OPENING LECTURE

F. BLOCH

Department of Physics, Stanford University, California 94305, U.S.A.

It is a great honour to have been asked to deliver the opening lecture of this Fourth International Symposium on Magnetic Resonance. Besides, feeling closely connected to the Weizmann Institute and the Hebrew University through long association and many old bonds of friendship, it gives me an extra pleasure to be among their guests on this particular occasion.

This is a very special occasion also inasfar as it is dedicated to the 25th aniversary of Magnetic Resonance. To most of you it must come as the natural tribute to a field of research whose origins belong to the remote past. But I have to forcefully remind myself of all that has been achieved in this field during the intervening years in order to fully realize that a quarter of a century has already gone by since the first modest beginnings. They are as vivid in my mind as if they had occurred just recently and I thought that some of my recollections may help to give you the flavour of these early days before we hear from the next speakers what has happened afterwards. In any event, you know that much better than I do and I can only hope that you are inclined to listen to some ancient history since that is the best I can contribute to this symposium. I also hope you will forgive me that my account will be highly personal. My selection of historical events is very narrow indeed, not because I consider others to be less important but merely because I shall limit myself to those of my own first-hand experience.

Now, every history has its pre-history and one does not have to be an expert archaeologist to know that nuclear magnetic resonance is older than 25 years, going back to the work of Rabi and his collaborators with molecular beams before the war. My own interest in magnetic resonance arose shortly afterwards through the measurement of the magnetic moment of the neutron with Alvarez in 1939, where we made another use of this method. Our main source of error had been in the determination of the resonance field and it was not until almost the end of the war that I was able to start thinking again how it could be improved.

I was at that time engaged in radar work at the Radio Research Laboratory of Harvard University while Ed Purcell—unknown to me—worked at the Radiation Laboratory of MIT. I did, however, discuss the problem of improved field measurement on walks with Rabi who likewise worked at MIT but lived close to our house in Cambridge. He offered, when back at Columbia, to calibrate a permanent magnet by resonance of an atomic beam of hydrogen and then to ship it to Stanford for comparison with the magnetic resonance of neutrons. Somehow, however, this seemed rather complicated and unsafe to me and I kept on thinking whether we could not do the calibration ourselves. We did not have

P.A.C.—32—4—B

molecular beam equipment and I had no taste to compete with the group at Columbia and their experience in this sophisticated technique.

But even in dry California we had sufficient water to provide us with the necessary protons and it was clear that, as far as their magnetic resonance was concerned, they would behave just like Rabi's. One only would have to find a different and, preferably, simpler way of detecting resonance and such a way occurred to me during an otherwise quite boring train trip to Chicago in the spring of 1945. By a quick-and-dirty calculation on the back of an envelope I convinced myself that the protons in about a cubic centimetre of water at resonance in a magnetic field of a few thousand gauss would induce in a surrounding coil a radio frequency voltage well above the noise of a normal radio receiver. Needless to say that I became rather excited but for quite some time I was far from being sure that I had not overlooked something which would spoil the game. I knew nothing of the previous attempts by Gorter nor of the work by Zavoisky to detect magnetic resonance through its reaction on electric circuits and this may have been one of the rare circumstance where ignorance helped. One of my principal worries was that the thermal relaxation time might be unfavourably long and it took a lot more thinking and calculation before I felt that, somehow, the thing really ought to be possible.

Despite my training in circuits which I had acquired during the war I needed far greater an expert in radio techniques than I was, and if there was ever a natural choice it was that of my late friend and colleague Bill Hansen of klystron fame. He came at that time often from the Sperry Laboratories on Long Island to Cambridge where he gave lectures at MIT and when I had told him my story once over lunch in the early summer of 1945 he immediately agreed to collaborate after our return to Stanford. I arrived there a few weeks before him, just at the end of the war. Shortly afterwards a young man, Martin Packard, who had heard rumours about our plans, came into my office to ask whether he might get a PhD thesis out of this work. I am usually quite reluctant to recommend to a student somewhat risky undertakings for his thesis but in this case I thought I could take a chance, particularly also since I was impressed by his quick understanding and his obvious qualifications. We were temporarily joined by another young man, Lawrence Manning, but he soon left us to go into electrical engineering.

After Hansen came back, the work was divided into three parts: Hansen and Packard took care of the radio frequency components, Manning was to work on the circuits necessary for the 60-cycle modulation of the magnetic field and I had to prepare the required d.c. field. While it was decided from the beginning that our test substance should be water, the real advantages of a liquid did not occur to us at that time since we did not think of motional narrowing. Consequently we estimated the width of the resonance from the field produced by the magnetic dipole of a fixed nucleus at the location of a neighbouring fixed nucleus, that is of the order of several gauss as it was indeed later observed in solids. Such a broad resonance did not seem to deserve any special magnet and our magnet was, in fact, anything but special. It had been used for a long time in simple lecture demonstrations and was less than mediocre both in homogeneity and field strength. About 2000 gauss was all we dared to produce, corresponding to a resonance frequency of protons around 8 megacycles, and the field

varied by at least a gauss over the size of the sample. After adjustment of the radio circuits to a given frequency, the current in the magnet had to be set so as to give the field required for proton resonance. The only luxury which we permitted ourselves was to stabilize the current by running it through our small cyclotron which had not yet been reactivated since the first years of the war. To ascertain the field in the gap of the magnet, I used the standard method of a flip coil and a ballistic galvanometer and I finally thought that I had done a pretty good job but, as you soon shall hear, it was not quite good enough.

We worked at a rather leisurely pace, strictly observing holidays and long weekends, and it was not until early in January of 1946 that everything seemed ready. So as not to be too much disturbed by voltage fluctuations we decided to meet one evening after dinner for our first run. There were several little spherical containers with water ready as samples. Since we thought that it might take several hours for the proton moments in pure water to reach thermal equilibrium in a magnetic field we took the rather unpromising step to place them for a good long time into the field of the cyclotron before transferring them to our equipment in the hope that this pretreatment would last during a test run. Actually, there would have been little chance to detect any signal from these samples if the thermal relaxation time had really been that long. But we did also something else which was considerably more clever. In some of the samples we had iron nitrate in fairly high concentration dissolved in water. By analogy with the known action of paramagnetic molecules as catalysts in the conversion of ortho- and parahydrogen it could be concluded that the thermal relaxation time would thus be shortened to about a millisecond which was highly desirable under the circumstances.

Nevertheless, when we came together that evening we placed one of those pretreated samples of pure water with about 5 millimetre diameter into the equipment, turned all the switches on and when the radio gear had been tuned and had somewhat quieted down I went over to the magnet to set the current to the supposedly right value. Hansen and Packard were watching the oscilloscope a few yards away but there wasn't a thing they could see on top of the noise fluctuations. So Hansen wanted to do some more adjusting of the amplifier and asked me to turn the current off. They were still watching the oscilloscope when I opened the switch and just then I heard Packard say to Hansen: 'Hey, did you see that? Something was just running across the screen!' I don't know whether Hansen saw it right away; in any case he asked me to close and open the switch a few more times and that thing repeated to run across the screen. Then Hansen and I changed places and I saw it too, a little hump, maybe three times above the noise, quickly travelling across the trace of the oscillograph after the switch was opened or closed.

What had happened was that my current setting had been too high by about one percent which was more than twice the amplitude of our 60-cycle sweep field. But when the current was turned on or off, the d.c. field in the magnet passed through the right value for resonance and the signal appeared while it was within the sweep range. I was not so sure, however, that this was the right explanation and wanted to go on trying whether we were not just tricked by some instrumental devil. But Hansen had enough faith to convince himself that this was 'it' and to declare categorically: 'All right, let's go to my home and get

drunk!' Well, I didn't have the strength of character to resist that temptation and consumed a fair amount of alcohol during the rest of that evening.

Although we felt rather elated, we did not get drunk, however, but kept on discussing what should be done next. In my usual conservatism I wanted to use the same equipment, tricky as it was, for a while longer to perform various tests. The worst feature was that the receiver coil had to be just in the right position relative to the transmitter coil in order not to pick up far too much of the driving radio frequency field. It needed Hansen's steady hand to bend it ever so slightly with a pair of tweezers in order to meet this delicate requirement and any little vibration was sufficient to disturb it. I couldn't blame him, therefore, for wanting a more stable construction before going on and he had the good idea that, with the receiver coil solidly positioned, one could mount a little copper paddle nearby which could be turned to effectively steer the flux from the transmitter coil. I must confess that I was rather impatient during the two weeks it took to build the new equipment but when it was functioning I had to admit that the delay was worthwhile. We firmly established the effect, found the relaxation time in pure water to be only about three seconds instead of several hours and also saw that it was greatly advantageous to use the iron nitrate solutions. The signal could now be kept steadily on the screen and we verified that, within the experimental error, the gyromagnetic ratio of protons in water agreed with the value, obtained earlier by Rabi and his collaborators in an atomic beam.

Thus assured of the reality of our findings, we sent at the end of January 1946 a short letter to the Editor of the *Physical Review* and it appeared in the issue following that which contained the first results of Purcell, Torrey and Pound. Shortly before, we had heard rumours that something called 'the poor man's molecular beam' had been found at Harvard. I heard a little more from Otto Stern who lived at that time in Berkeley and had followed our progress with interest. Although he did not know any details either, it sounded, at least in principle, very much like the thing we had done. Hansen brought back some more information after a visit in Cambridge where he had seen Ed Purcell. I did not meet Ed until the spring meeting of the American Physical Society where both groups presented their results. The two of us then had a private talk to compare our respective approaches and it seemed at first as if Harvard and Stanford belonged to distant countries of entirely different language. Where we spoke about precession of a nuclear moment, they spoke about transitions between Zeeman-levels and when we talked about an induced voltage they talked about absorption. It may be said to our honour, however, that it did not take us long to translate from one language to the other and by the time the extended papers were published the common basic features of our work were pretty well understood. After I had spoken last December about the early days of nuclear magnetic resonance in a meeting of the American Physical Society at Stanford, Ed Purcell told us also about the corresponding events at Harvard and I wish he were here again to have you appreciate both the apparent differences and the underlying similarity of our experiences. It may seem surprising that quite different considerations led us simultaneously to the same discovery but such coincidences have really quite often happened before. Another far more important example is the discovery of quantum mechanics within one year by

de Broglie in its wave form and by Heisenberg in the matrix form. It shows that science grows almost by itself like a tree which quietly draws nourishment from many roots until the fruits are ripe and can be picked by anybody who happens to see them at the right time.

I should like to use the rest of this lecture to tell you briefly about the sometimes quite unexpected shoots that sprouted out of our little tree during the next few years. It may be a useful reminder of the strength as well as of the weakness inherent in prophecy if I read first some of the remarks with which I concluded my extended paper in 1946:

> While the methods of molecular beams and of nuclear induction have a common ground of investigation it is evident that neither one makes the other superfluous. There are, on the other hand, many problems which become accessible or which can be more conveniently solved through nuclear induction and some of these will be mentioned here:
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> (1) The exact comparison of the magnetic moments of the neutron, the proton, and the deuteron is at present one of the most interesting problems, concerning nuclear forces. The main difficulty in this comparison was until now the sufficiently accurate calibration of the resonance field. It can be completely avoided by repeating the experiment of Alvarez and Bloch for neutrons and by observing through nuclear induction simultaneously and in the same field the resonances of protons and deuterons. The problem of comparison of their magnetic moments is thus reduced to that of their respective resonance frequencies and can be solved with high accuracy. It was indeed with this experiment in mind, and while searching for a suitable method of comparison, that the author was led to the thought of nuclear induction, and preparations are now under way at Stanford to carry out the measurement in the near future.
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> (2) One of the difficulties in the determination of the gyromagnetic ratios of many nuclei by molecular beams is that of finding suitable detectors. The method of nuclear induction is free from this obstacle and should be soon applied to all elements for which this determination is of interest.
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> (3) While even in its very initial stage, nuclear induction was observed with a sample of 100 milligrams, there are good reasons to believe that the sensitivity can still be greatly increased. This offers the possibility to observe the effect not only in liquids and solids but also in gases under no excessive pressure. With only small amounts of matter necessary for its performance, the experiment offers a convenient way of isotope analysis and particularly also for its application to radioactive nuclei.
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> (4) It was shown in Section 4 that the induced signals to be expected depend not only upon the nuclear susceptibility but also upon the relaxation times. By suitable choice of the variation with time of resonant field or frequency, it is thus possible to measure these quantities separately.
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> (5) As in comparing the moments of neutron, proton, and deuteron, nuclear induction can well be developed as a simple and practical method to calibrate and measure high magnetic fields with great accuracy, and to apply it, for example, in the construction of cyclotrons and mass spectrographs.
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> There are unquestionably more problems which will become tangible in further development of the new electromagnetic effects. The fact that they are simple to obtain and require only very modest equipment should make it possible for many investigators to enter this field of research.

Well, the truest of these remarks is probably the last, even though the requirements for equipment are not as modest any more as they were in the first

experiments where our total expenses amounted to 275 dollars, including 250 dollars for an oscillograph! Nevertheless, there are some other indications of the things to come in the preceding points. Regarding the first, the exact comparison of the moments of neutron and proton and their resultant in the deuteron was indeed carried out at Stanford although the 'near future' in which we hoped to have the results turned out to take almost three years. But the most interesting is probably the second point where the measurement of many other moments is foreseen. Notably Proctor and Yu and, later, Weaver indeed measured with great accuracy a large number of these moments some of which had not even approximately been known before and they were of considerable interest in connection with the then new shell-model of nuclei, particularly since in each case the sign of the moment was also determined.

Some of the most far reaching results of this work, however, came as byproducts which seemed even quite undesirable at the time of their appearance. This holds particularly for the chemical shift, found in 1950 almost simultaneously by Proctor and Yu and by Dickinson. In their investigation of nitrogen 14, Proctor and Yu found two resonances and since one did not know which to believe, they came as an annoying ambiguity in the determination of the nitrogen moment. It was first thought that this might be due to some novel double-nature of the nucleus but there was also a suspicion that the effect was of chemical origin since the solution contained nitrogen both in the form of NH_4^+ and NO_3^-. It came more as a disappointment than anything else when this suspicion was confirmed by showing that the effect depended indeed upon the compound used but appeared in the same relative magnitude for the two isotopes N^{14} and N^{15}. In fact, some such effect should almost have been predicted since Lamb had pointed out already in 1941 that the atomic electrons provided a shielding of the magnetic field although it was certainly remarkable that the small difference in the shielding due to a change in the orbital characteristics of the valency electrons could be so clearly demonstrated.

Another shift, due to the conduction electrons of a metal, had been found the year before by Knight but this Knight-shift had to be ascribed to the spin of the electron rather than to its orbital properties. In the same year in which they found the chemical shift, Proctor and Yu detected a beautiful fine structure of the antimony resonance in potassium antimony hexafluoride which likewise had to be ascribed to spin interaction, but this time it was the nuclear spin of fluorine instead of the electron spin which was responsible. From a mere curiosity, this nuclear spin–spin splitting likewise graduated in the course of time to an important feature in the application of nuclear magnetic resonance to chemistry.

Although this application blossomed up only several years later, most of the decisive steps which lead to it came at nearly the same time, that is about five years after nuclear resonance in ordinary matter had been established. It is through Hahn's discovery of spin echoes and his observation of echo modulation that a difference in the local field acting upon identical nuclei within the same molecule was first detected. Shortly afterwards, Gutowsky and his collaborators found in steady state resonance a spin–spin splitting between nuclei of the same kind but in different sites of a molecule and Hahn and Maxwell showed at about the same time that echo modulation, in addition to

internal chemical shifts, likewise revealed the presence of such an effect. This ingenious pulse method does not require great homogeneity of the d.c. magnetic field, even in the case of hydrogen where the spin–spin splitting typically amounts to a frequency difference of only a few cycles per second in contrast to the much larger splitting for nuclei of higher atomic number.

While these investigations were under way we gradually improved the homogeneity of our magnets but for quite different reasons. When we found the relaxation time of protons in water to be about three seconds it seemed that, in principle, one should be able to obtain resonance widths of the order of a cycle per second or, in field units, of a fraction of a milligauss. With our original magnet we were certainly very far from reaching this goal and it was soon replaced by better models which also allowed further improvement by the use of shims. Apart from the intriguing sport to obtain very narrow resonances, there were two major incentives to go further in field homogeneity. As they were pushed together into a smaller spread, the signals grew in intensity which was highly desirable. Another reason was that, from now on, nuclear moments would be measured by frequency ratios relative to a standard moment, notably the proton, and we wanted to establish this standard with respectable accuracy.

By the time internal chemical shifts of proton resonances in the order of 50 cycles per second, or about 10 milligauss, had been inferred from echo modulation, we had come to the point where the variation of the magnetic field over the sample extension had come down to just a few milligauss. Choosing ethyl alcohol, Arnold, Dharmatti and Packard thought it would be nice to display the shift between the three nonequivalent proton groups of the molecule by three separate resonance lines and that is exactly what they did. What, rather naively, impressed me most when I saw their first trace was that the intensities of these lines were indeed in the ratio 3:2:1 of the number of equivalent protons in the three groups of hydrogen atoms as claimed by the chemists and it then only dawned upon me that nuclear resonance and chemistry had much more to do with each other than we ever thought in the beginning.

Now it seemed doubly worthwhile to get still more homogeneous fields and it did not take too long, sticking to alcohol, until the much finer spin-spin splitting started to show up. But the going became hard until we fully realized the advantages of motional narrowing and nature was imitated through rapid rotation of the sample. It was then only that the lines began to approach their natural width and that the wealth of information, to be gained from high resolution, made its first appearance in the work of Arnold and Anderson.

I have warned or, better, I promised that I would only talk about some very old things and it would be presumptuous, indeed, if I would even begin to say something about the more recent developments or to describe the many other uses of nuclear magnetic resonance which have been found and keep on being found for research not only in chemistry but also in biology, geophysics and even in plain old physics. They certainly do not fall into the category of my first-hand experiences and I gladly leave it to the next speakers to present factual new information. There is only one more remark I wish to make on this memorable occasion: far from being disappointed that nuclear magnetic resonance has ceased to be an art for art's sake, I am happy that it has become a useful servant. In this age of extreme specialization it is heart-warming to think that the early

work has provided a link between different branches of science and I am sure that the strength of this link will be splendidly manifested in the following talks.

It is a great pleasure for me to be here and I wish to express my gratitude to Dr. Fiat and all others who have helped to organize this symposium.