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Sir Rex Richards FRS in interview with Max Blythe
Oxford, March 1988
Interview Two

MB Sir Rex, in the closing minutes of our last interview, we had you returning in 1955 from America working with Purcell¹ and then Pound,² and then moving progressively on to various interests with magnets, electromagnets, and then moving towards the 1960s and changes in interests, and also a meeting with Martin Wood – we'd just mentioned, I think, at the close of the interview – that was going to be quite significant.

RR Yes, indeed. Yes. Well, you see, at the end of the... by the late 1950s when high-resolution magnetic resonance had become quite well-established by then, although the equipment was still rather primitive, but my high-resolution permanent magnet instrument was behaving very well, and it was very productive in exploring the use of NMR [nuclear magnetic resonance] to study the structures of organic compounds of modest size.

MB This is the magnet made by Mullard?

RR Mullard. Yes, that's the magnet made by Mullard. And from that time onwards, this technique of high-resolution NMR was exploited; commercial equipment was manufactured by one or two major international manufacturers, and it has, of course, become a technique of immense importance in the organic chemical and pharmaceutical industry. It is the method of choice for obtaining the structures of organic compounds.

¹ Professor Edward Mills Purcell (1912-1997), Professor of Physics at Harvard University, 1949-77. In 1952 he shared the Nobel Prize in physics with Felix Bloch for work on nuclear magnetic resonance.

² Robert V Pound. In December 1945, he participated with his colleagues, E M Purcell and H C Torrey, in the first observation of nuclear magnetic resonance.

MB And all of that massive range of measuring that you carried out across the periodic table in the late Fifties.

RR Yes. Yes, well, that was mainly focused on hydrogen and fluorine resonances, and to some extent carbon-13, but during the late Fifties and Sixties, we explored a whole lot of the elements of the periodic table, looking at the kind of things that could be done. But few other people did that; there were a few laboratories interested in that, but technically it was much more difficult. And it's only in the last fifteen years, really, that a great deal of work on those elements has been done. But at that time, having seen how the technique could be applied to ordinary organic compounds, I was becoming interested in the possibility of extending it to biochemical materials.

Now, biochemical materials offer a particular difficulty. For one thing, they are substances of considerable complexity; they have high molecular weights, with a very large number of hydrogen atoms, and so the high-resolution proton resonance spectra were, are very complicated – there are very, very many lines. And you will remember that when we talked about the chemical shift, which is the effect which distinguishes the resonances of one hydrogen atom from another, this is field dependent – it depends on the applied magnetic field. And so at the modest fields that were then available, the separation of these resonances was not very great, and so if you had, say, a thousand hydrogen atoms, it was a really formidable problem. And, in fact, at that time, the spectra were so overlapping that there was no question of disentangling them. So the field strength was a major limitation, magnetic field strength. And one couldn't raise the field strength any higher than about 20 kilogauss, because that was the saturation field of iron. Now, there is another difficulty about biochemical materials, and that is that they're often present in only very low concentrations, and NMR is a technique, inherently, very insensitive technique. The signals are very, very weak and one always works with the highest possible concentration. So there was a problem of sorting out the nuclear resonances from the random fluctuations caused by the thermal motion of the sample, and the thermal oscillations and the motions in the equipment. So these were the two main difficulties about going into biochemical studies.

Now, they could be overcome by taking advantage of a very interesting effect, which was discovered by a number of people in the States, and exploited particularly

by Bob Sherman at Bell Telephone Laboratories and by Mildred Cohn³ at the University of Pennsylvania. This is an effect by which the effect of certain transition metal ions on the relaxation time of the water solvent is modulated by association between the paramagnetic ion and biochemical macromolecules. And this so-called ‘nuclear relaxation enhancement technique’ was developed, especially by Mildred Cohn, in the States, and we were very interested in it at that time, and some of my colleagues and I did some similar work. And so, that relaxation time work was going on during the Sixties. It didn’t prove to be very profitable, but rather interesting things came out of it, connected with the amount of molecular motion associated with certain macromolecules.

MB You mean they did indicate the kind of momentum that...

RR Yes. It got me interested in biochemical problems, really, and the big lesson it taught me was how difficult it is to do biochemical studies in a physical chemistry laboratory. We didn’t really know what we were doing. We were, in fact, making very precise and sophisticated measurements on samples we didn’t properly understand, although I constantly ran across to the biochemistry laboratory and the path lab, getting advice, it’s not very satisfactory. And I learnt that the hard way, over a period of a few years. So I was really interested in how to solve the problem of the field strength, and of the signal-to-noise [ratio]. And at about that time, a number of physicists, especially in Paris, were working on a technique known as ‘dynamic nuclear polarisation’, which produces dramatic changes in the signal, of an NMR signal, in certain circumstances. So I became fascinated by this, and set out to explore this in the hope that it might prove a way of getting something. Now, the way in which this works, it depends... it works when you have a mixture of paramagnetic substances with an unpaired electron in them – and we were using free radical – and an ordinary diamagnetic material with nuclei in it. A typical case might be a solution of an organic substance in which we were interested, with a minute concentration of a few parts per million of a free radical. And it turns out that if you... the relaxation of the nuclei and the electrons is coupled, that is to say, if you stimulate an electron from the lower energy level to the upper – remember that electrons have magnetic moments and behave just like the nuclei when

³ Mildred Cohn (b. 1913) held faculty positions at Washington University School of Medicine, the Institute of Cancer Research at Fox Chase Cancer Center, and the University of Pennsylvania.

you put them in a magnetic field; they have two energy levels arising from the interaction of their magnetic moment with the field, so there is an electron resonance phenomenon as well as a nuclear resonance phenomenon. And we were doing both of these experiments simultaneously in these solutions, and it turns out that if you disturb the populations of the electron spins, because of the mutual interaction between the nuclei and the electrons, this disturbs the population of the nuclei. And in favourable cases, you can cause the nuclear populations not only to be inverted, so that you have more nuclei in the upper level than the lower, but inverted by a factor of a hundred times as much. So, in a favourable case, you could take these solutions, saturate... that is to say, strongly irradiate the electron resonance, and the nuclear resonance turned upside-down and became a hundred times stronger – very exciting.

MB Massive effect.

RR Tremendous effect. So we set out to do this: this is technically very difficult. About the time I'd got it going, John White arrived as an 1851 Scholar⁴ from Sydney, and he and I set up the first viable experiment, and we pursued this until, I should think, about 1968 or '69, and had an absolutely wonderful time exploring the physics, and the nuclear spin physics in these solutions, and got all sorts of exciting and peculiar effects. But it turned out to be of no value whatever to the biochemical work. But, nevertheless, it was a very satisfying and amusing interlude.

MB Well worthwhile.

RR But it didn't... it turns out, for two important reasons: one is that it really isn't practicable to find a free radical stable enough to be introduced into the ordinary biochemical systems we were interested in, and secondly, the enhancement we got from large molecular waves was very low.

MB Right, but for a time, it increased the interest in this field of work.

RR Yes, yes. I mean, we thought it might, but as I began to understand the phenomenon more thoroughly, I did quickly realise that it wasn't going to be much use

⁴ Fellowship awarded by the Royal Commission for the Exhibition of 1851.

for the biochemical work. And, in fact, I read a paper at a meeting in Sweden, back in... oh, I think about '63 or '64, describing this effect and saying that it wasn't going to be much good for biochemical work. But it was such fun, from the physics point of view. And I gave a lecture to the Alembic Club, in which I took immense trouble, and we used a closed-circuit television because the equipment couldn't be taken to the lecture room. But we did, in fact, mount some of the most difficult experiments one evening and showed them in the lecture room, and we made a videotape of it, and to my great dismay, I discovered later that it had all been rubbed off. Because those experiments will never be repeated, I think. They were very difficult to do, and I can't think that anyone will want to do them. But, anyhow, they're published. But it was a pity. So that line of study proved fruitless, from the point of view of the biochemistry.

But, of course, as I did tell you, around about 1962 my friend Martin Wood⁵ came back from America with one of the first pieces of continuous superconducting wire, a niobium-zirconium wire, and he wound a little magnet, which, of course, because it doesn't need to have an iron core, will produce a field limited only by the physical properties of the wire. And he wound a little magnet, the sort of size that one could hold in one's two hands, and which, driven from an accumulator, produced a field of 4 Tesla, that's 40 kilogauss – twice the field that you could produce with a large iron electromagnet. So that was tremendously exciting. And I went to the Science Research Council and told them about this, and proposed to them that we should try to build a high-resolution superconducting magnet.

Now, of course, at that time, Varian Associates were also working on this and, in fact, in the middle Sixties, Varian Associates produced a commercially... a 200 megahertz – that's 4 Tesla, about – high-resolution magnet, which they sold. It wasn't a very good one, but they did sell quite a number. So we were some way behind them. And the Science Research Council, to their very great credit, I think, made me a very considerable grant, for those times; I forget what it was, but it wasn't a great deal of money in today's figures, but it was a big grant then. And my proposal was to build two magnets: a small model magnet, which would have a one-inch bore, in which we would learn the craft the hard way, and then build a more professional magnet, which

⁵ Sir Martin Wood FRS was the founder and chairman of Oxford Instruments Ltd from 1959-83. He has served as the deputy chairman of Oxford Instruments Group plc since 1983.

we would actually use – that was the idea. And we built the first magnet from niobium-zirconium, which is the alloy which was then used, and it was a simply awful struggle. We worked terribly, terribly hard, till late at night, night after night. The magnet was built, the cryostat – you know the thing has to be kept in liquid helium – and the cryostat when it used to go off into oscillations, it sounded like an organ note! It would make a deep, deep, kind of rather disturbing rumble, and as soon as it oscillated, the helium boiled off like mad. And trying to stop that... I can remember being there till midnight, night after night, struggling with this thing. And then we got that solved, and we got the magnet to go. But niobium-zirconium is a terribly unstable material, and you would get the field up and then the slightest little disturbance – a little pulse of a field, or a sudden movement of an iron object, or a little vibration – and the magnet would quench, all the helium would boil off in the most dramatic way, filling the room with steam. And I can remember Howard Hill and John Rackstraw and a number of other chaps there; we really sweated blood to...

MB A kind of nursing team, keeping it going.

RR It was terribly hard work to get it to go. But eventually we got quite good field stability and homogeneity with it. You see, by that time, having worked on the big permanent magnet, I'd thought a great deal about how to make homogeneous magnetic fields, and I'd had the great good fortune to know Marcel Golay – I think I spoke about him at an earlier stage – and his theory worked very much better in the cylindrical symmetry of a superconducting magnet than it did with an iron magnet. So we were able to take advantage of all that, for field corrections and so on. And I knew a lot about the materials that you could use, which would not disturb the field homogeneity, so I had a great deal of experience, as it were, soaked into the back of my mind, with which we were able to build this first magnet. And so, in the light of that, by the time that magnet... we'd learned all these lessons, niobium-titanium wires were becoming available, and this is a very much more stable conductor, and works at higher magnetic fields.

And so the second magnet was designed and built with a niobium-titanium wire, and that had a room temperature bore of about an inch and a half. It's not very much when you've got to realise you've got to get all your radio frequency equipment and the

sample, and it's right up inside a long thin tube, because, of course, it's got to have the helium around the magnet. But we built that magnet. It worked at a field equivalent to 320 megahertz, which is... let's see, that's about 6 Tesla – quite a high field – 60 kilogauss, three times the field of an iron magnet. And that magnet worked well. It had good... reasonably good resolution. It wasn't good enough for high-resolution proton resonances, but it was good enough for quite a lot of broad resonances. We studied some high molecular weight chemical materials; we looked at caesium resonances, all sorts of other elements, and had quite a jolly time doing a great variety of NMR work with that magnet. And that brought us to about the late 1960s. So, during those 1960s, we were doing a lot of work on elements right across the periodic table; we were exploring the ordinary high resolution proton resonances, using the old permanent magnet; we were doing the nuclear electron double resonance, which turned out to be just a physics, or a very chemical physics, perhaps, experiment; and then we were doing this engineering in preparation for the biochemical work.

And just at that stage, I was invited by the Fellows of Merton to go and become Warden of Merton, because I was, at the time... Oh, perhaps I should say, of course, in 1964 I was elected to the Dr Lee's Chair in succession to [Sir Cyril] Hinshelwood, and that didn't change things for me very much. I'd had excellent facilities in the physical chemistry lab. It put all sorts of responsibilities on my shoulders, which I hadn't had before, but I didn't find them too onerous. You know, it is rather awkward when an internal candidate is appointed some six months before the outgoing professor is retiring, and so as soon as I was appointed, I took leave and spent half the time in America, and half the time in the Soviet Union. I went off and gave a lot of lectures there. They worked me terribly hard there! And so I came back in the autumn, when Hinsh [Hinshelwood] was about to retire. And so I had a very, very nice time, because it was a time of great expansion in the universities, money poured in.

MB Money was available.

RR We built two new floors on the laboratory, I was able to revamp the teaching course in a very dramatic way, and we appointed quite a lot of new staff to the laboratory. We were much the biggest physical chemistry department in the country. And so it was a very thrilling time, really, for me.

MB The start of quite a long career as an Oxford statesman.

RR Yes. I had a very happy time, I mean, and my colleagues were very supportive, and it was a very good time, as I remember it, anyway. But then, in '69, the Fellows of Merton asked me if I would like to become Warden of Merton and my first reaction was, 'Good Heavens, no!' you know. But then when I started to think about it, I realised that if we were going to pursue the biochemical work, it was really hopeless because I didn't know enough about it, and I could see that the only really successful way of doing that was to do it in a department where you had biologists all round you, who really knew what they were talking about.

So I went over and talked to Rodney Porter,⁶ whom I knew well, in the Biochemistry Department, and told him about this, and said, 'What about it?' And he, with great generosity, I think, said, 'Well, look here, by all means, for goodness sake take the job and come over here. We'll find room for you somewhere.' And, of course, that was a very generous reaction. But, of course, finding room for... and you know, I was not... you know, I was bringing immense quantities of equipment, which was quite bulky, and the problem was where on earth was it going to go? And he solved... Rodney Porter solved it, by putting most of our equipment in what was then the cloakroom. There was a huge cloakroom on the ground floor of the Biochemistry Department. I don't know how he could have persuaded his colleagues to agree to it, but he just ripped all the insides of it out – lavatories and an enormous number of lockers and coat hangers and so on – they ripped it all out, and made a rather good laboratory for our heavy equipment, on the ground floor, you see. And I don't know what became of all the coats! But anyhow, that was... we moved in there. And I also had another room which he had, which was one of his own research suite next to his office, and he very generously shoved all his stuff into another room and gave us that as well. It was a very generous, and, as it turned out, quite a far-sighted thing to do because it all turned out rather well. But anyhow, he agreed to that, and so that altered my whole view of it.

⁶ Sir Rodney Robert Porter FRS (1917-1985), Whitley Professor of Biochemistry, 1967-85, University of Oxford. Awarded Nobel Prize in 1972 for Physiology or Medicine.

And so, at that time, the Fellows of Merton weren't inviting me to go as Warden of Merton, but they said, would I... I was one of three people they had in mind, and would I consider it? So I went back and said, 'Yes. If you decided you wanted me to go, then I should move all my equipment into the Biochemistry Lab, but I want to make it clear that I'm not coming just as a head of a college, I shall expect to have enough time to do some research.' In any case, it was my view that a head of a college ought to be seen to be seriously engaged in academic work; it's important for the young to see that going on. But, anyhow, that's as it was. And shortly afterwards, the Fellows came back and said yes, they wanted me to go. And they were extremely generous, they didn't ask me to do a lot of chores, which could perfectly well be done by other Fellows or by somebody else, and they did give me a lot of time free. And I'm eternally grateful to them. And I had fifteen years of the happiest time of my life in Merton, I think.

MB And very productive years in terms of the research.

RR And it turned out to be very productive, yes. So that was in the beginning of '69. Now, of course, I couldn't... and this had happened because Robin Harrison,⁷ who had been my predecessor at Merton, had a very serious illness and died quite suddenly and unexpectedly. And the old Merton statutes required that the Warden should be elected, I think, within two months of the death of, or departure of, the previous Warden. And, of course, that was a ridiculous situation! And so the Fellows moved like lightning, because the statutes provide that if they couldn't make up their minds in time, that the choice would fall to the Visitor, who was the Archbishop of Canterbury, and they didn't want... having someone foisted on them, obviously. So they elected me, but I couldn't possibly walk out of the Physical Chemistry Laboratory at such short notice. So they elected me as Warden of Merton and gave me instantly a year's leave of absence. This was how to get over the technicality. So I actually moved into the Warden's Lodgings at the Christmas of '69, but continued functioning as the professor until the following summer. And that was very good, it gave me time to get myself organised.

⁷ Alick Robin Walsham Harrison (1900-1969) was appointed Warden of Merton College, Oxford in 1963.

But at just that time, the... Sir Ewart Jones had been chairman of the Chemistry Committee of the Science Research Council, as it was then, and had been arguing that too much money was being spent on what was then called 'big science' – nuclear physics, space research, that kind of thing – and he had been challenged by the Science Council, and said, 'Okay, well, look, if you wanted it to spend more than the kind of small change,' which was what the Chemistry Committee was really spending of the total budget, 'what would you do?' And Tim Jones had said, 'Well, there are a number of big projects which I think we ought to stimulate. And one of them is to study enzyme chemistry, because enzymes are very extraordinary organic compounds, catalysts of quite incredible power and precision, may have great industrial importance. Why don't we make a big initiative and offer a lot of money to the community, the scientific community, to look at enzyme chemistry?' Well, we had been... and, of course, because Tim Jones was professor of organic chemistry at Oxford, he'd been chatting about this to everyone in Oxford, so we all knew about these ideas. And, of course, a lot of people in Oxford were, at that time, very interested in mechanisms of enzyme function, enzyme structures. Dorothy [Hodgkin]⁸ was working on enzymes, the people in the Organic Chemistry Department were working on mechanisms of enzyme reactions, so were the people in Biochemistry.

And so the idea gathered ground, and I don't know... I think it may have been Tim Jones's idea, originally, that in Oxford, we should try and get a group of people together to form a consortium, to have a real attack on enzyme chemistry. I think it was probably Tim Jones's original idea. But a group of people – and I think the prime movers were Jeremy Knowles,⁹ who's now a professor at Harvard; Bob Williams,¹⁰ who's a professor in Oxford now; David Phillips¹¹... I think they were the three prime movers, and George Radda.¹² They were, I think, the main movers, and felt that this

⁸ Professor Dorothy Crowfoot Hodgkin FRS (1910-1994), Wolfson Research Professor, University of Oxford, 1960-77. Awarded the Nobel Prize in Chemistry in 1964.

⁹ Professor Jeremy Knowles FRS, was a fellow and tutor of Wadham College, Oxford before joining Harvard University, USA in 1974. He was appointed Amory Houghton Professor of Chemistry and Biochemistry in 1979 and became Dean of the Faculty of Arts and Sciences in 1991.

¹⁰ Professor Robert Williams FRS was appointed Royal Society Napier Professor at University of Oxford in 1974.

¹¹ Professor Sir David Phillips FRS (1924-1999), Professor of Molecular Biophysics at University of Oxford, 1966-90. He was created a life peer in 1994, taking the title Lord Phillips of Ellesmere.

¹² Professor George Radda FRS, Chief Executive of the Medical Research Council since 1996 and British Heart Foundation Professor of Molecular Cardiology at University of Oxford since 1984. He was a University Lecturer in Biochemistry at Oxford, 1966-84.

was really something worth having a go at. And because, of course, with my biochemical interests, and because I was now Warden of Merton, and George Radda was a Fellow of Merton, I got very interested in this, and so we all started talking about what could be done. And as the nebulous ideas kind of gathered themselves in our minds, they came to me and said, 'Look here, you're moving out of the physical chemistry lab, you're going to be, as it were, somebody standing a bit on the side, would you care to become the chairman of a group and see if you can gather us all together and do something about it?' So I thought this was rather a thrilling idea. And so I started the thing up with these people, and we gathered together about twenty people, from eight different departments in the University, including Dorothy. Dorothy was one of the members. And they came from clinical biochemistry, biochemistry, organic chemistry, inorganic chemistry, physical chemistry, pathology, molecular biophysics – that's seven, and there's another one.

MB Did they come from pharmacology also?

RR There wasn't one from pharmacology. There was another... maybe crystallography, perhaps. But, anyhow, there were eight departments involved, originally.

MB Tremendous start.

RR A big group of people, and we talked about how we were going to get all these people together. Many of us didn't even know one another. And I felt that the only way to do it was to have some means... regular basis, when we would meet. And so we decided, in the first year, that we would meet every other Monday, have a simple meal in one of the Colleges – and we cycled round the Colleges of the twenty members – and after dinner, we would settle down at eight o'clock and work till ten thirty, talking science. And we started that off, and that was a terrific success. Having a meal together is a wonderful way of getting to know one another. It was all very informal. And we were very, very lucky with the particular personalities of Bob Williams and of Jeremy Knowles – both wonderful, original, sparkling people, with outward-going personalities, and as luck would have it, they were both Fellows of Wadham, knew each other well, so they could be frightfully rude to one another without causing

offence. Do you understand this? It's very, very important, a very important quality to have, to be able to argue and rubbish other people's ideas, without being offensive and destructive.

MB So they created a nice discussion temperature, a nice climate?

RR Oh, terrific! Oh, it was tremendously exciting! And I think we owe a lot to Bob and Jeremy for establishing that atmosphere. It was very... just lucky chance, you see. They knew one another well, and they were both the right sort of personalities. And so the whole thing sparkled terrifically, and people, quite soon, after a month or two of meeting regularly, quite soon got to the stage where they didn't mind a bit what they said; we just said what came into our minds at the time, and nobody felt offended by the criticism.

MB There must have been an immense benefit, from the many angles focused on this.

RR I think there was. I think there was. Oh yes, well, that came later. So we talked at some length about what could be done. And so gradually a kind of plan of attack evolved and, of course, partly because of my presence, and partly because of the time, it was realised that we were just poised on the brink where NMR might have a tremendously important part to play. And so we used this as an opportunity to go to the Science Research Council and say, 'Look, we want to establish the Enzyme Group.'

We wanted an enzyme preparation laboratory because, you know, preparing the enzymes, in those days, at any rate, was a fearful job to do in everybody's lab. You know, it was a colossal... you could sweat blood for months just to get a tiny sample before you could even start your experiments. So we thought we'd have a central laboratory with great cauldrons, you know, where you could make reasonable amounts of material, and one or two skilled technicians who would be able to keep the thing going. So that was one major plan. The second major plan was to get money to, really, make a big effort to make a high-resolution NMR machine that could look at biochemical materials – that was the second. And the third plan was to say, 'How are we going to knit all these people together?' Okay, you can have dinner together, but

it's not enough. And I thought of the idea of having a number of postdoctoral research fellowships, which would be assigned to projects which involved at least two of the members of the group, preferably in different departments. You see, the departments in the science area are quite close together, but, nevertheless, they are in different buildings, and if you're going to get people interacting, you can only do that if they're walking back and forth all the time. So we asked the Science Research Council to assign us... I forget what it was, four or five a year – quite a lot – which would be awarded by us, simply on the basis that they would be awarded for work which deeply involved at least two departments, and if possible, three. So these people were supposed to be the glue that was going to cement the departments together. And the Science Research Council, to their great credit, saw the point of this and gave us a very large sum so that we could do that. And it was of crucial importance, in my opinion.

So those are the three things. We got the money, and we set off. The enzyme prep lab just went ahead, because that was using all well-established technology, and one or two members of the group were skilled at that, and they just took responsibility for it, and it set off. It had its problems but, nevertheless, that worked. The shared postdoctoral fellowships worked very well too. That was a great success. And then the NMR thing had to be considered. And we debated how to tackle this, and decided it was too big a job for us to design and build the spectrometers, although I was very tempted to do it because I was interested in it. But in the end we decided against it, and we negotiated with Bruker Physik, which is a German manufacturer that makes very high quality equipment and was becoming the major international supplier of magnetic resonance equipment. We negotiated with them. I can remember a big meeting in the dining room of the Warden's Lodgings in Merton, where we discussed all this with their engineers. And the idea was that we would get them to build us a console with all the electronic and computing equipment to work at 270 megahertz, whereas a 100, 90 megahertz was their standard frequency, so we were to give a four-fold increase in one step. And we were going to design and build a magnet that would match that. And so that was negotiated, they agreed to do it at very, very low cost because, of course, it was a tremendous advantage to them. So they supplied us with a lot of equipment at virtually... probably less than it actually cost them to build. And then we set to work with Martin Wood's colleagues at Oxford Instruments, to design a magnet to go with it. And when we came to look into it, we found that the 320 megahertz magnet that they'd

built for us, which was now working quite well, but had too small a bore, we just did a few calculations and worked out that if we increased the bore of that magnet, until the field came down to 270, we would end up with something just about of the specification we wanted.

So the third magnet was built on the design of the second one, but with a bigger bore and a slightly lower field. And that magnet worked superbly and it's still working in the biochemistry lab. It was finished about 1970, end of 1970, early '71. And it remained at field until the late 1970s, when, on Christmas Day, one of my graduate students quenched it. The arrangement was... these magnets were... perhaps I'll come to that later. But, anyhow, that magnet, the 270 megahertz magnet, turned out to have fantastic resolution – something like a few parts in 10^{10} – and it was very stable; it didn't change by more than a few parts per million, over seven years. And it was a very great success. And the result of that was that Oxford Instruments started manufacturing this magnet in, really, quite considerable numbers. And Bruker Physik sold to the world at large, a 270 megahertz spectrometer. So that was, from the technological and engineering point of view, a great success.

MB And an immense support to the enzyme work.

RR And an enormous spur to the enzyme work. And with the aid of the Enzyme Group grant, we were able to appoint Iain Campbell, who had been a post-doc fellow working with me for some years, as a university lecturer to take charge of this high-resolution work. And he, together with Bob Williams, and Chris Dobson, did some tremendous work in the early Seventies, in which they actually laid down all the standard techniques for analysing the high-resolution spectra of proteins, small proteins up to a molecular weight of 7,000 or 8,000... 10,000, perhaps. And there's a whole series of publications in which they worked out how to set about this, and how to disentangle the spectra and assign the resonances, and interpret them in terms of the structure of the enzyme, the amount of molecular motion and so on, and the changes that occurred to the structure when the enzyme would bind the substrate. And a lot of that pioneering work was done in those early years, and, of course, it's all very much more elaborate and sophisticated now. But the basic techniques were worked out then, and Iain Campbell, I think, should take a large amount of credit for that.

So that was all a terrifically exciting time. But, by that time, by the early Seventies, I had lost interest in the high-resolution work, really. I could see how it was all going to go. And I had come from the stamp of scientists... I'm interested in exploring new ways of using a technique, rather, perhaps, than in focusing on one particular problem and sorting it out. So I could see how all that was going to go, and was getting interested in other things. And so I thought that, you know, when you're doing research, unless you're really interested in something, you don't do it very well. So I could see that it would be wise to be looking at something else.

So we moved the old 320 megahertz magnet over into the biochemistry lab, and George Radda and I started working together on phosphorus resonances in biochemical systems. Now, the advantage of doing that was that phosphorus resonances are... of course, there are many fewer phosphorus atoms in us, inside, and so the spectra are not nearly so complicated. On the other hand... therefore, one doesn't require such high-resolution. On the other hand, they're at a much weaker resonance – it's only about one-fifteenth, one over fifteen, as strong as proton resonances, so there's a technical problem there. However, we set off to see what we could do with phosphorus resonances in biochemical systems, and did all sorts of experiments on the molecular motion in enzymes by looking at the phosphorylated part of the enzyme. We did quite a lot of work on lipids, looking at the structures of lipids, because, of course, they all have phosphate groups in them. We looked at oriented lipids, and looked at the anisotropy, the way in which the phosphate groups were oriented in the lipid phase.

And at about that time, in the early Seventies, David Gadian had been studying physics at Merton, got a first, played football for the University – a very bright young man. And he came to see me and said, 'I don't think I'm frightfully interested in any of the physics research that I've been offered for a DPhil. Can you give me some advice?' So I said, 'Oh, why not do some biophysics?' I sent him off down to the laboratory, where he spent a little time. He came back, all filled with enthusiasm. And so he started to work for a DPhil with me, and I put him on to this phosphorus work, and he started looking at some phosphate groups. And then, at the same time, George Radda had working with him, a young man called Stephen Busby, and they were looking at the phosphorus resonances in extracts from muscle. George Radda, at the time, was

interested in muscle metabolism. You know, of course, that if we dash upstairs, our muscles do all the work to carry us up the stairs, and that the energy for that has to come from somewhere, and the question... and this had been studied for many years by muscle physiologists, especially at University College, London. And the mechanism of this was pretty well understood. The muscles store up glycogen and the glycogen can be degraded in a series of steps, enzyme-mediated reactions, and in the course of this degradation, they can produce ATP [adenosine triphosphate], which is a very energy-rich material. And this is a sequence of reactions called glycolysis, by which, effectively, sugar is converted into energy. And the energy which the muscles use is produced in the form of this triphosphate, adenosine triphosphate. But there is also another mechanism for producing ATP, which is by oxidative phosphorylation, using oxygen delivered by the blood to the site of the muscle. Now, when the muscle does work, the ATP is hydrolysed to ADP [adenosine diphosphate], and one of the phosphate groups is removed. But because of the very delicate biochemical balance, it's important that the ATP concentration should be maintained constant. So there's a rather wonderful buffering mechanism. The muscle stores up another phosphate called creatine phosphate in the muscle, and there's an enzyme that causes the creatine phosphate instantly to regenerate ATP from the ADP that is formed. So this rather lovely bit of machinery, which is set up in...

MB Bit of (?) biochemistry.

RR Yes. And this had been studied by muscle physiologists, by taking animal muscle and making it do a predefined amount of work, and then using a technique known as 'freeze clamp', by which the muscle was set up between the plates, two anvils, which were cooled in liquid nitrogen, and at the critical moment they were sprung together, so that the muscle was squished between the anvils and instantly frozen. And they assumed that the chemical reactions all stopped instantly, and then the stuff was scraped off and a chemical analysis done. Fearfully laborious business! It took them years to sort out all these reactions. Well, George Radda was trying to use NMR to make measurements of this kind, but by just doing extracts from the muscles, looking at the chemical extracts formed after digestion of the muscles. And Stephen Busby, who was working with George, one day said, 'Well, look, why don't we just put a piece of muscle into the NMR machine and see what we see?' And we all said, 'Oh,

you won't see anything at all. In the muscle the molecular motion is far too restricted, everything will be frightfully broadened.' But he went ahead and had a go, and to our amazement he produced the most beautiful phosphorus spectrum, half a dozen lines – three, four, five, six lines – all easily resolved, and we could instantly assign them, we knew what they were.

MB Incredible moment.

RR It was! We couldn't believe it! So we said, 'Oh, come on, Steve, we must do this again.' And he was working with rat muscles. So he repeated the experiment, not a thing. All we saw was just the single resonance due to inorganic phosphate. And we repeated it many times, got nothing. So it was all written off as some peculiar artefact. But George Radda and Stephen Busby kept worrying over this, and talking to the physiologists about it, and it turns out that he was quite extraordinarily lucky to get that to work the first time, because these muscles, when you kill the animal and get the muscle out, unless you do it exactly right, the muscle metabolism runs right down. If you let the animal shiver, for example, just before it's killed, it's all gone. And we were all amateurs, you see, we didn't really know what we were doing as physiologists, and so it was just an extraordinary stroke of luck that the first time he just got it right, the first time. But we tried it many times without! But anyhow, soon they discovered, they worked out a technique for getting these muscles out and could reproduce it beautifully. And that proved to be a discovery of very great importance because, as you probably know, George Radda now has an immense machine, worth millions of pounds, up at the John Radcliffe Hospital [Oxford], in which he could put you, and measure your muscle metabolism in your leg, or your metabolism in your brain, your liver, your kidney, your heart muscle, and see it all going on, and how it responds to stress and so on.

MB Formed the foundation of massive...

RR The foundation of what is called clinical magnetic resonance spectroscopy. Now, that mustn't be confused with NMR imaging – I'll talk about that later. But NMR imaging is a far more advanced technique than the clinical spectroscopy. But the clinical spectroscopy is potentially of very great importance, I think. But it came from

that... that casual experiment, really. So that made the study of phosphorus resonances very interesting. And so we persuaded the Oxford Instrument Company to design a much bigger magnet, with a bore big enough to put a whole animal into. And they designed a horizontal bore magnet which could be used for phosphorus resonances, and we could put... we could each of us put our arm into the magnet, and have measurements made on the muscles that run up and down the forearm here. And you could see, as you did work, by squeezing a rubber bulb, how the metabolism changed, and you could follow it and relate it to the amount of work your hand did. And George did a lot of beautiful experiments. And that work was all followed up by David Gadian.

And at the early stage of... when we realised what could be done, I realised that we weren't going to make much progress unless we involved a serious, well-respected physiologist. You see, at that time, magnetic resonance was a very mysterious and esoteric technique to physiologists, if not to biochemists, and if we started publishing numerical measurements, they would never have paid much attention, I think. And I happened to know Doug Wilkie,¹³ who is a professor at University College, London, and who had spent the greater part of his research career working on muscle physiology. And I went up to see him, and talked to him about this, got him interested, and he was tremendously interested, as you can imagine. And he came down twice, or three times a week and worked with David Gadian, and they repeated, over a period of about a year, all the muscle physiology experiments that he had done over the previous fifteen years, by the freeze clamp method. They got measurements which were considerably more accurate than the ones that had been done before. And because it was all published with Doug Wilkie's name on, it was instantly accepted by the physiology community. And I think that was a very important thing, because, you see, once that had been discovered, we were inundated with requests from people, from all over the place, saying, 'Oh, wouldn't you like to put a bit of our liver in?' or 'a bit of our kidney in.' You know, all sorts of people were interested in metabolism in all sorts of things. And we could easily have been side-tracked, by just popping a bit of this, and popping a bit of that in, and, of course, you know, you don't get any serious

¹³ Professor Douglas Wilkie FRS (1922-1998), Professor of Experimental Physiology, 1965-69, then Jodrell Professor and Head of Physiology Department, 1969-79, at University College London; Jodrell Research Professor of Physiology, 1979-88, then Emeritus Professor at the University of London.

scientific work done that way. It's what some people call the 'Ooh aah!' kind of experiment, which is a waste of time, really. One's very tempted to do that, of course, but I persuaded David Gadian that the sensible thing, particularly for him at his age, was really to focus on one thing and do it thoroughly. And that he did. And he's now a professor at the Royal College of Surgeons. But that was a very exciting period, I think. Now, where have we got to?

MB We're into second half of the Seventies.

RR Yes, that brings us up towards the second half of the Seventies. And, of course, by that stage, the technology of superconducting magnets was advancing very much – I was keeping a very close eye on that. There were new wires becoming available, multi-filamentary niobium-titanium wires were becoming available, and then someone produced some multi-filamentary niobium-tin wire. And niobium-tin is an alloy that will sustain much higher magnetic fields, and, obviously, you know, you can see that we were always looking to higher and higher fields. And so I was arguing with the people at Oxford Instruments and saying, 'Look, you want to get up to 500 megahertz.' And we talked endlessly about it. Now, niobium-tin presents terrible problems because the wire is terribly brittle. Once the niobium-tin is formed, you can't bend it, you can't make any change in the shape of it at all. So there was no question of winding it on a coil. So there was a rather wonderful technique you might be interested in, for doing this. What you do is to take a billet of bronze, about a metre long, and perhaps this diameter, and you use a rifle drill, and you drill, say, 2,000 holes through it, longways, so that it looks just like a collection of tubes. And in each of these holes, you put a rod of niobium, tight fit. Then you start drawing it, stretching it, and then you stretch it, and then you push it through a die, and you draw it and draw it and draw it until it ends up miles long, and you end up with, as I say, a half millimetre wire, which is a bronze wire with 2,000 filaments of niobium in it – a nice bit of technology involved in that. But, of course, that's not the superconductor. But this is a wonderfully ductile, flexible material, and if you take a piece of it and just dissolve away the bronze in acid, you get this marvellous little brush comes out with 2,000 filaments of niobium at the end. It's a tremendous lot. So what you do, you take this cable, you wind your magnet with it, you wind the cable and wire on the magnet, you fix it all down in special technical ways, you make the joints at the end, all ready, and then you take this magnet, and you

put it into a furnace where it can be heated through a very carefully controlled heating cycle, in a hydrogen atmosphere. And during the course of this, the tin of the bronze – you know bronze is a tin/copper alloy – the tin of the bronze diffuses into the niobium and forms the niobium-tin conductor. And when you've done that, you try it, if it works as a superconducting magnet, you say, 'Hooray!' If it doesn't work, you drop it in the bin because there's nothing whatever you can do with it.

So that was the technique that was going to be employed. And because of the difficulty of this technique, we designed a magnet which would have niobium-tin in the inner part, where the field strength was the highest, and have niobium-titanium in the outer part. And so this was going to be a nesting set of magnets, really. There were going to be three, actually – an outer niobium-titanium one, a middle one, and then the niobium-tin in the middle.

MB I'm just thinking of the distance from the first magnets you...

RR Yes. This is getting a very...

MB This is light-years away, isn't it.

RR ...getting a sophisticated design, it was getting quite big, and... oh, when we were starting on this, I remember, we used to meet every fortnight, down at Oxford Instruments, for about half a day, to discuss the design and the progress of the experiments they'd done there. And we focused all our attention on the niobium-tin magnet, because this was where we... this had never been done before, this is where we foresaw all the difficulties. How were we going to hold the wire steady? How were we going to make the joints? Because the joints were very critical, and a difficult part. How was it all going to be held together? Because, of course, you don't want gaps. And yet it's got to be... it's all got to withstand immense forces because the magnetic field gradients generate huge forces on the windings. So we set off on this, and the first magnets quenched, that is to say, they became non-superconducting at too low a field. And it turned out that we never had any trouble with the niobium-tin part. It all went perfectly because we'd focused all our energy and attention on that, and hadn't worried too much about the outer part because we thought we knew all about that. But, in fact,

all the troubles came with the outer part of the magnet, because, as the fields went up, the forces on these outer windings became enormous, and as the forces went up, we found that the windings were moving very, very slightly – only a few millionths of an inch, but enough to cause it to quench. And so the technical problem became an engineering problem, of how to make this whole thing rigid enough so that it was stable. And in the end, I can't remember the dates, I'm afraid, but in the end, Oxford Instruments made a magnet which worked at 470 megahertz, we didn't quite get to 500. And we have that in the laboratory now and it's been working beautifully. And they won a great prize from America for innovation in getting that thing to go. And then they very soon after that, learnt the other technical problems, and they have been manufacturing 500 megahertz magnets, I forget, five or six a month, I expect, for years. So it's a big business there, being sold all over the world.

MB Sir Rex, you've had many many problems and challenges with the magnet side and the techniques and technology involved. I've got a problem because we've got about three four minutes left to wind this section up. Perhaps, looking at the science, and that technology of the Seventies, I could leave it for you to begin to sew that up for the end of this second interview. Could I leave that with you, to sew up the Seventies for me?

RR So, I think, looking back at the Seventies, from the scientific point of view, certainly from my point of view, it was the most wonderfully thrilling and exciting time.

MB It sounds marvellous.

RR I was having a wonderful time in Merton; I was very interested in Merton College, though I haven't mentioned any of that. But the scientific work went very well. It was just the lucky juxtaposition of particular individuals, I think, there; that it was the right time, technology became available which wasn't available before. And I think we broke a lot of new ground and did a lot of innovative work, which has been developed enormously ever since, I think.

MB It's had the most marvellous repercussions in all kinds of areas as well.

RR All sorts of things. But, of course, looking back on it, we were all pretty naïve at that time. But, nevertheless, I think we did get it all started. And I think it wouldn't have happened but for that very interesting mixture of people who were prepared to get together. I ought to have said that one of the conditions of joining the Enzyme Group was that you would agree to devote not less than one-fifth of your effort to the work of the Enzyme Group. That didn't mean a fifth of your time, but a fifth of the effort you made had to be that. So it was a deep commitment from very senior, distinguished and original people, who had all sorts of exciting things of their own going on. But they were prepared to give a really serious commitment to the work. And for those early years – well, certainly for the first six or seven years of the Enzyme Group – I think the attendance at the meetings, every other Monday, without fail, the attendance of the meetings, must have been rarely less than fifteen out of twenty. And then in the later years, you know, these things wax and wane, it did fall away a bit for a time, and then it all gathered momentum again as people became excited. But I think that was a very thrilling time, certainly from my point of view.

MB Sir Rex, I'm very grateful for that step-by-step personal journey through what was an enormous period of development in NMR work, with all the repercussions we've suggested. This is the end of our second talk. We still have quite a lot to talk about because we haven't talked about Merton at length, or you being Vice-Chancellor here in Oxford, or about your colossal rise in interest in art.

RR Oh yes, well, of course that's a very big hobby.

MB This, perhaps, we should leave to another occasion.

RR We'll leave that to another occasion, yes. Thank you.