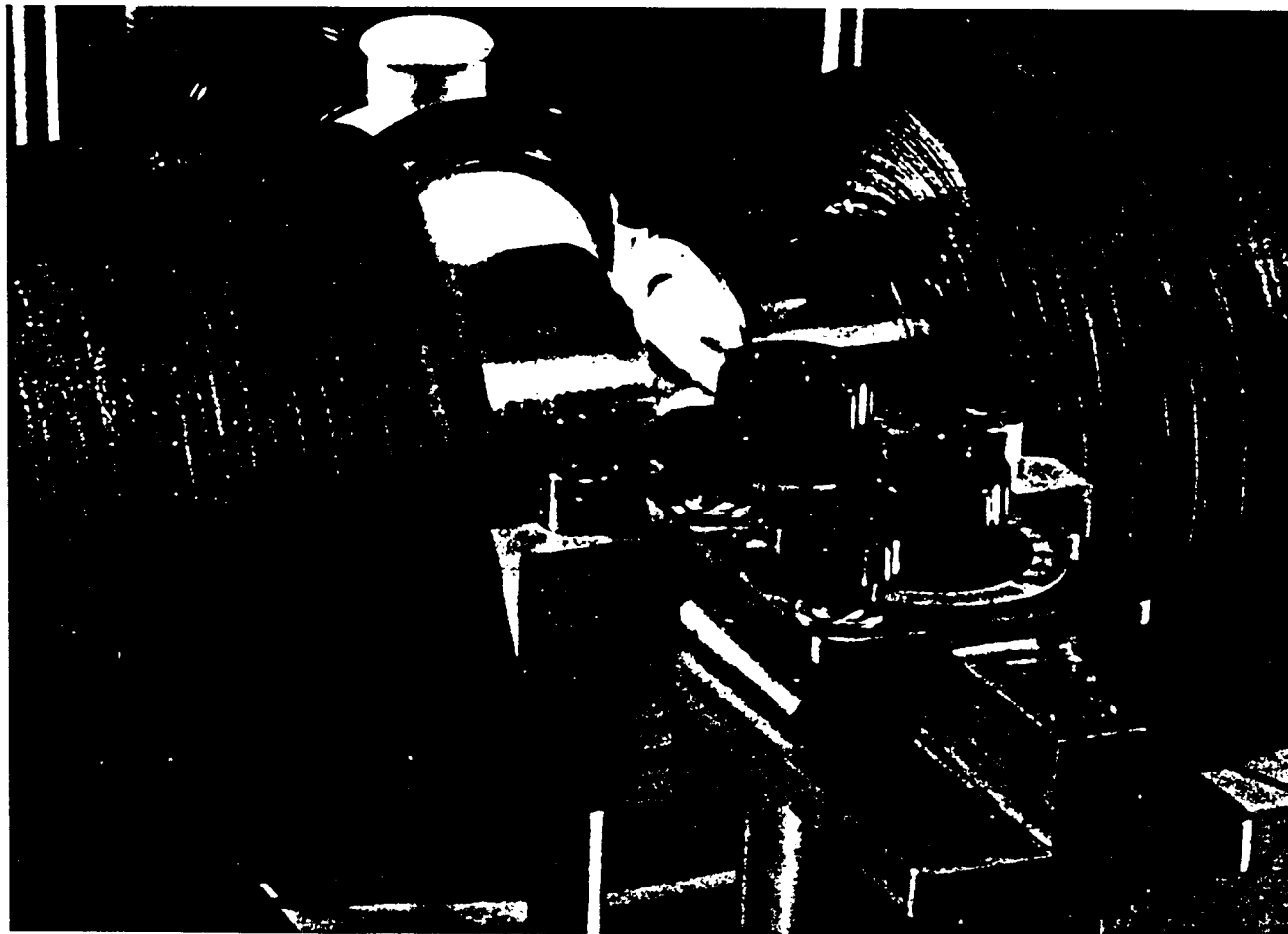
by George E. Pake

Early in 1946 Edward Purcell at Harvard University and Felix Bloch at Stanford University announced, almost simultaneously, an interesting discovery in physics. They had found a way to tune in on the magnetic fields of the spinning nuclei of atoms.

The work was important enough to win the 1952 Nobel prize in physics for Purcell and Bloch.

It is doubtful that many people outside the field of nuclear physics were much excited by or even took notice of these experiments at the time they were

announced. But by now the phenomenon in question, called magnetic resonance, has become a matter of very wide interest indeed. Scientists in various distantly separated lines of work—geologists, chemists, biologists—are, if anything, even more excited about the discovery



MAGNETIC-RESONANCE EXPERIMENT on electrons in chlorophyll demonstrates that photosynthesis involves free radicals. The sample of chlorophyll is in the upright tube in the center, be-

tween the poles of the magnet. The light source which illuminates sample is behind magnet. This photograph was made in the laboratory of Barry Commoner at Washington University in Saint Louis.

than nuclear physicists. For it has led unexpectedly to the development of a sensitive tool useful for a multitude of purposes, from prospecting for minerals in the earth to analyzing the chemistry of living organisms.

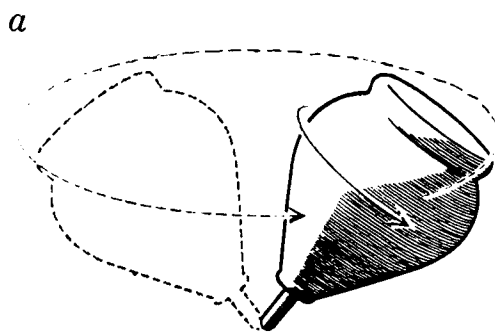
We must start this story by giving thought, as Purcell and Bloch did, to the spinning behavior of the proton. Like the rotating earth, a proton constantly spins around its axis (as do all the other elementary particles of the atom). It spins eternally with a certain momentum, reckoned in the proton's case as one-half unit. Since the proton carries an electric charge, its spin generates a magnetic field; in other words, the proton is a tiny magnet. Now we can ask ourselves the intriguing question: What will happen if we apply an outside magnetic field to this little magnet? Purcell and Bloch fell to wondering (independently) whether it would be possible to use a magnetic field to manipulate the spinning protons in a piece of matter: say, flip them over so that their north and south poles were reversed.

Here it is useful to think of an ordinary spinning top or a gyroscope. As everyone knows, a gyroscope tipped from the vertical does not fall down; instead its upper end circles slowly (precesses) around the vertical. That is to say, the downward gravitational pull of the earth acts to swing the axis of the spinning gyroscope around rather than to tip it further. Similarly, if we apply magnetic force to a spinning proton it will make the proton precess, not tip over. Brute force, in the form of stepping up the strength of the magnetic field, will avail us nothing: it will merely cause the proton to precess faster.

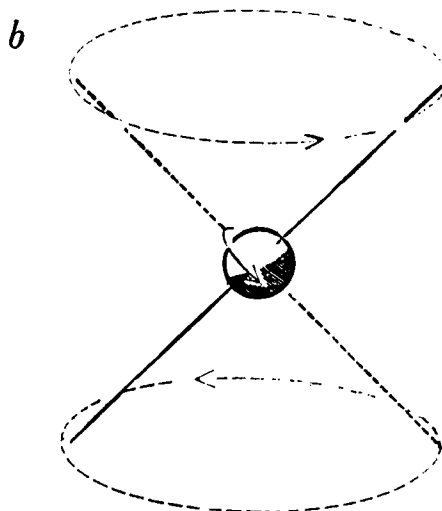
But there is a way to outwit the spinning particles. Suppose we apply a second magnetic field at right angles to the main field. Theory says that if we make the second field rotate around the first (by means of an alternating electric current in a coil), and if we time the rotation so that it coincides exactly with the rate of the proton's precession, we should be able to tip the proton over. In short, with proper tuning (at radio frequencies) the feat may be achieved by a magnetic-resonance effect.

A New Spectroscopy

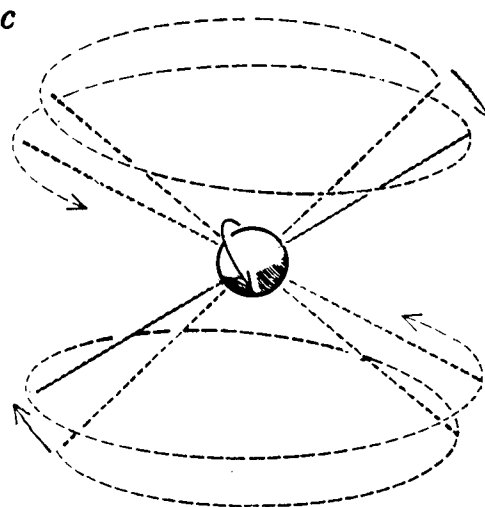
The problem, then, was to find the resonance frequency and to detect the effect on the protons. Purcell and Bloch employed different methods to look for the effect. In Purcell's apparatus the sample of matter was placed between



GRAVITATIONAL FIELD

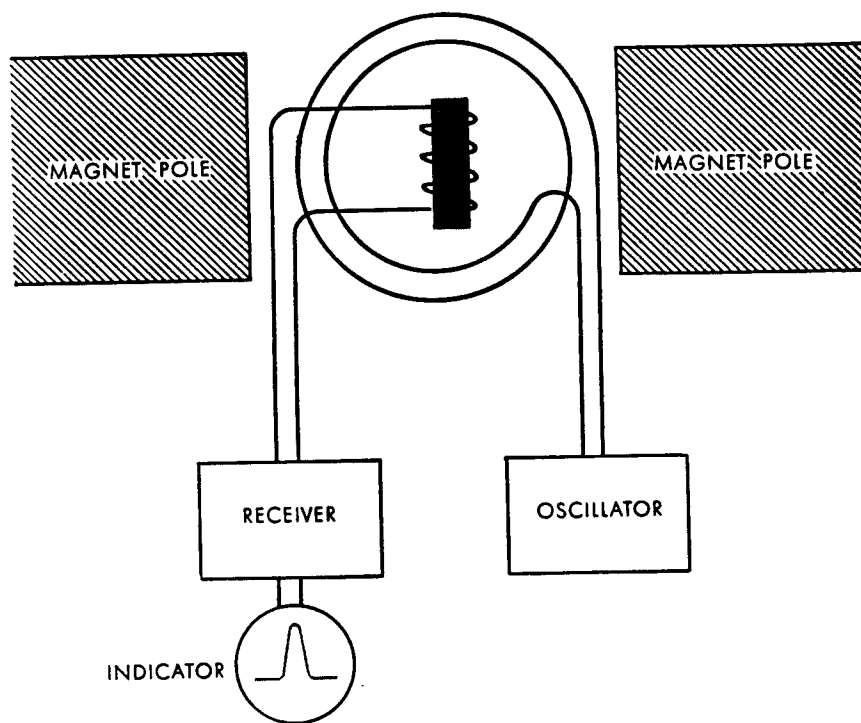
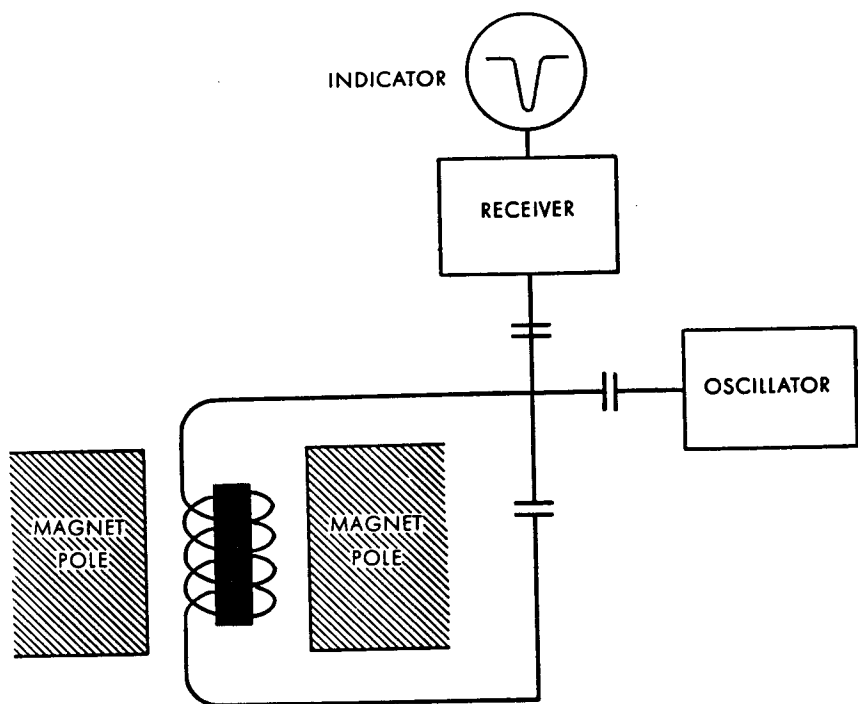


MAGNETIC FIELD



MAGNETIC FIELDS

GYROSCOPIC ACTION of a spinning top or particle causes it to revolve or precess around a vertical field tending to tip it over. Particle can be tipped, as shown in the diagram at the bottom, by applying in addition a rotating horizontal magnetic field (right), which revolves at exactly the same rate as the axis of the precessing particle in the vertical magnetic field.



NUCLEAR-RESONANCE DEVICES designed by Edward Purcell and Felix Bloch are diagrammed schematically. In Purcell's arrangement (top) a single coil passes radio waves from oscillator into sample (gray bar) and feeds into receiver. Resonance is indicated by a dip in received energy. In Bloch's apparatus (bottom) a separate coil picks up energy from tipping particles. Resonance shows up as an increase in energy reaching the receiver.

the two poles of a magnet and surrounded with a coil which produced the second, rotating field [see upper diagram at left]. When the frequency was just right, energy passing along the coil was absorbed by protons in the sample of matter as they flipped over; this absorption of energy was recorded by a sudden dip in the strength of the signal reaching a radio receiver. Bloch's group, on the other hand, devised an instrument which recorded the event by induction of a voltage. As the protons flipped over, the motion of their magnetic fields induced a voltage in a second coil, and this signal was registered on an oscilloscope [see lower diagram at left].

The electron, like the proton, is a charged particle; it, too, spins and has a magnetic field—far stronger than the proton's, because it spins much faster. The electron also exhibits magnetic resonance. Since it is a stronger magnet and much lighter than the proton, it precesses much more rapidly in a given magnetic field. Whereas the proton is probed with radio waves in the range of a few megacycles per second (near the frequencies of ordinary home radio), for electrons the frequencies employed are in the microwave range, around 10,000 megacycles per second.

The magnetic resonance of protons and electrons makes it possible to learn many things about atomic nuclei, atoms and molecules. The magnetic probe amounts, in effect, to a new kind of spectroscopy. This brings us to the varied uses of the discovery in chemistry and biology.

The Structure of Molecules

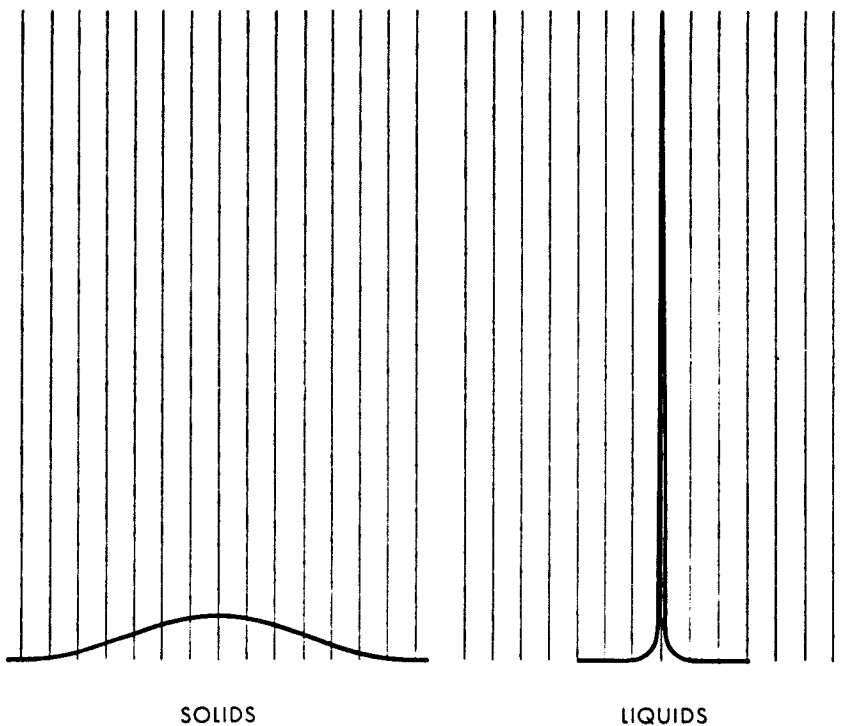
Let us look, for example, at an organic compound such as cyclohexane (C_6H_{12}). We shall examine its resonance spectrum by means of nuclear magnetic resonance (NMR). We measure the substance's resonance in terms of the precession speed at which the nuclei flip over. That is, instead of tuning in to the resonance by varying the frequency of the rotating magnetic field, we use a fixed frequency and vary the strength of the main magnetic field, which controls the precession speed; when the nuclei flip, the resonance reading is taken as the strength of the magnetic field at that point (measured in gauss or oersteds).

When we subject a sample of cyclohexane at room temperature to the proper magnetic field, we get a sharp resonance reading. The compound's hydrogen nuclei flip simultaneously at a certain field strength (the carbon atoms are not

affected). Now the sharpness of this response has to be explained. In any collection of atoms we must reckon not only with the applied magnetic field but also with the little nuclear magnets of the atoms themselves. Each nucleus is subject to the magnets of its neighbors as well as to the applied field. The total magnetic field acting on a nucleus must vary from place to place in the material, because of the varying orientation of the nuclear magnets that happen to surround it. As a result of these variations, the responses to the external field should vary: it should take a slightly stronger applied field to flip some nuclei than others. This means that the resonance range for the whole group of nuclei should be a broad band rather than a sharp line. However, in a liquid the local variations are so short-lived, because of the rapid random motions and mixing of the molecules, that in effect all the nuclei are subject to about the same average field. Thus cyclohexane, a liquid at room temperature, gives a sharp magnetic-resonance line.

The situation is different in a solid. Because the molecules occupy fixed positions, there are persisting local differences in the magnetic field, and accordingly solids tend to have a broad resonance. The resonance band may be as wide as 20 gauss, as against a sharp line as narrow as one 10,000th of a gauss for some liquids. But here cyclohexane offers an unusual and illuminating case. When it is frozen to the solid state, it still has a sharp resonance down to a temperature of 90 degrees centigrade below its freezing point. This tells us that the molecules in the solid must be in some kind of motion. Evidently they rotate around their positions in the crystal lattice, so that the magnetic field averages out to uniformity.

More detailed study of various sub-

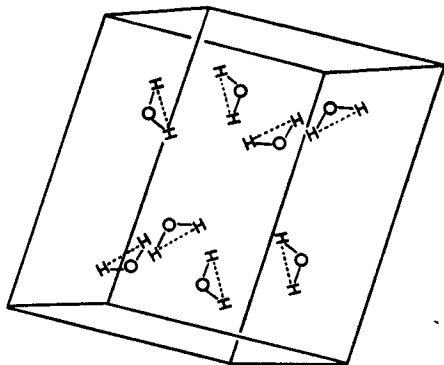


NUCLEAR-RESONANCE CURVES are broad for solids, narrow for liquids. The difference is actually greater than indicated here: the ratio of widths may be as great as 100,000 to 1.

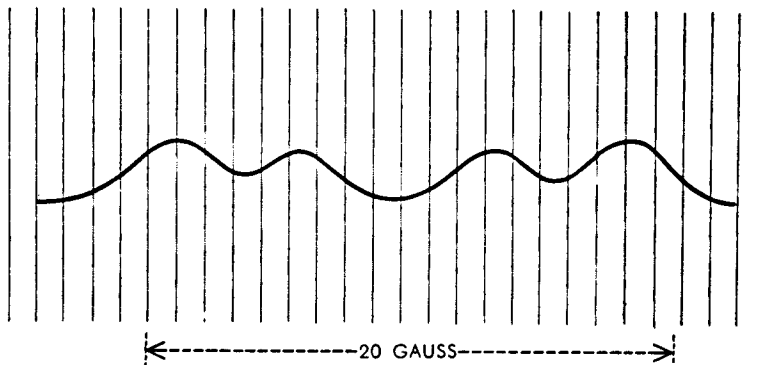
stances, solid and liquid, leads to still more interesting developments. In 1947, while working as a graduate student with Purcell at Harvard, I found that the resonance of the hydrogen nuclei in gypsum was split into four distinct lines [see chart below]. Clearly these must reflect certain definite variations of the magnetic field within the gypsum crystal. By a theoretical analysis it was possible to translate the information into a picture of how the hydrogen atoms lie in the crystal structure. Here, then, was a new tool for analyzing the structure of crystals—a supplement to probing them with X-rays and neutrons. It is particularly useful for locating light atoms such

as hydrogen and lithium, which deflect X-rays only weakly. Nuclear magnetic resonance has now been applied to the study of crystals by scientists in many parts of the world.

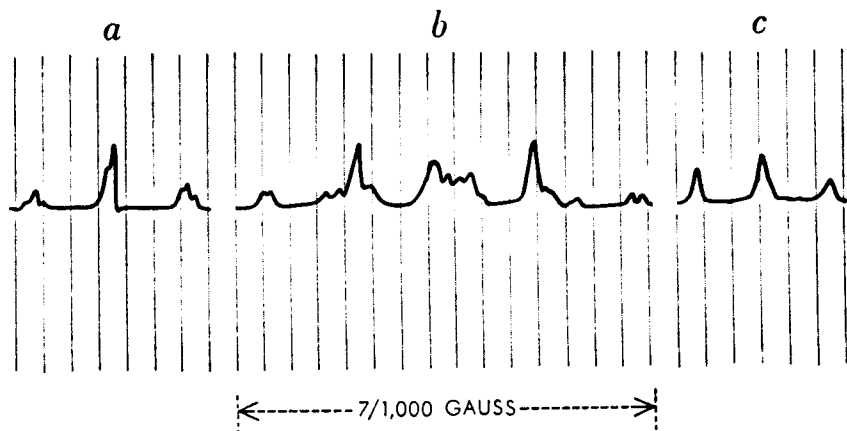
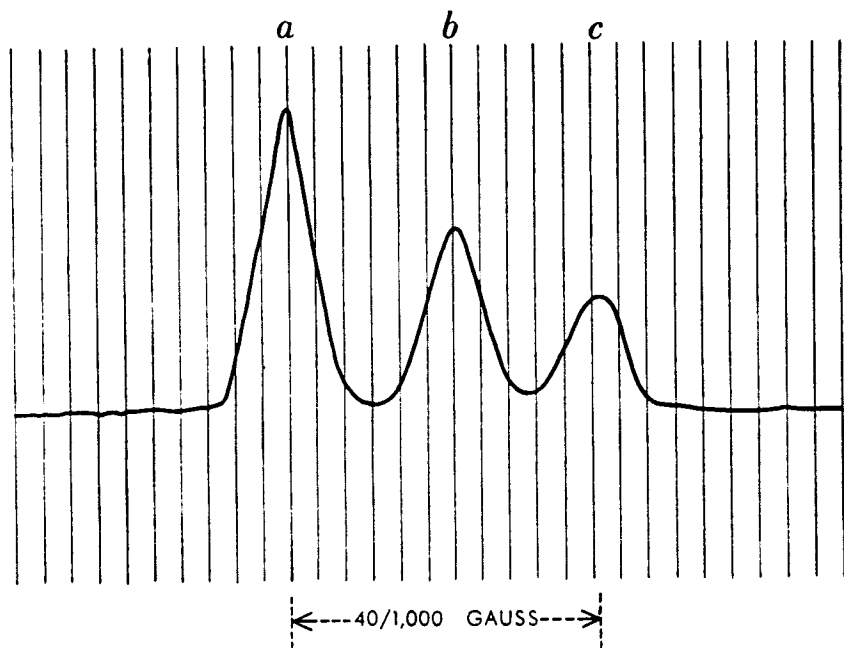
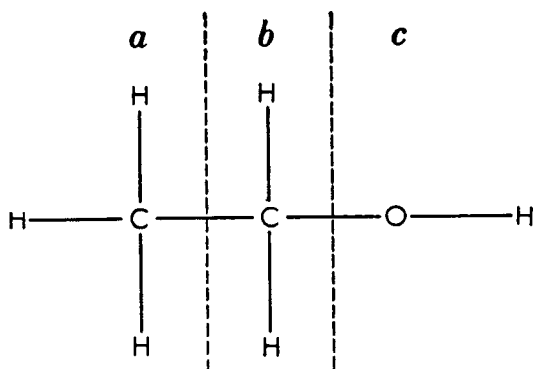
From crystals it was a logical step to go on to study the structure of giant molecules, such as rubber, polyethylene and other plastics. One of the problems in analyzing such molecules is to find out how much of their structure is orderly, or crystalline [see "Giant Molecules," a special issue of *SCIENTIFIC AMERICAN*; September, 1957]. C. W. Wilson, III, one of my graduate students at Washington University in Saint Louis, was able to show that nuclear magnetic reso-



GYPSUM CRYSTAL contains molecules of water, indicated in drawing at left as H-O-H. From the shape of the nuclear magnetic



resonance (NMR) spectrum of gypsum (*right*) the positions of the water molecules in the structure of the crystal can be calculated.



ETHYL ALCOHOL, whose chemical formula appears at top, has a three-peaked NMR spectrum (*center*) when examined with a uniform magnetic field. Letters match hydrogen atoms in various sections of the molecule with their corresponding resonance curves. With a still more uniform field the central part of each curve splits further, as shown at bottom.

nance could be used to examine the structure of these huge molecules.

Fingerprints of Molecules

It is in liquids rather than solids, however, that the technique of nuclear magnetic resonance has achieved its most important triumphs of structural analysis. As we have seen, liquids show sharp resonances, because the magnetic field through the material is almost completely uniform. But a few irregularities can be detected when a liquid compound is examined under a very uniform applied field. Under these circumstances it becomes possible to read the resonance spectrum as a "fingerprint" of the structure of the molecule.

For example, James Arnold and Martin Packard at Stanford University, working with an extremely uniform applied field, were able to resolve the resonance of the hydrogen nuclei in the ethyl alcohol molecule ($\text{CH}_3\text{CH}_2\text{OH}$) into three separate resonances [*see upper chart at left*]. These singled out the three different groups that make up the molecule: CH_3 , CH_2 and OH . The explanation is that the hydrogen nuclei in the three groups respond differently to the applied magnetic field because of a shielding effect of the atoms' electrons. The electrons themselves show no magnetism, for in a molecular combination electrons usually are paired off so that each cancels its partner's magnetic field. But an applied magnetic field slightly alters the motions of electrons around their atomic nuclei; the induced motions of the electrons in turn produce weak magnetic fields opposed to the applied field; this "diamagnetism" partly shields the nuclei from the external field. The amount of shielding differs in the different groups of a molecule, and this explains why the hydrogen atoms in the three groups composing ethyl alcohol have different resonances.

With higher resolution (*i.e.*, under a still more uniformly controlled magnetic field) the magnetic spectrum of the ethyl alcohol molecule splits up into an amazing array of separate resonances [*see lower chart at left*]. The spectrum is a fingerprint of the molecule which not only identifies it but also tells much about its structure. Indeed, from such a fingerprint a chemist can sometimes predict the behavior of a molecule.

Chemists in all branches of their discipline are now busily employing nuclear magnetic resonance to unlock the secrets of structure of many kinds of substances, from soap and motor oil to the extremely

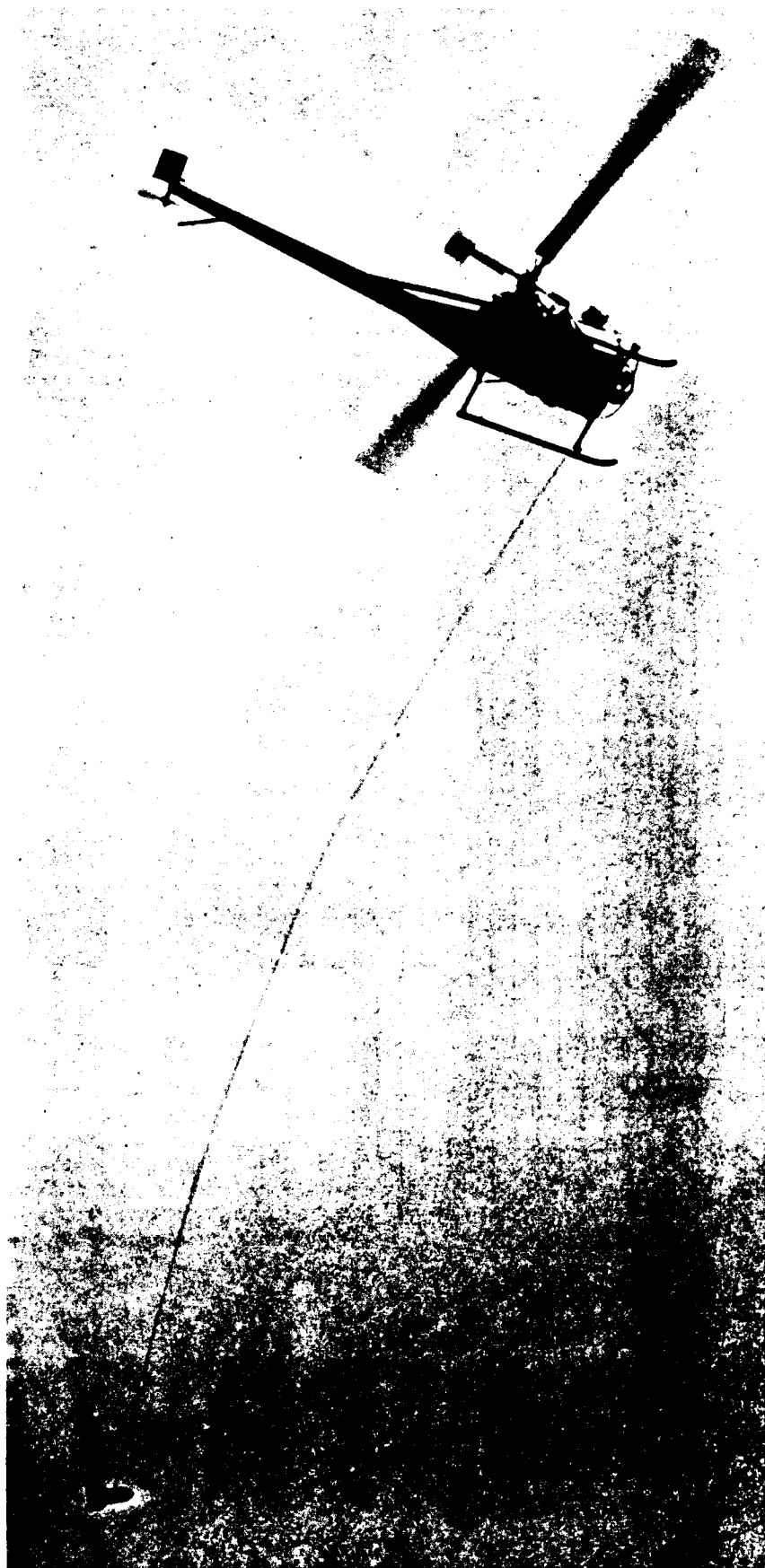
complicated molecules of living matter. One of the virtues of this new analytical tool is that it does not destroy the chemical under analysis. The chemist simply puts the sample in a coil, turns on the radio waves and the magnetic field, records the resonance spectrum and then takes out the sample intact.

Measuring the Earth's Field

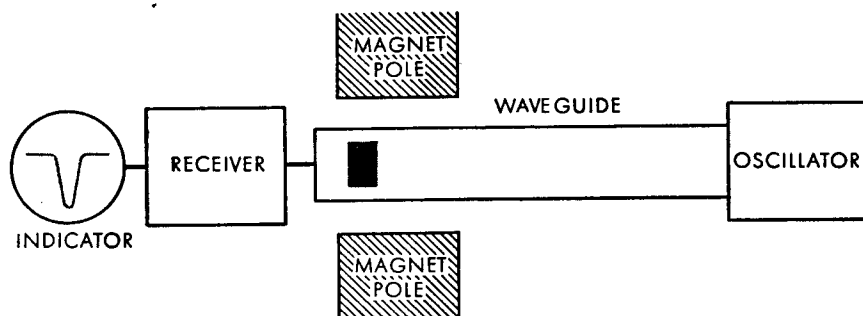
As a final illustration of the versatility of NMR let us look at a very different use—namely, exploring the earth's magnetic field. If very sharp precision in the strength of the applied field is needed to hit the resonance of a liquid, why not reverse the procedure and use resonance for precise measurement of magnetic fields? The difficulty about the earth's field is that it is extremely weak—only about half a gauss. To measure this by the resonance phenomenon, which previously had been studied in the laboratory with fields of thousands of gauss, posed quite a challenge. But Russell Varian and Packard, now with the Varian Associates, have solved the problem with an ingenious device.

Their instrument first lines up the protons in a sample of liquid with a moderately weak magnetic field. The protons are all oriented in one direction so that the whole sample, in effect, is a weak magnet. Then the polarizing field is suddenly switched off; the magnetic rug is pulled out from under the group of protons, so to speak. The nuclear magnets, which have been lined up in a direction *not* parallel to the earth's field, now begin to precess around the axis of this field. Their alignment rapidly breaks down, but in liquid benzene it lasts up to 20 seconds. This is long enough to measure the strength of the earth's magnetic field to an accuracy approaching one part in 10 million. The measurement is made simply by tuning in to the precession rate of the group of protons: since the earth's field produces the precession, the rate is a measure of the strength of the field.

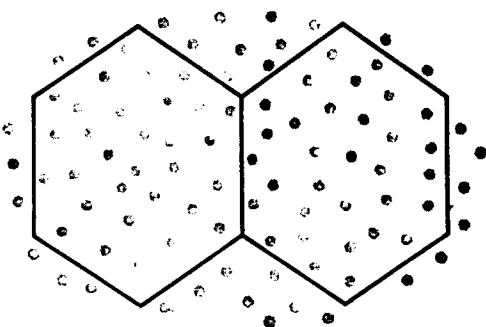
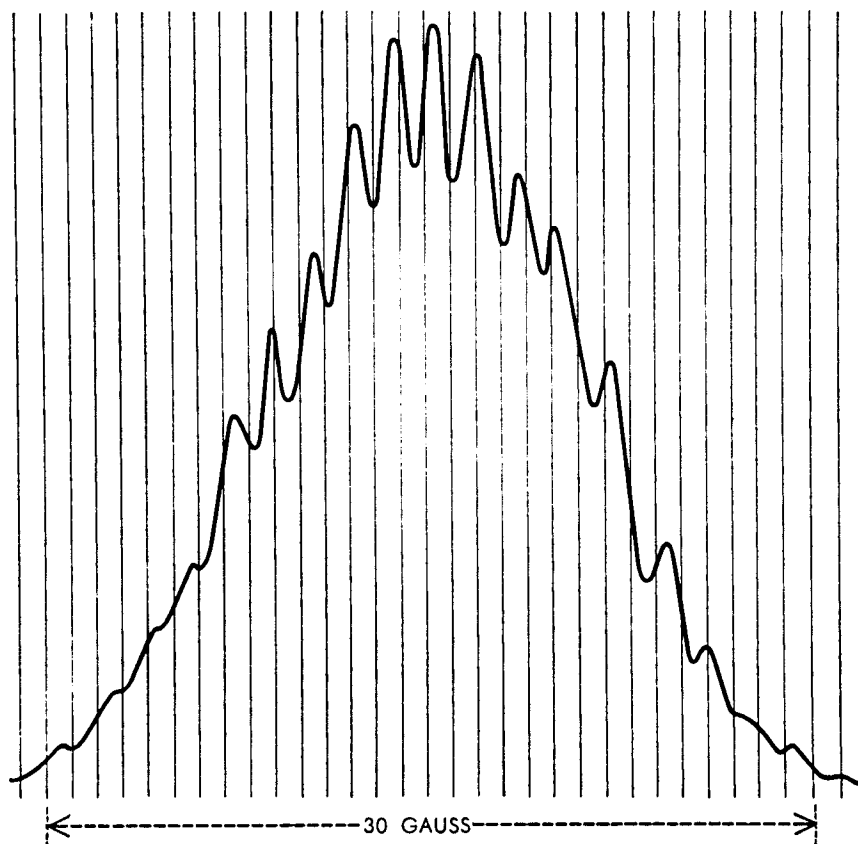
Varian and Packard named their instrument the proton precessional magnetometer. Obviously this amazingly sensitive device could serve to measure variations in the earth's magnetic field. It has already been put to use in prospecting for mineral deposits, from the air and on the ground [see photograph at right]. The instrument has also been shot in rockets to measure the strength of the earth's field at various heights above the surface. A magnetometer of this type is scheduled to go up in



MAGNETOMETER based on nuclear magnetic-resonance principle measures small variations in the earth's field. Here it is towed by a helicopter in a mineral-prospecting survey.



ELECTRON-RESONANCE APPARATUS operates on the same principle as Purcell's circuit shown on page 4. A microwave oscillator sends three-centimeter radio waves through the waveguide. The sample (gray rectangle) is mounted on the inside of the guide. Resonance is indicated by a decrease in the power delivered by the waveguide to the receiver.



HYPERFINE STRUCTURE (jagged splitting) of an electron-paramagnetic-resonance (EPR) spectrum indicates various positions of the unpaired electron in a free-radical molecule. This curve comes from naphthalene radicals. Gray dots in the structural outline of the radical at bottom indicate that the free electron wanders over many parts of the molecule.

one of the U. S. artificial satellites soon. Surely Purcell and Bloch could hardly have foreseen that their exploration of the magnetism of the proton would lead to such developments.

The Resonance of the Electron

Let us turn now to the magnetism of the electron. The magnetic resonance of this particle was discovered by a Soviet physicist, E. K. Zavoisky, in 1944, before Purcell and Bloch tuned in on the proton. But curiously enough the Russians apparently were not as quick to exploit the discovery as physicists in the U. S., Great Britain and the Netherlands. At all events, the electron's resonance, called electron paramagnetic resonance (EPR), has now been forged into a tool as important in its area of usefulness as nuclear magnetic resonance.

As we have seen, the electron, because of its smaller mass and faster spin, is a much stronger magnet than a proton. As a result, a given magnetic field makes it precess far more rapidly. Its precession rate in the standard laboratory magnetic field is in the range of the frequency of radio microwaves—that is, about 10,000 megacycles per second, or a wavelength of about three centimeters.

When microwaves travel down a rectangular waveguide (the tube used to conduct such waves), they produce a rotating magnetic field at any fixed point. This field can serve to flip over the electron magnets in matter, just as a rotating field in a coil flips protons. The experimenter may place the sample of material on a side wall of the waveguide, turn on the radio waves and apply an external magnetic field to make the electrons precess. When the precession rate reaches the resonance value and the electrons flip, they extract energy from the radio waves, and the reading on a receiver at the end of the tube dips accordingly.

Now this technique obviously can tell us nothing about substances in which the electrons are all paired, *i.e.*, where the electrons' magnetism is neutralized. But it has proved very helpful indeed in studying material with unpaired electrons. Electron resonance was first applied to investigate crystals containing elements with unfilled electron shells (therefore unpaired electrons)—elements such as manganese and iron. Much has been learned about substances of this kind, particularly about those used for "magnetic" cooling of matter to very low temperatures.

But more exciting has been the discovery that electron resonance can be used to investigate free radicals, the

transitory molecular fragments that play a crucial role in many chemical processes, including the chemical activities of living cells [see "Free Radicals," by Paul D. Bartlett; *SCIENTIFIC AMERICAN*, December, 1953]. Free radicals, of course, have unpaired electrons, and with the electron-resonance technique it is sometimes possible to detect these fleeting substances and to learn something about their structure and behavior.

At first thought one might suppose that the resonance spectrum of the unpaired electron in a free radical should always be the same—one free radical indistinguishable from another. But this is not the case. The electron is affected by the magnetic field of the nuclei in whose neighborhood it happens to be, and as the free electron wanders about in the molecular fragment, it is subjected to varying magnetic fields. As a result its resonance may be split into a "hyperfine structure" [see chart on page 8]. From the splitting we may learn where the electron spends its time and at what rate the free radical is likely to enter into chemical reactions.

Such studies are not limited to natural free radicals. With high-energy particles from an accelerator it is possible to break a molecule into fragments, and the fragments can sometimes be frozen in their tracks, so to speak, by keeping the sample at a very low temperature. We can then see what has happened to the molecule by examining the electron resonances of the fragments. This kind of investigation could be useful for studying the chemical effects of radiation on certain plastics; irradiation is known to strengthen some plastics by causing them to form new chemical bonds. Magnetic resonance also looks promising as a tool for investigating the free radicals that catalyze the synthesis of high polymers such as rubber or polyethylene [see "How Giant Molecules Are Made," by Giulio Natta; *SCIENTIFIC AMERICAN*, September, 1957].

Resonance in Living Cells

To illustrate the interest of biologists in magnetic resonance, I shall close this account with an episode that began in Saint Louis one evening in 1951. After attending a chamber music concert, a few members of the Washington University faculty repaired to someone's home for coffee, and the conversation turned (probably to the wives' chagrin) to shop talk. Barry Commoner of the botany department fell to discussing the theory that free radicals play an important role in the processes of oxidation

and reduction in living cells, and he remarked how difficult it was to detect free radicals in living systems. I suggested that electron resonance might be helpful, and offered to help Commoner and his group learn how to use the method. Thus began a most interesting series of experiments.

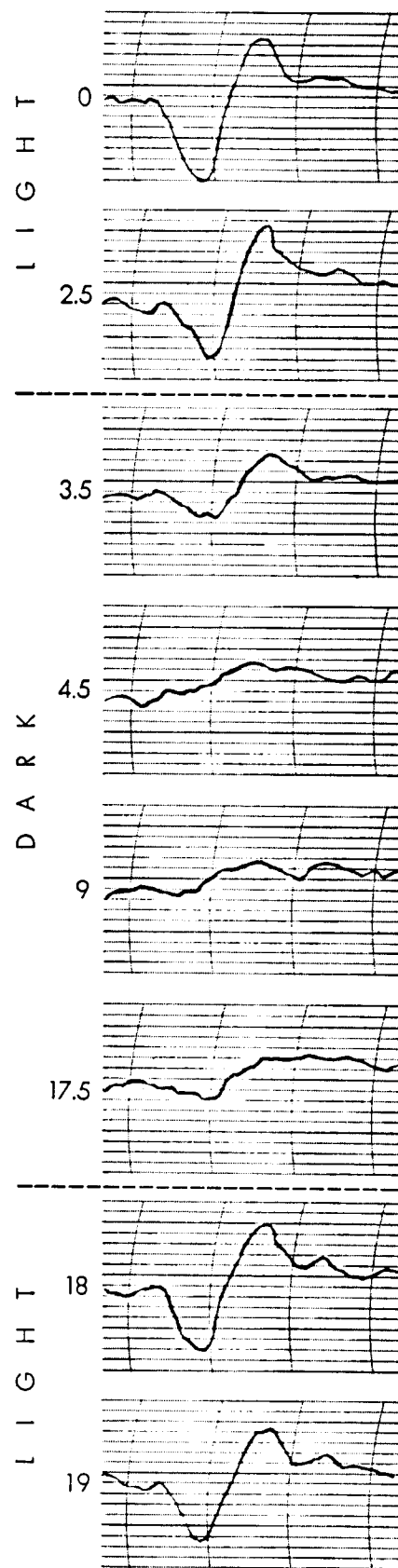
The first results were disappointing. Since the experiments involved cultures of cells (yeast and other organisms), there was moisture in the microwave apparatus, and moisture absorbs microwaves. This absorption of course masked the dip in radio energy produced by magnetic resonance. Even so, the experimenters finally detected a weak resonance from yeast and found that its intensity varied with the rate at which oxygen was consumed by the yeast cells. Then a resonance was discovered in green leaves ground up and quickly freeze-dried to eliminate the absorption by moisture.

To study the active process of photosynthesis in its necessary moist environment, however, called for a much more sensitive apparatus. Jonathan Townsend of the physics department succeeded in devising one, and it became possible to work with living cells. The cells selected contained chloroplasts—the small, green, chlorophyll-packed bodies which are thought to carry out most if not all the steps of photosynthesis.

The cells were placed in the sensitive magnetic resonance apparatus and were simultaneously irradiated with white light from a 50-candle-power lamp. The chloroplasts immediately showed a dramatic resonance spectrum [see charts at right]. When the light was turned off, the resonance soon weakened or disappeared entirely. Next the cells were exposed to light of various specific wavelengths; it turned out that the resonance appeared at the very same range of wavelengths of light that produces photosynthesis.

Commoner and Townsend have gone on to further experiments which not only have linked free-radical activity firmly to photosynthesis but have also indicated that free radicals are involved in the metabolism of cancer cells. And biological investigators in many other laboratories have begun to adopt electronic resonance as a tool in their researches.

That basic discoveries in science invariably bear fruits which cannot be foretold is an old story to scientists. Even so it has been a great thrill to see what has grown out of the work of Purcell, Bloch and Zavoisky, who were seeking only to get a better understanding of the magnetism of the particles in the atom.



CHLOROPHYLL SAMPLE gives sharp EPR spectrum when irradiated with light. This proves that free radicals are involved in photosynthesis. Numbers at left indicate minutes from the start of the experiment.

The Author

GEORGE E. PAKE was Edward Purcell's graduate student at Harvard University when Purcell was just beginning his Nobel-prize-winning work on magnetic resonance. Pake, who is now professor of physics at Stanford University, has been investigating magnetic resonance ever since. Pake grew up in Kent, Ohio, where his father taught English at Kent State University. As a student in the University's "laboratory" high school for teacher training, he had access to the University library, and there his interest soon turned from baseball and model airplanes to physical science. With the help of Kent State's faculty, Pake received a head start in physics which served him well when, as a Westinghouse Scholarship student at the Carnegie Institute of Technology, he received his B.S. and M.S. degrees just 32 months after matriculating. "My undergraduate career whizzed by in a kind of blur," Pake reports. "I often think I would never have survived the concentrated dose of studies had it not been for my music and the opportunity to play French horn in the Carnegie Tech or-

chestra." Pake worked at Westinghouse Research Laboratories for a year, then went to Harvard, where he received his Ph.D. in 1948. Four years later, at the age of 28, he became chairman of the physics department at Washington University in Saint Louis. He has been at Stanford since 1956.

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the thermocouple and heater wires must be connected to a proper vacuum tight feed through² which is attached to the middle cylinder. The system is then operated by simply pouring liquid nitrogen into the dewar. The sample temperature stabilizes at some temperature above -196°C . We usually obtain a temperature of -120°C easily, and with better vacuum and shielding against thermal radiation from outside, one should get better results. As the nitrogen vaporizes, the sample temperature begins to rise. The heater may be used to obtain higher temperatures. One may use a combination of the above temperature controller and the cryostat to cover a wider range of temperatures. Note that a J-type thermocouple³ provides an easy means of sensing the low temperatures the cryostat can achieve.

When dealing with various properties of semiconductors and other solid samples, it is absolutely essential to be able

to control their temperature. Despite their obvious limitations, the systems described above provide a low-cost and low-maintenance alternative to the commercially available units.

¹For a table of various types of windows and their transmission properties, see D. L. Greenway and G. Harbecke, *Optical Properties and Band Structures of Semiconductors* (Pergamon, Oxford, 1968), Table 3.2.

²A typical feed through with eight wires on 1.33-in. flange may be obtained from Huntington Mechanical Laboratories, Inc., 1040 L'Avenida, Mountain View, CA 94043.

³J-type thermocouple consists of iron and constantan (copper-nickel alloy) wires, welded at their tips. Commercial J-type thermocouples may be obtained from Omega Engineering, Inc., 1 Omega Dr., Box 4047, Stamford, CT 06907. The Omega catalog contains information about a variety of thermocouples, the principles of their operation, and the range of their application.

Comparison of the gyromagnetic ratios of the ^1H and ^{19}F nuclei—A student experiment

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An exercise sometimes included in senior undergraduate teaching laboratories is that in which a nuclear gyromagnetic ratio is determined by magnetic resonance. The experiment is normally performed using protons (e.g., in the form of glycerol). The sample is contained within a coil that forms part of an oscillator resonant circuit. Frequently a marginal oscillator is used—see, for example, Ref. 1. In the usual absorption form of the experiment the coil is lo-

cated in a uniform steady magnetic field B_0 on which a small alternating component is superimposed at mains frequency. Provided the oscillator frequency f is close to the resonant value f_R given by

$$f_R = \gamma B_0 / 2\pi,$$

where γ is the gyromagnetic ratio of the nucleus concerned, then resonance occurs twice in every cycle of the alternating component of the magnetic field. The absorption signals are usually displayed on an oscilloscope which is also swept at mains frequency. A phase shifter enables the absorption signals to be superimposed and then the frequency (or magnetic field) is finally adjusted to centralize them on the oscilloscope trace. Knowing B_0 (e.g., from Hall probe measurements) and measuring f_R then γ is obtained.

An instructive modification of this experiment that may not be generally recognized permits a comparison of the gyromagnetic ratios of the ^1H and ^{19}F nuclei without the need either for magnetic field measurement or for probe head change. The sample can conveniently take the form of a cylindrical rod of PTFE (polytetrafluoroethylene) with a hole drilled axially through it; this rod has the oscillator resonant coil wound round it, and it is immersed in glycerol. The PTFE rod supplies the fluorine nuclei and the glycerol the protons. For operation in the region of 10 MHz, say, the rod can be some 12 mm in length and 6 mm in diameter with an axial hole 2.5 mm in diameter. Although the fluorine resonance is weaker than the proton resonance, it can be detected quite readily given a sufficiently uniform magnetic field over the volume of the sample. The gyromagnetic ratios of the two nuclei differ by only about 6%. Thus a single oscillator range from say 8 to 12 MHz

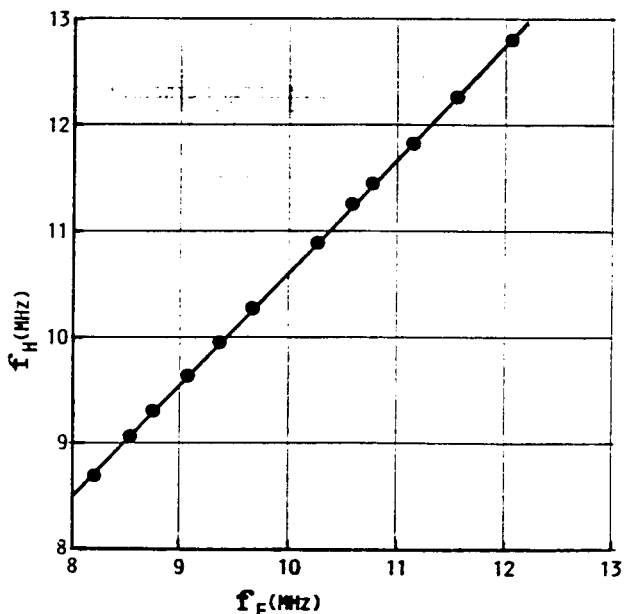


Fig. 1. ^1H resonant frequency plotted against corresponding ^{19}F resonant frequency for a range of magnetic field values.

can cover both resonances for a considerable range of values of magnetic field current.

The procedure is first to find the proton resonance for a given magnetic field current and then to decrease the oscillator frequency by a few percent until the fluorine resonance comes in. This pair of frequency readings is repeated for successively increasing magnetic field currents until the full oscillator range has been used.

Figure 1 shows a recent student's experimental results in which the two resonant frequencies (for various magnetic fields ranging from 0.2 to 0.3 T) are plotted against each other.

The slope of the graph gives a value for the ratio of the gyromagnetic ratios of the ^1H and ^{19}F nuclei as

$$1.06 \pm 0.01.$$

This agrees with the generally accepted value to within 1%.

ACKNOWLEDGMENT

I am indebted to third-year student Jeanette Bird for permission to use her recent experimental results.

'Ijaz-ur-Rahman "Transistorized marginal oscillator NMR detector with improved performance," Am. J. Phys. 47, 1004 (1979).

GUESS WHAT? THE FOUR-YEAR COLLEGES ARE STILL WITH US

...my uneasiness grows out of my partisanship toward the four-year college and toward physics. It is from the viewpoint of this partisanship that I am disturbed as I wonder: Can the four-year college prepare physics majors?... I think that, for a minimum of the next generation or so, we can safely presume the existence of the four-year liberal arts college. The question is simply whether or not physics is to be a part of it.

George E. Pake, "Can Four-Year Colleges Prepare Physics Majors for Graduate Work in Physics?" Am. J. Phys. 29, 678-684 (1961).

The 50 liberal arts colleges [discussed in this report] appear prominently among the most productive institutions *per capita* on six measures of student outcome: receipt of NSF Fellowships, earned doctorates in the sciences, membership in *American Men and Women of Science*, listing in *Who's Who in Frontier Science and Technology*, appearance among the 1000 authors of scientific literature whose work is most often cited in subsequent publications, and membership in the National Academy of Sciences. When ranked with the 20 top-rated research universities, the 50 colleges command a majority of the 25 most productive institutions *per capita* on fully five of the six outcomes measures. The colleges form a majority of the ten most productive schools on two of the measures, and represent five of the top ten institutions in *per capita* productivity on two other measures.

Sam C. Carrier and David Davis-Van Atta, *Maintaining America's Scientific Productivity: The Necessity of the Liberal Arts Colleges*, Report of the Second Oberlin Conference, Oberlin College, 1986.

Z^2 , Z^3 , X , Y , XZ , YZ , XY , X^2 , $-Y^2$, etc.) before each spectrum is taken. With the advent of microprocessor-controlled spectrometers, the bulk of these adjustments are now accomplished automatically.

We are left with a paradox. To get an acceptable signal, we need to have as many nuclei as possible in the sample region (remember the minute difference between spin state populations?). But we must restrict our sample to the smallest possible volume in the interest of precision and resolution. The eventual compromise results in a sample cavity of $\sim 0.05 \text{ cm}^3$ for instruments that accommodate narrow-bore (5-mm-o.d.) tubes to $\sim 1.0 \text{ cm}^3$ for instruments using wide-bore (10–20-mm-o.d.) tubes. [However, for medical use, some low-resolution NMR instruments have been constructed that accommodate entire human bodies! (See Chapter 16)] Typically, ^1H and ^{13}C spectra require ca. 5 and 15 mg of sample, respectively.

■ **EXAMPLE 3.3** A typical thin-wall narrow-bore NMR tube has an outside diameter of 5.00 mm (0.500 cm) and an inside diameter of 4.20 mm. It is usually filled to a height of ~ 1 in. (2.5 cm). (a) What is the wall thickness of the glass tube? (b) If the total volume of the sample cavity (including the tube) is 0.050 cm^3 , what are the dimensions (radius r , height h , and volume) of the space that is actually occupied by sample? [Hint: The volume of the cylinder is $\pi r^2 h$.]

□ **Solution:** Refer to Figure 3.6.

- (a) Wall thickness = $(5.00 \text{ mm} - 4.20 \text{ mm})/2 = 0.40 \text{ mm}$.
 (b) The diameter of the sample is the same as the inside

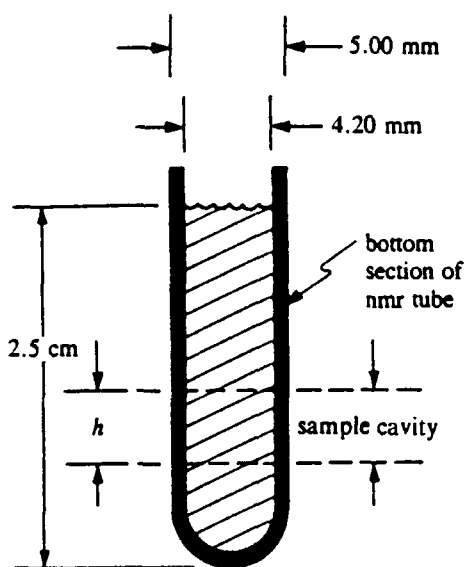


Figure 3.6. Bottom section of an NMR sample tube and the sample cavity where the NMR signal is generated.

diameter of the tube, 0.42 cm. The height of the sample cavity is given by

$$h = \frac{V_{\text{total}}}{\pi r_{\text{total}}^2} = \frac{0.050 \text{ cm}^3}{\pi(0.25 \text{ cm})^2} = 0.255 \text{ cm}$$

Since $r_{\text{sample}} = 0.42 \text{ cm}/2 = 0.21 \text{ cm}$,

$$V_{\text{sample}} = \pi r_{\text{sample}}^2$$

$$h = \pi(0.21 \text{ cm})^2(0.255 \text{ cm}) = 0.035 \text{ cm}^3 = 35 \mu\text{L}$$

Thus, only 70% of the sample cavity is filled with sample in this case. Clearly, the thinner the wall of the tube, the more sample actually gets into the sample cavity. Furthermore, for samples in very limited supply (<1 mg), precisely machined Teflon inserts for the tubes are available to both reduce the amount of dead volume in the tube below the sample cavity and prevent formation of vortices (whirlpools) of the solution within the tube when it is spun. □

There is one more thing you should know about the powerful magnets used in today's NMR spectrometers. If you get too close to the magnet itself, you run the risk of demagnetizing anything on your person, such as credit cards, magnetic tapes, and computer diskettes. (This fact was central to the plot of a recent novel by Joseph Wambaugh.) But no need to worry; it will not affect your magnetic personality!

3.2.2 Assembling the Pieces

We are now ready. The magnetic field is locked at 5.87 T and a sample containing a substance with ^1H nuclei, dissolved in a deuterium-containing solvent, is spinning in the probe. We activate the rf oscillator in the transmitter coil, producing a B_1 field oscillating at 250 MHz radiation, and . . . yes! A weak signal is detected in the receiver circuit! But let us not celebrate yet. What has this told us, except that we have ^1H in the sample, precessing at 250 MHz? Certainly, we would like to be able to adjust parameters to test for nuclei precessing at other frequencies as well. How can we accomplish that?

3.3 SIGNAL GENERATION THE OLD WAY: THE CONTINUOUS-WAVE (CW) EXPERIMENT

Recall from Chapter 2 that, at a given field strength, each magnetic isotope ($I \neq 0$) precesses at a unique frequency governed by its magnetogyric ratio [Eq. (2.6)]; see Figure 3.7. Thus, if we intend to use our spectrometer to observe nuclei other than ^1H , there must be a way to vary either the operating (B_1) frequency or the magnetic field strength.

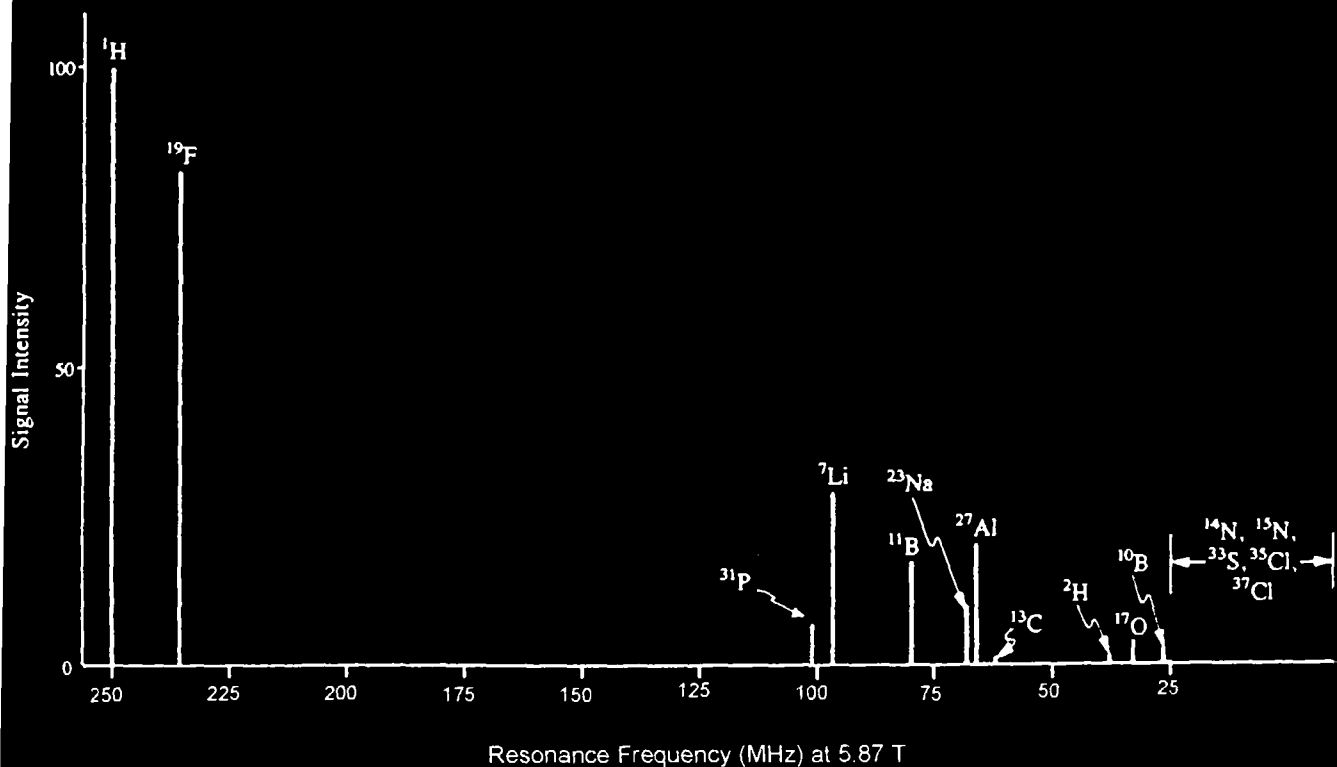


Figure 3.7. Resonance frequencies and relative sensitivities of several common isotopes at 5.87 T; compare with Table 2.1.

From the discussion in Section 3.2, it is clear that the field strength of any type of electromagnet can only be varied within an extremely narrow range. This means that the nominal operating frequency for, say, ^1H nuclei is also fixed. (In fact, the model number of most commercial NMR spectrometers is the same as the ^1H operating frequency in megahertz.) Since, for a given instrument, we cannot change \mathbf{B}_0 , the only way to investigate nuclei other than ^1H is to switch to a different rf oscillator (\mathbf{B}_1 source) with a frequency appropriate for the specific nucleus of interest (e.g., ^{13}C or ^{31}P). In the old days, switching oscillator circuits could be a rather tedious process, but these days it requires little more than pushing a few buttons or typing a few commands into the computer that controls the instrument.

However, as we will see in Chapter 5, the real value of NMR does not come from generating one signal for each isotope present in the sample (e.g., one signal each for ^1H , ^{13}C , or ^{31}P). Rather, we will find that even the individual nuclei of the same isotope in different molecular environments can precess at *slightly different* frequencies (on the order of parts per million), and these small differences can tell us much about the details of the molecular structure involved. Thus, we normally examine only one isotope (e.g., ^1H) in each NMR spectrum; that is, each spectrum is **homonuclear**. Since we are examining only one isotope at a time, we only have to

vary the magnetic field (field sweep) or rf frequency (frequency sweep) over narrow limits to see all of the nuclei of that specific target isotope. All older NMR spectrometers, equipped with conventional electromagnets, used either field- or frequency-sweep technology. Because both involved continuous operation of the rf (\mathbf{B}_1) oscillator, they were both referred to as continuous-wave (cw) techniques.

3.3.1 Frequency-Sweep Mode

In the case of a frequency-sweep cw experiment, the magnetic field strength (\mathbf{B}_0) was fixed. Suppose our sample contained two different nuclei (A and B) characterized by slightly different resonance frequencies, with $\nu_A > \nu_B$. The spin state energies of these two nuclei are depicted in Figure 3.8a. In order for nuclei A and B to generate resonance signals, Eq. (2.7) requires they be irradiated with \mathbf{B}_1 frequencies given by

$$\nu_A = \frac{\Delta E_A}{h} \quad (3.2a)$$

$$\nu_B = \frac{\Delta E_B}{h} \quad (3.2b)$$

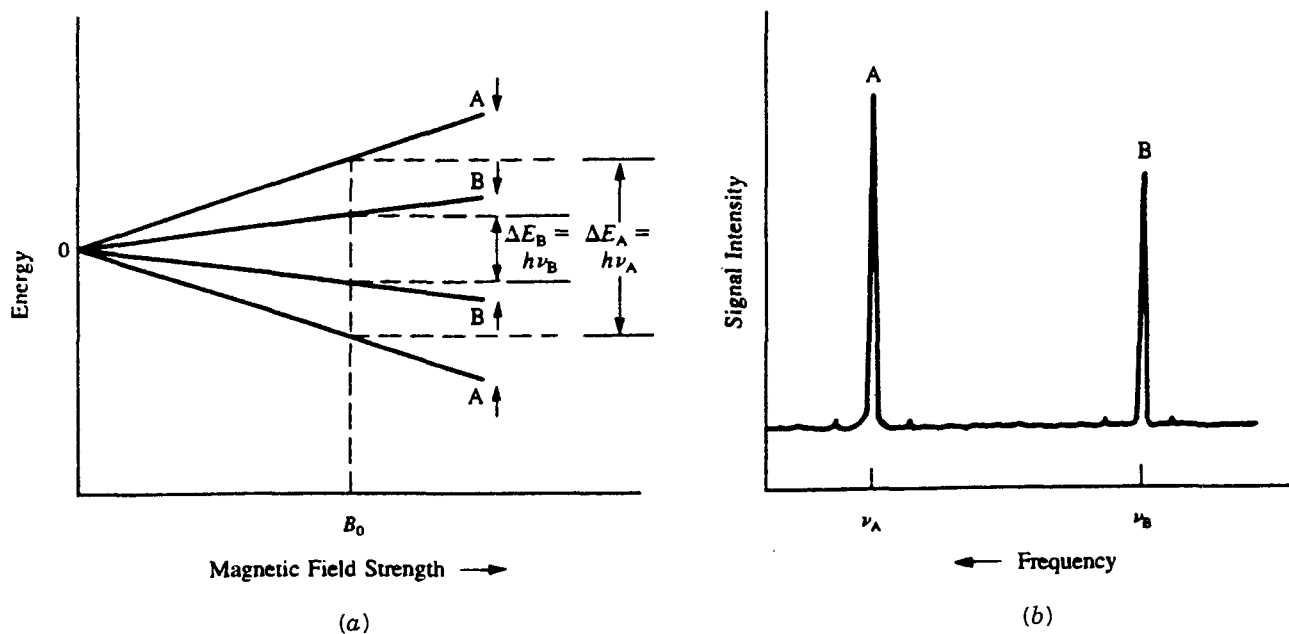


Figure 3.8. (a) Spin state energy gaps (ΔE) for two different nuclei at field strength B_0 . (b) Resulting frequency-sweep NMR spectrum.

Thus, it was necessary to sweep the operating frequency over the range ν_A to ν_B (or vice versa) using a *variable-frequency* rf transmitter. This *range* of frequencies ($\nu_A - \nu_B$) is called the **spectral width** (or sweep width), SW, of the spectrum and was limited to about 2000 Hz. Beginning at a frequency a little less than ν_B , the frequency of the continuous rf radiation was gradually increased to a value above ν_A while the receiver circuit was constantly monitored for a signal. As the frequency passed first through ν_B , then through ν_A , two separate signals were detected. A plot of the intensity of these signals versus frequency (Figure 3.8b) is our first **frequency-domain** NMR spectrum, with frequency increasing from *right to left* (as is the convention).

3.3.2 Field-Sweep Mode

Although some early NMR spectrometers did employ the frequency-sweep (at constant field) technique, it turned out to be electronically simpler to maintain the constant B_1 oscillator frequency appropriate for the target isotope and sweep (vary) the magnetic field to achieve resonance for the nuclei in the sample. By passing a slowly increasing direct current through **sweep coils**, the magnetic field B_0 could be varied through a limited range while maintaining its homogeneity in the sample area. Let us investigate how this change affected the spectrum.

Because the operating radio frequency (ν_0) was now constant, only photons of energy $h\nu_0$ were available in the experi-

ment [see Eq. (1.3)]. Thus, the *energy gap* [ΔE , Eq. (2.4)] for *each* nucleus had to be adjusted by varying the magnetic field strength B_0 . By rearranging Eq. (2.7), we can solve for the field strength at which nuclei A and B entered resonance:

$$B_A = \frac{2\pi\nu_0}{\gamma_A} \quad (3.3a)$$

$$B_B = \frac{2\pi\nu_0}{\gamma_B} \quad (3.3b)$$

Figure 3.9a depicts the situation graphically. This time, instead of varying the B_1 frequency until it matched the precessional frequencies of nuclei A and B, we varied the precessional frequencies (by varying the field strength) until they matched the B_1 frequency. Most importantly, the resulting spectrum (Figure 3.9b) was *indistinguishable* from the frequency-sweep spectrum, except that the abscissa was calibrated in magnetic field units increasing from *left to right*.

Comparing Figure 3.8b with Figure 3.9b reveals that nucleus A enters resonance at a higher frequency (at constant field) or at a lower field (at constant frequency) than does nucleus B. For this reason, the right-hand (low-frequency) side of an NMR spectrum is often referred to as the *high-field* (or *upfield*) side, while the left-hand (high-frequency) side is called the *low-field* (or *downfield*) side.

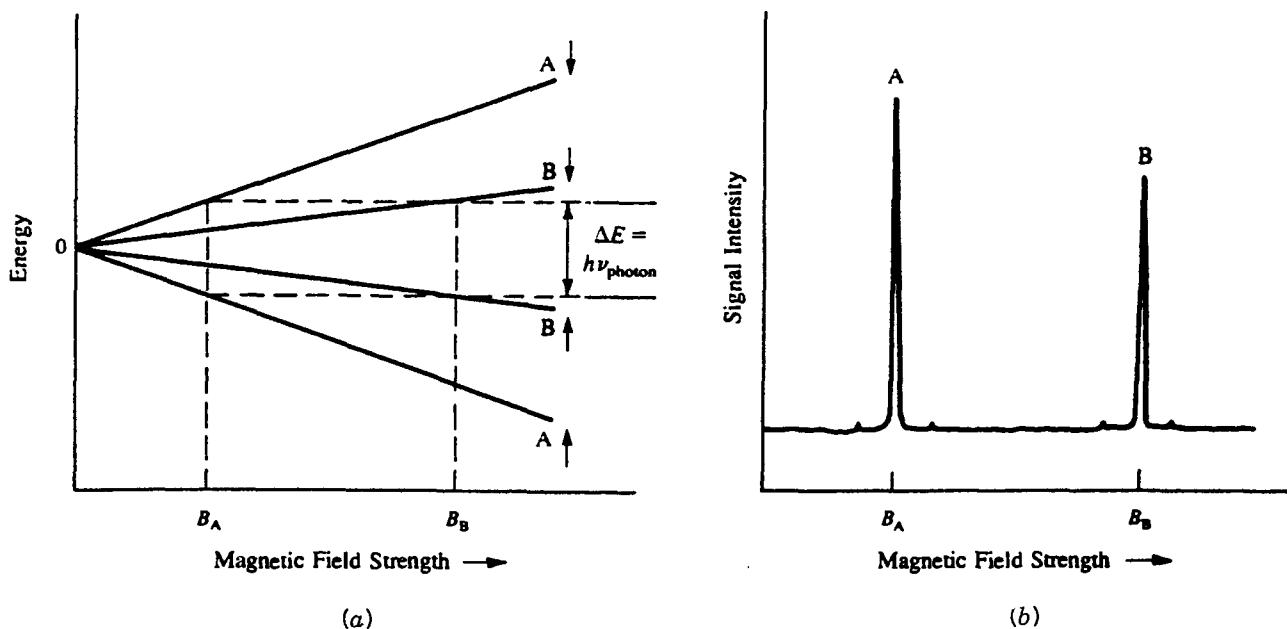


Figure 3.9. (a) The B_0 field strength required for two different nuclei to attain the same spin state energy gap ΔE . (b) Resulting field-sweep NMR spectrum.

■ **EXAMPLE 3.4** Suppose that, at a nominal field strength of 2.35 T, NMR signals were detected at 100 and 25.2 MHz. (a) What are the two isotopes giving rise to the signals? (b) If the spectrum were obtained by the field-sweep method, what field strength would be required to observe the latter signal using an operating frequency of 100 MHz?

□ **Solution:** (a) By referring back to the ν column in Table 2.1, we see that isotopes are ^1H and ^{13}C , respectively. (b) Use Eq. (3.3) and the value of γ for ^{13}C from Table 2.1:

$$B_{\text{C-13}} = \frac{2\pi\nu_0}{\gamma_{\text{C-13}}} = \frac{2(3.14 \text{ rad})(100 \times 10^6 \text{ s}^{-1})}{67.3 \times 10^6 \text{ radT}^{-1} \text{ s}^{-1}} = 9.33 \text{ T}$$

It is impossible for an NMR electromagnet designed for 2.35 T to produce a 9.33-T field! □

3.3.3 Spinning Sidebands and the Signal-to-Noise Ratio

A closer examination of the signals in Figures 3.8b and 3.9b brings up some additional points. Figure 3.10 is an enlargement of one of the peaks. Notice the two small signals symmetrically flanking the large signal. These so-called **sidebands** or **satellite peaks**, marked with asterisks in the figure, are an unavoidable result of spinning the sample to improve field homogeneity (Section 3.2.1). If the field has been well shimmed, such **spinning sidebands** rarely exceed 1% of the height of the main peak. Moreover, they will always be

separated from the main peak by *exactly* the spin rate in hertz. This is, in fact, the most direct way to measure the sample spin rate. One can, of course, completely eliminate spinning sidebands by turning off the spinner. But this would cause substantial broadening of the signal (with an accompanying decrease in signal height) because of the small inhomogeneities present in the magnetic field.

■ **EXAMPLE 3.5** Suppose the two sidebands in Figure 3.10 are each separated from the main peak by 58 Hz. (a) What

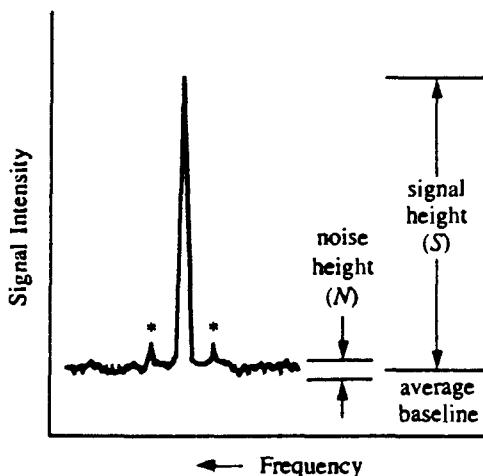


Figure 3.10. An NMR signal peak showing sidebands (*) and signal (S) to noise (N) ratio.

is the spin rate of the sample tube? (b) How could you confirm that these peaks were indeed spinning sidebands and not due to something else?

□ **Solution:** (a) Because the frequency separation of a sideband from the main peak is equal to the spin rate, the latter must also be 58 Hz. (b) Varying the spin rate (by adjusting an air flow directed at the spinner paddle) causes spinning sidebands to shift position accordingly. If the peaks do not shift position, they are not spinning sidebands. There are other types of satellite peaks that we will encounter later. □

You will also notice in Figure 3.10 that the signal baseline is not perfectly flat. Instead, there is perceptible random background noise causing a continuous wiggle in the baseline. Even in the most carefully built and tuned spectrometers there will always be some electronic noise generated by the various circuits within the instrument, and the way the signal data are processed. Normally, this does not present a problem, provided the sample gives signals strong enough to be easily differentiated from the noise. But what about really weak signals? For example, a sample of natural hydrogen (Table 2.1) contains 99.985% ^1H with a relative sensitivity of 1.00, while a sample of natural carbon contains only 1.1% ^{13}C , which has a relative sensitivity of 1.59×10^{-2} . These two factors, low natural abundance and low relative sensitivity, combine to make the carbon signal only about 2×10^{-4} times as intense as a hydrogen signal for equal numbers of atoms of each element. Thus, a ^{13}C signal is much harder to distinguish from noise than is a ^1H signal.

To deal with this problem, we define a quantity called **signal-to-noise ratio** (S/N), where S and N are approximated by their respective peak heights, as shown in Figure 3.10.

■ **EXAMPLE 3.6** Using a ruler, estimate S/N in Figure 3.10.

□ **Solution:** The exact values of S and N will depend on the scale of your ruler. But the ratio of the two numbers, S/N , should be about 20. □

The goal in an NMR experiment is to maximize S/N , and this can be achieved in several ways. One method is to use higher rf power and a series of rf filters to remove some of the noise. While this technique results in some improvement, care must be taken to avoid saturation problems (see Section 2.3). A far better improvement can be obtained by relying on a result of the **central limit theorem** from information theory. This theorem tells us that if the spectrum is scanned n times and the resulting data are added together, signal intensity will increase directly with n while noise (being random) will only increase by \sqrt{n} :

$$\left(\frac{S}{N}\right)_n = \left(\frac{S}{N}\right)_1 \left(\frac{n}{\sqrt{n}}\right) = \left(\frac{S}{N}\right)_1 \sqrt{n} \quad (3.4)$$

where $(S/N)_1$ is the ratio after a single scan. Thus, S/N improves linearly with \sqrt{n} .

To make use of this multiple-scan technique, we first need an extremely stable field. Then we need a computer to collect the signal data (digitally) from each scan, add the data together, and then divide the sum by n . The technique is known as **signal averaging** or **CAT** (computer-averaged transients, not to be confused with the diagnostic X-ray technique called *computer-aided axial tomography*). Because each scan of an older cw instrument could require 10 or more minutes, this process used to take hours, during which time the magnetic field had to be kept as perfectly stable and homogeneous as possible. A momentary flicker in the building power during an overnight experiment could cause all the data to be useless.

■ **EXAMPLE 3.7** A single 10-min cw NMR scan of a certain highly dilute sample exhibited S/N of 1.9. How much time would be required to generate a spectrum with S/N of 19?

□ **Solution:** We can rearrange Eq. (3.4) to calculate the required number of scans:

$$\sqrt{n} = \frac{(S/N)_n}{(S/N)_1} = \frac{19}{1.9} = 10$$

$$n = 10^2 = 100$$

The time required for 100 scans is

$$t = (100 \text{ scans})(10 \text{ min per scan})$$

$$= 1000 \text{ min} = 16 \text{ h } 40 \text{ min}$$

No sleep tonight! □

3.4 THE MODERN PULSED MODE FOR SIGNAL ACQUISITION

Further improvement in S/N had to await the development of faster computer microprocessors, which was exactly what happened during the 1980s. Armed with very fast and efficient microcomputers with large memories, chemists discovered they could now generate NMR signals in an entirely new way.

Have you ever been sitting in a quiet room when suddenly a fixed pitch noise (sound waves) causes a nearby object to vibrate in sympathy? This is an example of acoustic resonance, in which the frequency of the sound waves exactly matches the frequency with which the object naturally vibrates. If the pitch of the sound changes, the resonance ceases.