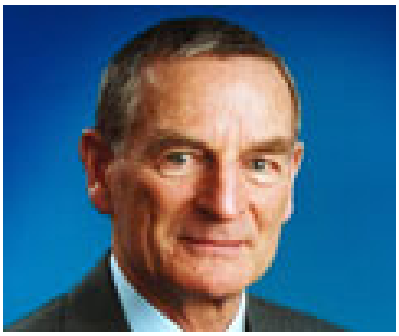
1965-6 Rex Richards



I followed Norman Sheppard as Chairman of the Group but the late David Whiffen remained as Vice-chairman. Like Norman, I served for one year only so this account will be concerned with my general involvement in NMR. As a result of my interests the Physics applications of NMR, I also was involved in the formation of the British Radiofrequency Spectroscopy Group (now affiliated to the Institute of Physics) which was founded in 1956.

This is a very personal account of some of the stages which I found particularly exciting in the research in my laboratory at Oxford on magnetic resonance. I became interested in NMR in 1948, but Bernard Rollin, working in the Clarendon Laboratory, published his first observations of NMR in 1946 very soon after the original announcements from Harvard and from Stanford. Rollin used the simplest possible system in which a signal generator passed an appropriate radio frequency through a high impedance to a tuned rf sample coil which was thus supplied from a constant current source. The voltage on the coil was measured with an rf amplifier and homodyne (phase sensitive) detector; when energy was absorbed in the coil the voltage across it dropped and a NMR signal could be detected. Bernard Rollin was very kind to me and gave me a lot of very helpful

advice to enable me to set up a simple NMR instrument, though he did not believe that we would find anything of use to chemistry!

The magnet we started with had very limited homogeneity, so only broad lines could be measured, and this meant working with solids. Most of our instrument was built in the laboratory from components obtained by carefully unsoldering them from ex-service racks of electronics which we were able to get at virtually zero cost. My research training with H. W. Thompson in infra-red spectroscopy had taught me many laboratory arts and crafts and to be ready to improvise and have the confidence to make whatever is needed; an excellent preparation for the early days of NMR.

This work led to numerous publications in which the line shapes and widths of resonances in solids were interpreted in terms of the structures of the molecules involved. The discovery of the chemical shift was of immediate significance to anyone brought up in the early days of infra-red spectroscopy and we set to work to build a better magnet with the very limited funds at our disposal, and constructed an electromagnet with 11" pole faces and a gap of 2". In spite of much care and adjustment, the performance of the magnet was not good enough for proton shifts,, so the obvious answer was to use it to study heavy nuclei. We were able to study a very wide range of chemical problems using the nuclei of cobalt, thallium, gallium, indium, and many other elements.

By this time, more detailed study of magnet design and consideration of the factors affecting homogeneity suggested that a well designed permanent magnet might give a very cost effective solution for high resolution NMR. I was able to raise £2,000 and to persuade the Mullard company to build a permanent magnet.

In the course of conversation with Marcel Golay over dinner, I told him about my design for a permanent magnet and about the problem of compensating for residual field inhomogeneities arising from imperfections of gap geometry and from the grain structure of the pole pieces. I later had a letter from him setting out a detailed theory of a design for a set of correcting coils which could, in principle, cancel out any field gradient with a set of orthogonal adjustments. He had some sets of printed circuits made, and very kindly sent me one. We installed this on the Mullard permanent magnet, and they worked extremely well!. This permanent magnet became the basis of a very simple and reliable high resolution spectrometer; although the field, at 30MHz for hydrogen, was very modest, the field value and the very good homogeneity were remarkably stable. We used this instrument to explore a wide variety of high resolution NMR applications many of which would seem commonplace today. This simple NMR spectrometer was subsequently used as the basis of a series of relatively inexpensive but reliable instruments manufactured by the Perkin Elmer Co Ltd, in the UK and later by other companies.

The commercial production of Nb/Zr superconductors in the early 1960s brought the possibility of the construction of higher field homogeneous and persistent magnets, and indeed Varian Associates were very quick to take advantage of this and produced their pioneering 220MHz spectrometer. This instrument was too expensive and too inflexible for our purposes at Oxford so I resolved to raise funds to develop a magnet ourselves, knowing that Martin Wood (now Sir Martin) had already made a small magnet at the Oxford Instrument Co and the engineers there were rapidly acquiring the skills required. It was agreed that Oxford Instrument Co would build two magnets; the first to be a small model to test the design details and the second, a bigger one, to take advantage of lessons learned from the first. The first

magnet had a room temperature gap of only 2.2 cm, yet it produced a truly persistent field of 5T and the field homogeneity could readily be adjusted to about 1 ppm over 1 cm^3 without spinning. This seemed too good to treat purely as a design exercise, so we designed a spectrometer to use the magnet; although the homogeneity was not good enough for proton high resolution work, there were plenty of other nuclei to study. In the meantime, Oxford Instruments were building the second magnet using the newly available Nb/Ti conductor which was much more stable than Nb/Zr. This magnet was persistent at about 7.5T (320MHz for protons) in a 3cm room temperature bore and has been in use more or less continuously since 1969.
I decided to aim the new magnet particularly at phosphorus resonances on the grounds that our new spectrometer would be sensitive and homogeneous enough and the phosphorus spectra would be simpler in biological materials than the proton ones.

In 1969 I was appointed Warden of Merton College and Professor R. R. Porter very generously welcomed me and my colleagues into the Biochemistry Department with all our equipment and engineering. The obvious success of the 7.5T magnet made it clear that the Oxford Instruments design was a good one, and should be exploited immediately. At the same time it was clear that a larger bore was required to give more room for the probe and to make homogeneity adjustment easier, and it was decided to invite Bruker Physik to collaborate with us. The same basic design of magnet was to be used, with the bore increased and the field reduced to a value corresponding to 270MHz for protons. The new 270MHz magnet was a great success; it had excellent resolution and stability.. It formed the basis of a long line of high resolution magnets manufactured by Oxford Instruments and a later version is a 750MHz persistent magnet in use in Oxford for proton resonance

work on proteins. At the same time, David Hoult and David Gadian developed a new pulsed phosphorus spectrometer for the 7.5T magnet which was quite sophisticated for the time and had a good performance. The great advantage of having moved into the Department of Biochemistry was that we were surrounded by people who knew what problems were worth tackling and how to handle the complex materials involved. In particular we were able to start a long and fruitful collaboration with Dr George Radda and his colleagues who were very quick to see the possibilities of NMR techniques and ready to make the effort to understand them. The 7.5T instrument was used initially to do a thorough study of the effects on the chemical shifts of phosphorus resonances of typical biological materials of temperature, pH, ionic strength, and the presence of other salts in the solution. Because we were members of the Oxford Enzyme Group which was particularly studying the glycolytic pathway, it was also decided to start to look at the phosphorus resonances of muscle extracts. Many experiments were done, and it could be shown that glycolysis was fully operational in these extracts with appropriate additions. There was speculation at the time about whether there was any hope of observing these processes in intact muscle, but the expectation was that the relaxation times would be too short. After a few false but very promising starts we used the hind leg of a rat which had been very extensively studied by classical methods.. Techniques were developed for maintaining perfused organs in the spectrometer. Collaboration with D. Wilkie and his colleagues at University College, London, led to a careful re-analysis of muscle metabolism in working muscle which largely confirmed earlier work by freeze-clamp methods but with greater accuracy. G. K. Radda and his colleagues extended the measurements to perfused kidneys, liver, and heart.

In 1977 I became Vice-Chancellor of Oxford University and my active participation in day to day laboratory work inevitably ceased