NMR SPECTROSCOPY IN SOLIDS
A HISTORICAL PERSPECTIVE

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Although NMR spectroscopy in solids is now less popular than in liquids, it was not always so. Purcell, Torrey, and Pound discovered NMR in solid paraffin (1), and Bloch, Hansen, and Packard independently discovered it in liquid water (2)—it would not have dawned on anyone that there was any essential difference between their discoveries. In early NMR experiments the apparatus did not appreciably distinguish between solids and liquids. Continuous wave (CW) excitation and incoherent (diode) radio frequency (rf) detection were the rule, and spectra were recorded as the magnetic field was swept.

In liquids and solids alike, the rf excitation was normally kept very weak so as to obtain undistorted spectra by satisfying the requirements for unsaturated slow passage. (However, if the goal was to measure the spin-lattice relaxation time T_1, usually the rf power level was progressively increased and broadening and attenuation of the signal were observed.) There was only one minor difference between solid and liquid NMR spectroscopy: For solids, which often have broad resonances, a small audio field modulation was often superposed on the field sweep and accompanied by synchronous lock-in detection in first-derivative mode to improve stability.

The first age of solids

The earliest applications of NMR spectroscopy tended to favor the solid state because the dipole–dipole interaction, dominant in many solids, depends on internuclear distances and directions strictly as $r^{-3}(3\cos^2\theta - 1)$. Thus, as Pake (3) and van Vleck (4) first demonstrated, shapes of absorption lines could be used to determine molecular and

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crystal structures. In addition, the onset of molecular motion with increasing temperature could narrow these lines, creating a new way to study slow (kHz) random motions and phase transitions (5). Polymer scientists in particular benefited from this approach.

An early CW NMR spectrometer is shown in the photo on p. 726 A. In this instrument the magnet was powered from World War II surplus submarine batteries whose discharge could be used to sweep the field through resonance. This was the first NMR spectrometer that could plot out the spectrum on a chart recorder.

The spectra of solids tend to be broad and lack resolved detail. They are low in information content because of the very dependence of the dipolar interactions on geometrical structure that Pake and van Vleck exploited. The interaction is anisotropic, and molecules differently oriented in the external magnetic field give different spectra, leading (except in single crystals) to serious overlap. The interaction also falls off very slowly, as r^{-3}, with the distance between a nucleus and its neighbors. The number of neighbors at distance r increases as r^2, so that the presence of many neighbors splits and resplits the resonance into an ultimately unresolvable pattern.

The age of liquids

It turned out that weaker interactions such as chemical shielding, σ, (discovered by Proctor and Yu [6] at Stanford and by Dickinson [7] at MIT), and indirect spin–spin interaction, J (discovered by Hahn and Maxwell [8] at Berkeley and by Gutowsky, McCall, and Slichter [9] at Illinois), formed the basis of a much more useful type of NMR spectroscopy. This type worked only in

liquids, where the very rapid molecular motions result in an averaging of interactions over all orientations.

Several factors are important. First, the average of the dipolar interaction is exactly zero, so this otherwise dominant influence is removed altogether. Second, σ and J are also anisotropic, but their angular averages are *not* zero, so some information remains. Finally, the J coupling among N neighboring spins such as the dipolar interaction leads to about 2^N lines. However, the J coupling falls off much more rapidly with distance, making N effectively small and often leading to usefully resolved multiplets.

The result is the familiar NMR spectrum consisting of a chemically shifted multiplet for each distinct species in a molecule; the multiplet structure gives information about the arrangement of near neighbors. One has enough information to be useful and not so much as to be an embarrassment of riches. Moreover, the values of σ and J are easily extracted and can be interpreted on the basis of empirical correlations without the need for theoretical analysis. This almost magical set of properties quickly made NMR the premier spectroscopic technique used by chemists.

Credit belongs to H. S. Gutowsky and his group in Urbana for developing this field in its early stages and to Varian Associates for bringing about its commercialization. Russell Varian was the inventor of the reflex klystron, on which the largest part of the business was founded. He was also an enthusiastic amateur scientist and encouraged the company's foray into NMR instrumentation. Among the outstanding staff of scientists and engineers he assembled were Warren Proctor, Martin Packard, Jim Shoolery, Emery Rogers, Harry Weaver, Wes Anderson, Ray Freeman, and Richard Ernst. For several years this group was the source of most new theoretical and experimental developments in NMR, dominating the best scientific journals in this field and surpassing the contributions of the university laboratories.

Because of its dominance in fundamental discovery, application, and patents, Varian enjoyed a near monopoly in commercial NMR instruments for several years. Apparently instrument sales did not yield sufficient profits, however, for after the death of the Varian brothers there were several episodes of cutting back development resources for NMR in-
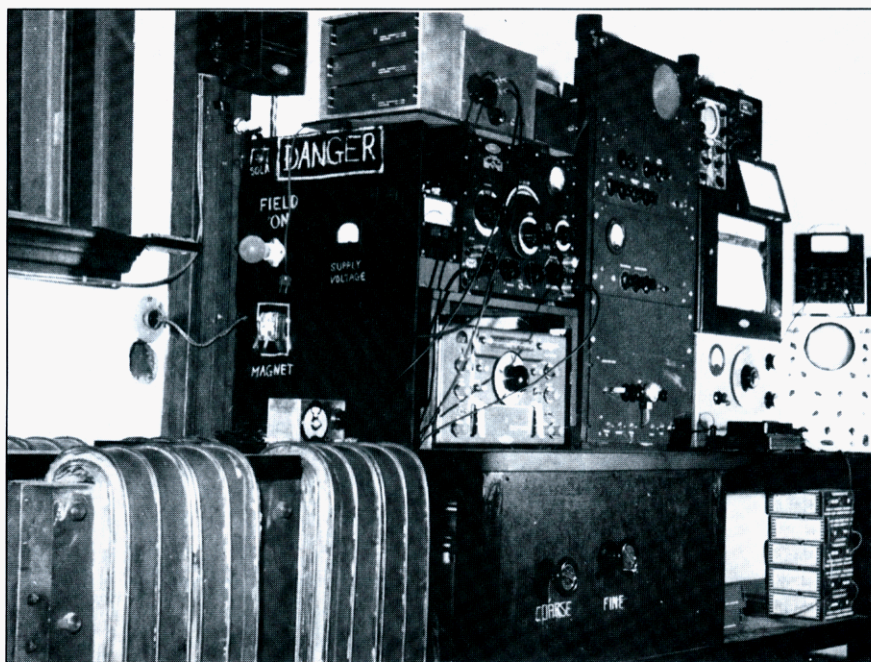
Early CW spectrometer built at Caltech in 1951 for the study of solids.

struments. A particularly serious instance occurred after Anderson and Ernst pointed out the advantages of the pulsed Fourier technique in liquid-state NMR spectroscopy (*10*). The company delayed applying this revolutionary development to its instruments, thus opening the door to competitors such as Bruker Physik and to the ultimate departure or transfer of most of the scientific staff who had symbolized Varian's halcyon days in NMR research.

Guenther Laukien and Toni Keller of Bruker recognized the importance of FT-NMR spectroscopy and quickly developed commercial instruments based on this approach. Their first spectrometers used Fabri-Tek (now Nicolet) signal averagers to acquire the free induction decay (FID) data and Digital Equipment PDP-8 minicomputers to perform the Fourier transforms. Subsequently these functions were combined in the Nicolet 1080 (and, later, 1180 and 1280) computers. The 1080 in particular showed its heritage as a sort of 20-bit PDP-8: 20 bits apparently represented the precision required, in someone's judgment, for storing NMR data.

During this period, Varian was completing development of its XL-100. The last of the large CW spectrometers, this instrument had a basic rf design that was not easily converted to pulsed operation. By the time a serious attempt was made to change this design, Bruker had assumed the dominance it retains to

this day, and other companies—notably JEOL, Nicolet (later absorbed by GE), and IBM Instruments (later absorbed by Bruker)—became major players as well.

The Fourier transform relationship between the transient response and the CW spectrum had in fact been discovered earlier by Lowe and Norberg (*11*), whose concern was with solids. At that time there may have appeared to be little, if any, practical advantage in using the pulsed Fourier technique experimentally in broad-line systems; it was in the rich and resolved spectroscopy of liquids that the multiplex advantage of the Fourier method would become essential. Moreover, the small laboratory computers needed to exploit the method were not yet available, a situation that began to change when Anderson and Ernst became involved.

Simultaneously, high-field, high-resolution superconducting magnets began to appear. The combination of these developments led to dramatic improvements in sensitivity and dispersion, which in turn led to a revolution in liquid-state NMR spectroscopy: the use of the technique with nuclei other than protons, the study of large biological molecules, and the emergence of multidimensional techniques.

Spin alchemy and the second age of solids

While all this was going on, developments were occurring that would ul-

timately revive interest in NMR spectroscopy of solids. The growing popularity of the pulsed Fourier approach was an important impetus in that it focused on the dynamic behavior of spin systems rather than exclusively on transition probabilities between eigenstates of the spin Hamiltonian.

Spin dynamics had not been altogether ignored; however, pulses had been widely used in only a few situations, such as in the inversion-recovery method of measuring T_1 and in Hahn's spin-echo method for measuring T_2 (12). In their simplest forms each of these required only a pair of pulses, although "method B," as Carr and Purcell called it (13), required the use of a long train of refocusing 180° pulses following a single preparative 90° pulse. The possibilities inherent in more complex pulse sequences, however, had been largely untapped.

For this to change, the technology of phase-coherent NMR apparatus had to be developed. In early times the pulses were produced by gating electrode voltages on free-running rf oscillators, so that the rf phase of one pulse was unrelated to that of its predecessors or successors. In addition, the square law detectors used to observe the responses were oblivious of rf phase.

Meiboom and Gill (14) were perhaps the first researchers to switch the carrier phase of a pulse transmitter between pulses, inventing a useful modification (CPMG) of the Carr–Purcell multiple-echo sequence. The rationale for this step was easy to understand with the help of "hand-waving" vector precession pictures. CPMG represented the first demonstration that coherent pulse transmitters with control of carrier phase could be important. At about the same time, rf phase detectors were used to preserve the phase information in the transient response.

One result was that workers using NMR techniques began to think increasingly in the time domain, but their experiments temporarily fell into two incompatible groups. Physicists such as Irving Lowe and Richard Norberg were largely interested in the solid state. It was believed that the "irreversible" FID made it unprofitable to apply long pulse trains but the single pulse needed to excite the FID required a high-powered transmitter. Chemists found useful applications for T_1, T_2, and diffusion measurements in liquids. Some of these measurements

needed the capability to program long pulse trains with some control of phases, but they did not require high transmitter power.

The Harvey Wells Company, which had made amateur radio equipment in the 1930s, emerged after World War II as a small manufacturer of CW NMR spectrometers based on the "Pound box," or marginal oscillator (15). It was natural for the company to enter the laboratory electromagnet business, and subsequently it merged with another magnet company, Magnion. Under Edward Ostroff, vice president of engineering, the new company developed a line of pulsed NMR spectrometers.

To appeal to chemists and physicists alike, it offered a pulse programmer capable of the relatively long and complicated pulse trains needed by the chemists as well as the option of high-rf power required by the solid-state physicists. Using

NMR Scientists Began to Think Increasingly in the Time Domain

this previously unavailable combination, Ostroff, experimenting with solids having T_2 values in the range of tens of microseconds, applied a CPMG sequence modified by reducing the flip angle of the normally 180° pulses. He was surprised to see trains of thousands of echoes lasting as long as a second. Although the "solid echo" was known from the work of Powles' group (16), Ostroff's observation directly contradicted the general belief that transient NMR signals in homogeneously broadened solids could not last longer than a few times T_2. For reasons that need not be discussed, the pulse sequence ultimately became known as MW4. Magnion sold a few pulse spectrometers, but because of management changes and legal expenses associated with the defense of Erwin Hahn's patent on spin echoes, the company eventually went out of business.

Ostroff's discovery (17) forced a new theoretical approach to spin dynamics and fostered a series of new

advances. It had been customary in analyzing spin dynamics to concentrate on the quantum state (or density matrix ρ) of the spin system as it evolved under the influence of its natural internal Hamiltonian, supplemented by a train of strong rf pulses. (This point of view was a natural one for thinking about simple situations such as inversion recovery or spin echo, in which a vector precession model was adequate.) In thinking about the new pulse experiments it proved profitable to focus instead on the time development operator $U(t_2, t_1)$ that carries the system from an initial time t_1— perhaps that at the beginning of a FID—to a later time t_2 when the magnetization signal will be sampled. Although development of the FID under the natural spin Hamiltonian may have been interrupted by strong time-dependent fields, the overall time development operator can always be thought of as having arisen from a fictitious time-independent average Hamiltonian (18). This concept is a simple consequence of the unitary aspect of U.

If the pulses were designed so that by themselves they would have restored the system to its initial state, the average Hamiltonian would resemble a new and now unnatural internal spin Hamiltonian, under which the spin system would have executed a FID if there had been no irradiation. This strange transformation depends entirely on the rf irradiation chosen, so that within limits it becomes possible to design the experiment to attain a desired result. It is as if a magic wand (the rf pulses) had changed the physical nature of the system, which is akin to an alchemist's transformation of base metals into gold.

The first experiments performed at MIT (19) in which this approach was used were designed to erase the homonuclear dipolar interactions that had broadened the resonances of solids and at the same time preserved the small, underlying chemical shifts and J couplings. A striking example is shown in Figure 1. In other words, this work is a sort of "high-resolution" NMR spectroscopy of solids. For a long time, however, this multiple-pulse NMR technique was not exploited commercially, because the experiments were (and in fact still are) exceedingly demanding on the instrumentation and its operator.

The idea of using the average Hamiltonian, however, was adopted for many less difficult situations in
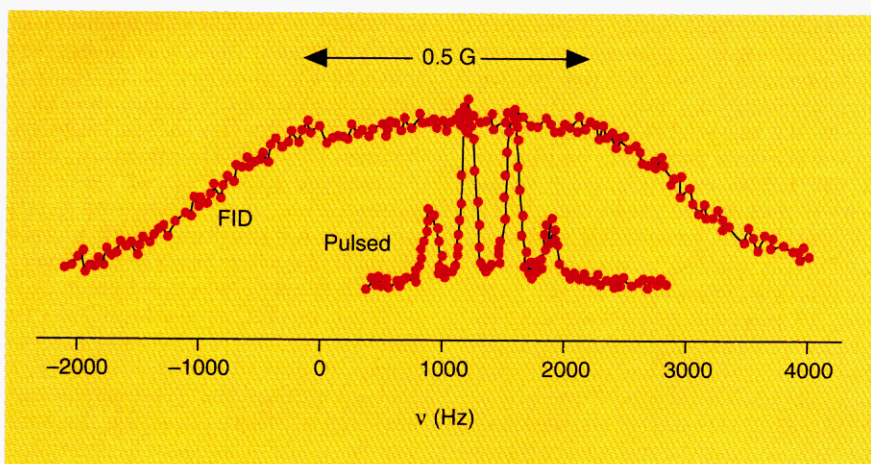
Figure 1. ^{19}F spectra of solid perfluorocyclohexane.

The broad spectrum is the Fourier transform of a conventional FID. The resolved spectrum, taken a few minutes later on the same sample, is the Fourier transform of the pseudo FID obtained by sampling in the windows of a multiple-pulse sequence. In the latter, the (intermolecular) dipolar broadening is removed, but the chemical shift between axial and equatorial fluorines is preserved, as is the scalar coupling between them.

liquid-state NMR spectroscopy, some of them already well known and understood in other ways. For example, a pair of 180° pulses applied to a spin system having only inhomogeneous broadening is equivalent to a reversal of the Hamiltonian during the intervening interval; the average of the normal and reversed Hamiltonians over equal times is zero, and the initial point of a FID returns as the peak of an echo. Or, continuous irradiation near resonance of the second (I) of two distinct spin species results in a FID of the first species (S) from which the J interactions of I and S are decoupled (removed from the average Hamiltonian).

At the same time, the realization that the effective Hamiltonian of a spin system could be changed at will from one form to another contributed to the invention of new experiments, such as numerous multidimensional FT-NMR methods (20). The essence of many such experiments is that the effective Hamiltonian is different during the times $\tau_1, \tau_2, \ldots$ which correspond to the frequency variables $\omega_1, \omega_2, \ldots$ into which they are mathematically transformed. Most of these methods have been applied in liquids and are reviewed by Ray Freeman in his Waters Symposium presentation (21).

For commercial purposes, attention remained focused on the much larger and technically easier field of NMR spectroscopy in liquids, and further developments in pulsed NMR spectroscopy of solids remained in the hands of private researchers. The MIT group and its descendants in Heidelberg and Dortmund as well

as Vaughan's group at Caltech and its satellite at the Jet Propulsion Laboratory were particularly involved in such research, and there was some derivative activity in the United Kingdom as well as in East Germany.

Their task was formidable. The broad lines of solids impose difficult demands on the instrument. To say that the resonance lines are broad is to say that the interactions are strong in energetic terms, which means that the time scales (T_2 values) are short. Thus the power of the pulse transmitter must be high enough, perhaps a few kilowatts, to achieve a large flip angle in a time much less than T_2. Immediately thereafter a sensitive receiver must recover from this high-powered pulse quickly enough to record a transient NMR signal of perhaps a few nanowatts before it is over or before the next pulse in a sequence has to be applied. A brute force approach based on linear receiver circuits with large dynamic range is hopeless: The noise threshold of the required receivers is below the peak transmitter power in the probe by ~ 180 db!

The necessary transmitter–receiver isolation was achieved by duplexers based on nonlinear passive elements (diodes) and tuned elements such as unmatched coaxial lines. Such circuits grew out of amateur radio practice and circuit elements developed during World War II for microwave radar that were adapted for the lower frequencies used in NMR instruments. The relatively large bandwidths and phase control required for solid-state NMR

spectroscopy were achievable by the fortuitous development of passive modular circuit elements that acted as rf analogs of waveguide-based microwave elements. These included 0°, 90°, and 180° hybrid junctions made by companies such as Merrimac, Anzac, Adams-Russell, and Olektron.

Highly stable rf carriers with precise control of frequency became available from frequency synthesizers produced by Schomandl, General Radio, Hewlett Packard, and Programmed Test Sources, among others. The carriers were gated by wideband double-balanced mixers based on hot carrier diodes and ferrite transformers, which were also used for up-and-down conversion and phase detection.

The first double-balanced mixers were marketed by Hewlett Packard in the mid-1960s and cost $500 each; their cases were milled out of solid metal and cleverly sealed, perhaps to prevent the user from easily seeing how little was inside. Equivalent mixers are now available for under $10 each from Mini-Circuits and other companies. In addition, broadband modular VHF amplifier modules became available, notably from Avantek. All of these components had 50-ohm input and output impedances and were well characterized; thus, researchers lacking sophisticated knowledge of circuit design could put together complete high-performance rf systems without difficulty.

During the same period, MSI and LSI integrated logic circuits became available. Thus the design of pulse programmers and computer interfaces offered the same sort of building-block simplicity provided by rf modules. Of course, digital computers became cheaper because of the same technology.

These advances in technology created a climate in which individual academic researchers could develop powerful and versatile NMR spectrometers without relying on the instrument manufacturers (22). Ultimately their developments converged with commercial practice, largely because more attention was paid to NMR spectroscopy of dilute species such as ^{13}C, ^{19}F, and ^{15}N. For a long time NMR spectroscopy had, for all practical purposes, meant *proton* spectroscopy because protons offered an irresistible combination of spin 1/2, large magnetic moment, and high abundance in a wide variety of important sample materials. Magnets and spectrometers are still identified by labels such as 500,

which refers to the Larmor frequency, in MHz, of protons.

It was not until the late 1960s that a substantial number of researchers began paying attention to "other" nuclei, a development made possible by advances in sensitivity arising from stronger superconducting magnets and, particularly, FT-NMR spectroscopy.

In solids, the low sensitivity of these other nuclei is exacerbated by their characteristically long T_1 values, which are a consequence of their low abundances and magnetic moments. This situation was changed by the introduction of proton-enhanced NMR spectroscopy by our research group at MIT (23). Cross polarization (CP) through Hartmann–Hahn double resonance (24) confers on the dilute species some of the benefits of the shorter T_1 and high abundance of surrounding protons. Following CP, broadening by the surrounding protons is removed by strong heteronuclear decoupling while the signal of the dilute spins is recorded. The result is a pure chemical shift spectrum.

Because the chemical shift is anisotropic, the spectra exhibit powder patterns in samples that are not single crystals. Although the chemical shift tensors constitute new and often valuable information, the powder patterns overlap in all but very simple samples. What it took for routine use of this method was removal of the powder broadening by magic angle spinning (MAS) (25).

MAS was an old technique, discovered independently by Andrew and co-workers (26) in the United Kingdom and by Lowe (27) in St. Louis. Both groups regarded it as a means for removing homonuclear dipolar broadening. Because this broadening is homogeneous, the spinning speed must exceed the dipolar linewidth, which is often large. Thus technical difficulties restricted these MAS experiments to a few specially chosen samples, and the method remained largely a curiosity. The chemical shift broadening, however, is inhomogeneous and can be effectively removed at spinning frequencies lower than the spectral width, which in any case is ordinarily smaller than dipolar widths.

The intensities of the resulting CP/MAS powder patterns are concentrated in sharp lines, conferring an apparent increase in sensitivity in addition to the obvious improvement in resolution. If the spinning sidebands are removed by rapid spinning or pulse techniques, the spectra become very much like the chemical shift spectra of liquids and are susceptible to the same sort of empirical interpretation in terms of structure that has made liquid-state NMR spectroscopy such a powerful analytical technique. In this sense the art of NMR in solids had come full circle.

The importance of the development of CP/MAS NMR was obvious, and many prospective purchasers of high-resolution NMR spectrometers began to demand accessories for performing CP/MAS. It is an interesting sidelight on scientific fashion and sociology that some of the purchasers seemed to have no actual use for such accessories and that some of the ones offered and sold did not actually work. However, the technical demands of CP/MAS NMR—mainly the need for fast and stable sample spinners—are relatively modest compared with those of the multiple-pulse methods.

Commercial designs were developed by Bartuska of Chemagnetics (which emerged from Maciel's group at Colorado State University) and by Doty of Doty Scientific (which emerged from Ellis' group at the University of Southern California). These startup companies concentrated on CP/MAS. Chemagnetics subsequently expanded into the manufacture of complete spectrometers specially adapted to solids; the company survives as a part of Otsuka Ltd. Ultimately, other manufacturers—notably Bruker—produced high-performance spectrometers, and private researchers no longer have to make their own instruments.

The study of solids has become an established part of the NMR field. However, it is—and doubtless will remain—less important than the powerful modern uses of NMR spectroscopy in liquids and much less visible to the general public than the dramatic NMR imaging methods.

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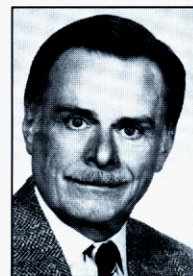
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