RAY FREEMAN

6 January 1932 – 1 May 2022

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Elected FRS 1979

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Ray Freeman pioneered many of the important advances in the technique of liquid-state nuclear magnetic resonance spectroscopy: his worked changed fundamentally the ways in which chemists and structural biologists use NMR spectroscopy. Born in Nottingham, he was an undergraduate chemistry student at Oxford after National Service working with radar, and completed his Part II and doctoral research with Rex Richards FRS. After brief spells with Anatole Abragam in Saclay, France, and at the National Physical Laboratory in Teddington, he worked for ten years in the research department of Varian Associates, Palo Alto, USA. He was appointed as Lecturer in Physical Chemistry and Tutorial Fellow of Magdalen College, Oxford, in 1973, and subsequently promoted to Aldrichian Praelector. In 1987 he was appointed to the John Humphrey Plummer chair at the University of Cambridge, where he remained active in research long after his retirement in 1999, publishing his last paper at the age of 84.

EARLY YEARS 1930-1951

Ray was born in Long Eaton, Derbyshire, in 1932, the only child of Albert and Hilda Freeman. Tragedy hit the Freeman household in 1940 when Albert, a builder and joiner by trade, died as a result of an infection contracted after a routine surgical procedure. This had a profound effect on Ray; it perhaps accounts for how intensely he felt about his own children and grandchildren, and also how much he valued the fatherly guidance and mentorship of figures such as Sir Rex Richards. Hilda had an interest in art and painting, but at that time this was not considered to be a suitable occupation for a young woman. Ray’s eye for graphic art and his beautiful handwriting were most definitely things he acquired from his mother.

Hilda Freeman supported herself and Ray after the death of Albert. She was immensely proud of Ray’s achievements at school and supported his ambition to carry on with his studies, despite pressure from the rest of the family to do otherwise. Ray won a scholarship to Nottingham High School, which had high academic standards and, as Ray recorded, some excellent teachers. Here Ray developed a determination to study science, but it seemed that the headmaster thought that bright pupils such as Ray should be directed to study the classics – science being thought rather second-rate. The intervention of his kindly physics master, Dr Somekh, rescued Ray from classics so that he could pursue his passion for science. It is typical of Ray that many decades later he recalled both the incident, and the name of the teacher whose intervention was so critical.

Further academic success followed with Ray gaining a scholarship to Lincoln College Oxford in 1949, seemingly to the surprise of his headmaster who continued in his low opinion of science and, by extension, the pupils who studied it. At this time an eighteen-month period of National Service was compulsory, so Ray's initial plan was to complete this first and then go up to Oxford in 1951. He duly joined up with the Royal Air Force, but not long afterwards hostilities started on the Korean Peninsula and National Service was extended to two years. Ray's duties with the RAF involved learning about radar, which give him some experience of radio-frequency circuits, much to his advantage later on. At the last moment the authorities relented on the extension of National Service, thus allowing Ray to start his course in Oxford in October 1951.

OXFORD 1951–1957

No doubt Ray learnt a great deal of chemistry from his Tutors at Lincoln College, who included the then youthful Rex Richards who was to have such an influence on Ray. However, in time-honoured student tradition he found the time for some non-academic activities which led him to two of the great loves of his life. The first was his discovery of the exuberant joy and energy of traditional jazz, and the second was meeting a young Frenchwoman, Anne-Marie, who was also studying in Oxford and was destined to become Ray's wife.

Then, as now, Oxford undergraduate chemists had the great privilege of devoting the entirety of their fourth year (Part II) to a research project. Ray chose to work with his Tutor, Rex Richards, who had just completed building a nuclear magnetic resonance (NMR) spectrometer – one of the very first in the UK. At this time chemists were just beginning to realise that NMR spectroscopy could be a valuable tool for determining molecular structures and properties, and Rex was at the forefront of these developments. The spectrometer itself was a formidable piece of equipment put together from 'war surplus' electronics (including a large bank of ex-submarine batteries used to power the magnet) and featuring a home-made (and indeed, largely hand-made) electromagnet to Rex's design. Ray's doctoral work with Rex involved spending much of his time developing the spectrometer. His first paper (1), on the proton NMR spectrum of polycrystalline potassium amide, reported the H—H distance in the water of crystallisation. Ray recalled this as very painstaking work for little reward. More profitable was his work searching for the resonances of nuclei such as ^{7}Li, ^{59}Co, ^{71}Ga, ^{115}In, and ^{205}Tl (2, 3, 4). The precise resonance frequencies of these nuclei were not known, so looking for the resonance was very much like looking for the proverbial needle in a haystack. However, the process was greatly aided by Ray's use of a sensitive super-regenerative detector, popular with amateur radio enthusiasts at the time and adapted for NMR by Robert Pound (and hence known in the NMR world as a 'Pound box').
Based on this work, Ray reported (2) measurements of the chemical shifts of ^{59}Co in a series of transition metal complexes and the good correlation of these values with the magnitude of the ligand field splitting, as predicted by Ramsey's theoretical treatment of the chemical shift. Ray greatly appreciated, and benefitted from, Rex's light touch when it came to supervising graduate students. Advice was freely given and guidance was gentle, but above all Rex encouraged his students to explore and to be adventurous. Ray's own style of supervision was to become much the same, and later proved to be equally effective with his own students.

SACLAY 1957–1959

After Ray completed his D.Phil., Rex – knowing that Anne-Marie had returned home to Paris – suggested that he might like to spend a period working at Saclay in the group of Anatole Abragam. Ray leapt at the possibility of working in France and duly arrived in Paris in 1957. Abragam already had a formidable reputation by this time. His group in Saclay saw NMR very much from a physicist's point of view, with heavy doses of theory and attendant mathematics. Ray commented of this time that his rather more pragmatic chemist's approach was regarded with some suspicion. Perhaps this was responsible for Ray's long-held belief that if you could only explain something with heavy-duty theory and mathematics, you probably had not really understood what was going on. Ray always felt that a physical picture, combined with a good dose on intuition, was the best way of explaining something.

At Saclay, Ray was pleased to encounter Robert Pound (of the eponymous Pound Box) and the two of them worked together on various refinements and adaptations of the a regenerative detector (5). Somewhat disappointingly, it soon dawned on Ray that such a detector was not suited to high-resolution work (such as was required for proton NMR in solutions). However, the detector proved to be an excellent basis for stabilizing the resonance frequency of the spectrometer, thus enabling Ray to construct an instrument with exceptional stability (6). At Saclay Ray also encountered Ionel Solomon; although they appear not to have worked on any projects together, Ray greatly revered Solomon for his insight and advice, and included him in his select list of the six 'sorcerers' from whom he learned much as an 'apprentice'.

In 1958 Ray and Anne-Marie married. The wedding itself was touch-and-go as French bureaucracy did not appear to look too kindly on an English–French conjunction, but in the end, and with some timely intervention from well-placed friends and relatives, all was well.

NATIONAL PHYSICAL LABORATORY, TEDDINGTON 1959–1963

After a profitable and stimulating two years at Saclay, Ray returned to the UK to work at the National Physical Laboratory (NPL) in Teddington, Middlesex, moving with Anne-Marie and their baby daughter Dominique to New Malden in Surrey. A second daughter, Anne, joined the family the following year. Ray's time as a senior scientific officer at the NPL was highly productive, leading to a string of notable papers on double and even triple resonance methods for the determination of the relative signs of coupling constants and for the analysis of complex spectra. It was also an opportunity to collaborate with a wide range of scientists, including Ray Abraham, Peter Diehl, Laurie Hall (who would also go on to be a Professor in Cambridge), Keith McLauchlan FRS (for many years a colleague of Ray's in the Physical Chemistry Laboratory at Oxford), Klaus Pachler and David Whiffen.

Ray's work in Saclay with Bob Pound on the use of super-regenerative oscillators led to a characteristically elegant method (7) for automatically mapping magnetic field contours in the pole gap of an NMR magnet. Two probes were used, one fixed and the other movable. Electric motors were used to scan the movable NMR probe over the pole face, and to scan a pen in sympathy over a piece of paper. Both probes were wired into super-regenerative oscillators to generate continuous signals at their local Larmor frequencies. The two super-regenerative oscillator output signals were mixed, and the difference frequency (in the audio range) was fed to a lock-in detector wired to drop the pen onto the paper whenever the difference frequency corresponded to an odd harmonic of a reference frequency set to half the desired contour spacing. The result was that as the movable probe scanned over the pole face, the pen would alternately drop and lift, tracing out the magnetic field contours. Years later, Ray's Oxford students would adopt a very similar approach to plot out contour maps of early two-dimensional NMR spectra using an analogue chart recorder (36). At the time of Ray's field mapping experiments, the active components used were still thermionic valves, the descendants of the valves used in the wartime short-wave radio communication equipment that provided the electronics for early NMR spectrometers, but already Ray's circuit used germanium semiconductor diodes, and within a few years almost all NMR equipment would use solid-state electronics. Sixty years on, automated field mapping ('gradient shimming') is used in virtually all modern high-resolution spectrometers to allow the static magnetic field homogeneity to be optimised.

Ray had a healthy respect for the role of blind chance in science. In the early 1960s, many British scientists followed a well-trodden path to the USA, attracted both by the resources for research and standards of living that were difficult to match in the UK. Ray had received an invitation to join the group of Britton Chance in Philadelphia. When he approached his boss at the NPL, John Pople FRS (Nobel Laureate 1998), for permission to spend a sabbatical in Philadelphia, Pople immediately agreed but suggested that Ray should first look into other possibilities. Ray contacted John Baldeschweiler at Harvard, Paul Lauterbur at the Mellon Institute in Pittsburgh, Britton Chance, and Wes Anderson at Varian Associates in California. The first to come up with financial support was Wes Anderson; had he delayed just a few hours, Ray would instead have gone to Harvard and the history of NMR would have been quite different.

VARIAN ASSOCIATES, PALO ALTO, CALIFORNIA 1963–1973

Ray's 1961 sabbatical from NPL, the California weather and the warm welcome he received from Wes Anderson and colleagues, laid the foundations for his subsequent move to Varian Associates in 1963. The family settled very happily – and grew, with the arrivals of Louise, Jean-Marc and Lawrence – in the community of Ladera, not far from Palo Alto. Ladera, which was also home to Sigurd Varian, was originally founded on socially liberal principles and was popular with employees of nearby Stanford University.

At that time Varian's research was world-leading, eclipsing that of almost all university groups. Initially Ray worked with Wes Anderson on a variety of double resonance methods. Spin tickling (8), the use of a very weak continuous second radiofrequency (RF) field to perturb a coupled spectrum to reveal connectivities between different transitions, is nowadays little remembered. However, like many of the methods pioneered by Ray at Varian, it had a lasting impact through the subsequent developments it inspired, and indeed was responsible for the joint award to Ray and Wes of the Russell Varian Prize, in 2012. In allowing experimenters to anatomise complex coupled spin systems it sowed the seeds for later two-dimensional NMR methods such as COSY and eCOSY (Aue *et al.* 1976, Griesinger *et al.* 1985). Similarly, the principle established in Ray's and Wes's papers on the indirect detection of one nucleus by its effect on the signal of another (9, 11) can be traced through to such diverse experiments as the two-dimensional heteronuclear correlation techniques HSQC and HMBC (Bodenhausen & Ruben 1980, Bax & Summers 1986), the mapping of protein energy landscapes by detecting transient 'dark state' protein conformations (Anthis & Clore 2015), and chemical exchange saturation transfer (CEST) (van Zijl and Yadav 2011) and magnetization transfer contrast (MTC) methods (Henkelman *et al.* 2001) in magnetic resonance imaging (MRI).

As early as 1963, Ray and Wes were using double-quantum transitions as a tool for spectral assignment (10). Almost twenty years later, Ray was to exploit such transitions in what is still one of the most powerful structure elucidation methods in organic chemistry, the INADEQUATE (Incredible Natural Abundance DoublE QUAntum Transfer Experiment) technique (41, 45). This traces out the bonds between carbon atoms by detecting the double-quantum coherence created through the one-bond scalar coupling between two carbon-13 nuclei. From 1963 onwards, attention began to shift towards experiments using RF pulses, as opposed to the constant low-level RF magnetic fields used for single and double resonance alike, in the 'continuous wave'

(CW) experiments used for almost all NMR work up to that point. (Wes Anderson did, however, investigate the possibility of a motor-driven device for multifrequency excitation and detection of NMR, to improve sensitivity, that Ray christened the 'Prayer Wheel'; figure 1 shows Wes with his invention.) The use of pulsed RF fields made it possible to study the relaxation processes by which nuclear spins reach thermal equilibrium with their environment, and hence to gain access to a wide range of information about molecular structure and dynamics. As was usually the case with new experimental techniques at this stage, it needed bespoke electronics to generate and control the pulses (14). Later, Ray was to pioneer the use of real-time computer control to enable new experimental methods to be developed and applied without the need to construct any dedicated hardware.

Figure 1. Wes Anderson with his 'Prayer wheel' device for multifrequency NMR, on the occasion of its donation to the Smithsonian Institute. **[permission needed from John Wiley and Sons]**

While Ray was using pulsed irradiation for double resonance and relaxation experiments (12,13), another young European researcher at Varian, Richard Ernst ForMemRS (Nobel Laureate 1991) was – also in collaboration with Wes Anderson – doing the first practical experiments using the pulse Fourier transform (FT) method that was to revolutionise the practice of NMR. 'Practical' is perhaps stretching a point; the experiments required the nuclear free induction decay to be recorded, digitised, transferred to punched cards, transported by car to a remote mainframe computer, Fourier transformed by brute force numerical integration, and finally, a day later, plotted out to produce a spectrum. With hindsight, the sensitivity advantage brought by the Fourier transform method made it inevitable that it would supplant the much slower and less sensitive CW method, but at the time Varian's management were slow to appreciate this, not least because the minicomputers that would make such methods accessible to the general user of NMR were only just being developed. Referees were equally slow on the uptake: Ernst and Anderson's paper was rejected twice, before being published in the *Review of Scientific Instruments* (Ernst &

Anderson 1966). It took the Nobel Committee for Chemistry another 25 years to recognise the importance of this idea, in 1991.

By 1970, the development of Varian's first commercial FT NMR spectrometer, an adaptation of the XL100, made it possible for both double resonance (15) and pulsed relaxation (16) experiments to be carried out using the Fourier transform method. This coincided with the arrival from England of a new collaborator, Howard Hill, forming a highly creative partnership. In the three years that followed, Ray published with Howard and other collaborators a series of classic papers that presaged many of the important developments of the next 20 years. The reason for the initial success of the Fourier transform NMR method was its dramatic sensitivity advantage over the continuous wave method, but it gradually became clear that a secondary advantage was if anything even more important. This was the added flexibility afforded by separating the preparation of the nuclear spins for measurement – their excitation – and the measurement of the resultant free induction decay (FID). Ray rapidly showed that by controlling the timing of the proton decoupling irradiation used in measuring carbon-13 spectra it was possible to produce not only proton-decoupled carbon-13 spectra enhanced by the nuclear Overhauser effect (NOE), but also decoupled spectra without NOE enhancement (54) (thus allowing the NOE to be measured), and carbon-13 spectra with NOE enhancement but without proton decoupling (18) (allowing proton-carbon couplings J_{CH} to be measured with enhanced sensitivity). He was also able to show that the spin-lattice relaxation of carbon-13 nuclei may change in the presence of proton decoupling (20).

Ray's collaborative work with Iain Campbell FRS on the effects of dipolar cross-relaxation (22, 23) helped lay the foundations for the major impact of NMR, and in particular the nuclear Overhauser effect, on the determination of biomolecular structure in solution. Campbell went on to become one of the pioneers of the use of NMR in structural biology, making major contributions to the determination of the structure of proteins and protein complexes in solution. Experiments combining heteronuclear double resonance with rapid spin echo trains (21) showed that the transfer of magnetization between spins, mediated by dipolar couplings, that Hartmann and Hahn had observed in continuous spin lock experiments ion solids, could also be observed in discontinuous irradiation experiments on liquids, this time mediated by scalar couplings. This transfer of transverse magnetization between coupled spins is the basis of the subsequent TOCSY experiment (Braunschweiler & Ernst 1983), a key tool in modern methods for structure elucidation by NMR.

The most far-reaching product of Ray's collaboration with Howard Hill was probably their invention of '*J*-spectroscopy' (17), in which the measurement of a train of spin echoes as a function of time maps out the modulation of the echo amplitude caused by homonuclear scalar couplings. The motivation for this was that the use of the spin echo suppressed the contribution of magnetic field inhomogeneity to the widths of the spectral lines measured, and hence enabled both the detection of very small couplings (as low as 0.05 Hz), and the measurement of couplings with unprecedented accuracy. The principle of mapping out signal evolution in a series of measurements using incremented time intervals was proposed independently by Jean Jeener as the key principle of two-dimensional NMR spectroscopy, at almost the same time, and demonstrated practically by Richard Ernst four years later. Ray was thus one of the first to appreciate the full power of Jeener's innovation, and was able very rapidly to apply it to the development of two-dimensional forms of *J*-spectroscopy.

For many years Varian Associates had thrived as a relaxed and creative research community as well as a commercial organisation, but by the early 1970s commercial considerations had begun to play an ever-increasing role in company decision-making. The failure to capitalise on the development of Fourier transform methods opened the door to more agile competition, notably from the Bruker company in Europe. Varian began to lose both its pioneering mentality, and some of its best scientists. When Ray received a letter from his former NPL colleague David Whiffen that mentioned an opening for a physical chemist at Oxford, he initially put the letter straight into the waste bin as the salary looked so poor. When he realised that the university Lectureship was accompanied by a college Fellowship with its own salary, he retrieved the letter and sent a Telex message to apply for the post. Shortly after returning to California from his interview in Oxford he received a telephone call in the middle of the night telling him that he had been appointed. In Ray's words, "It turned out to be a brilliant move."

OXFORD 1973–1987

After over fifteen years working in pure research environments, renewed immersion in academic life as a Lecturer in Physical Chemistry and Tutorial Fellow at Magdalen College posed significant challenges for Ray. His first priority was to prepare for the demands imposed by the Oxford teaching system, which required him to give multiple weekly tutorials to groups of 2–3 students at a time. He therefore joined the undergraduate audiences for the lectures on physical chemistry. Somewhat conspicuous in such a young milieu, he was thought by the students to be some sort of government inspector. His second priority was to acquire an NMR spectrometer, which he did by submitting a research proposal (on stopped flow kinetics, inspired by the work of Britton Chance that first made him consider working in the USA) to the Science Research Council. While no kinetic results were ever obtained, it is fair to say that the SRC received good value from this grant; methods that were originally developed using this spectrometer are still in use in almost all chemistry departments worldwide.

The spectrometer Ray purchased, and installed in room 049 in the Physical Chemistry Laboratory on South Parks Road, was a Varian CFT-20 (figure 2). This latest Varian product was designed as a low-budget instrument for carbon-13 NMR, with a small water-cooled electromagnet. Varian engineers felt aggrieved at the use of cheap plastic knobs for controls, but the decision to economise on parts by using the built-in minicomputer (a Varian Data Machines 620L) to control as many functions as possible was providential. The instrument was controlled through a keyboard, and a small oscilloscope tube, driven directly by the computer, served both to display small amounts of text and to show spectra. All the key functions for acquiring spectra, generating RF pulses at the carbon-13 and proton Larmor frequencies of 20 and 80 MHz respectively and digitising, recording and averaging free induction decays, were controlled by the computer and ancillary timing electronics. The great advantage of this tight integration between computer and spectrometer was that new experiments could be set up and tested in a matter of hours, simply by reprogramming the CFT-20 control software, rather than requiring bespoke electronics to be constructed.

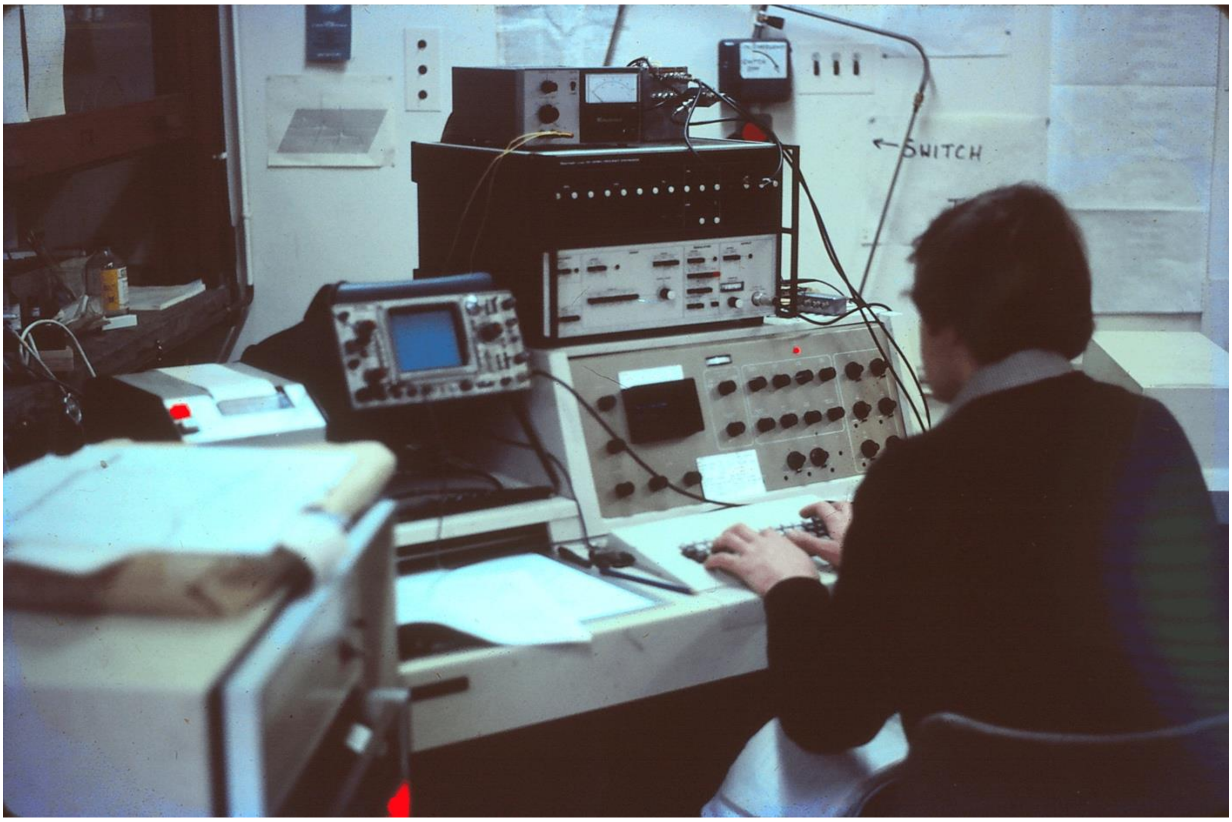


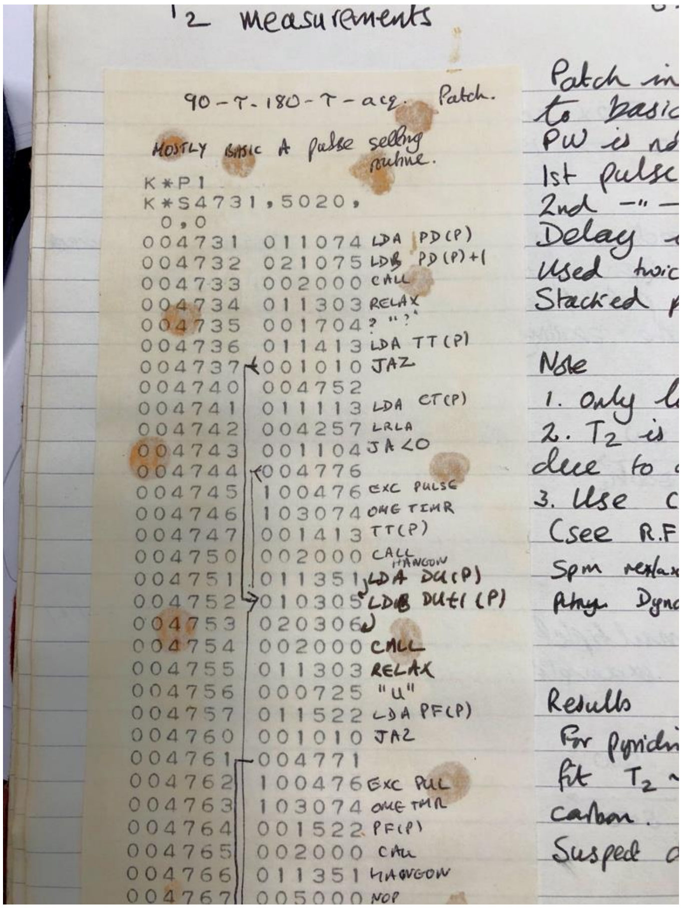
Figure 2. The CFT-20 spectrometer, with an unidentified graduate student (possibly JK or Tom Frenkiel) at the console. Photograph dated August 1982, kindly provided by Professor Peter Barker.

Ray's first two Oxford PhD students, David Turner (who began his Part II undergraduate project with Ray in autumn 1974) and Geoffrey Bodenhausen (who arrived in January 1975, having done some undergraduate research with Richard Ernst), set out to explore the possibilities of the new instrument. Initially, David worked on carbon-13 spin-lattice relaxation, using differences between the T_1 values of the three carbons in the pyridine molecule to demonstrate the anisotropy in its motion caused by hydrogen bonding (24). Geoffrey investigated using spin echo trains for T_2 measurement, which both revealed the problems with the timer electronics, and required great ingenuity in adapting the machine code control programme of the spectrometer to perform arbitrary sequences of RF pulses. The next October they were joined by one of the authors (GAM) as a 'Part II' (12 month undergraduate research project) student, who set out to build a high-power RF amplifier to allow 'spin-locking' measurements of transverse relaxation. Alas the first test of this amplifier was the last, the expensive power transistor in the output stage failing almost immediately. Fortunately, Ray had also suggested looking into an experiment for measuring T_2 using transient nutations, and while this proved impractical the same computer code allowed a completely different experiment to be performed. This was what became known as the DANTE pulse sequence ('Delays Alternating with Nutations for Tailored Excitation'), which allows short, powerful RF pulses to achieve the same sort of frequency-selective excitation as a long, low-power pulse (25, 34, 73, 144; Morris 1996). The name DANTE was suggested by the resemblance between the trajectories of magnetizations subjected to a 90° DANTE sequence and the reverse of the trajectory taken by Dante and his guide Virgil up through Mount Purgatory in the *Divine Comedy*. (The name was given extra resonance by a fancied resemblance, spoilt only by the lack of glasses, between Ray and the portrait of Dante in Domenico di Michelino's depiction of the *Purgatorio* in the cathedral in Florence.)

At first sight it seems counter-intuitive to choose to excite just one peak in a spectrum. The whole point of the FT method is that measuring many resonances at once is much more sensitive than detecting them one by one, as in CW NMR. However, in FT NMR the excitation of the nuclear signal is separate from its measurement, so as Geoffrey Bodenhausen rapidly pointed out it is possible to excite selectively a decoupled ^{13}C signal, but then measure it without decoupling so that all the multiplet structure caused by proton-carbon couplings J_{CH} is recorded. In this way the morass of overlapping multiplets typically observed in ^{13}C NMR when proton decoupling is not used can be neatly decomposed into a set of distinct multiplets, by selectively exciting each chemical shift in turn and recording its proton-coupled spectrum (25, 26). Selective excitation in FT NMR proved a very fruitful idea, and while the original DANTE method is now relatively rarely used, a wide range of more sophisticated methods using amplitude- and phase-modulated RF pulses went on to be developed, many of them by Ray and his students (60-62, 72, 74-78, 80, 84, 88, 91, 98, 104, 117).

Using DANTE to disentangle proton-coupled ^{13}C spectra brought an alternative method (Müller *et al.* 1975), published a few months previously by Richard Ernst and based on an unpublished idea of Jean Jeener, to Ray's attention. This was Ernst's second paper on double Fourier transform (two-dimensional, '2D') NMR spectroscopy, in which he showed that ^{13}C signals could be dispersed in one dimension according to both chemical shifts and couplings, and in the other just according to chemical shift, thus separating the multiplet structures of different chemical sites. While the results were less impressive than those obtained with DANTE, and the effort required far greater, the power and potential of the 2D approach were immediately obvious. Ray saw straight away that a much more effective solution to the problem of unravelling ^{13}C multiplet structure was to add a 180° pulse to Ernst's pulse sequence, creating the first 2D *J*-spectroscopy experiment (27). This not only separated the individual multiplets out, by dispersing signals according to chemical shifts and scalar couplings in orthogonal frequency dimensions, but as a bonus it removed the limit imposed by magnetic field inhomogeneity on signal linewidths. The choice of pyridine as the first sample to be analysed (as a consequence of David Turner's work on motional anisotropy) was a fortunate one, as it revealed very early on the complications caused by strong coupling in 2D methods, and led to the production of software for the simulation and iterative analysis of *J*-spectra (29, 31). Later, the loan of a new FT-80 spectrometer by Varian, to enable a 2DFT software package to be developed for other users, gave Ray's group access to proton NMR measurements and allowed similarly detailed analysis of strongly-coupled homonuclear *J*-spectra (35).

Performing and processing 2D FT experiments on the CFT-20, with its very limited computer memory (32 kilobytes, in the form of 16k 16-bit words), was a formidable technical challenge. Geoffrey Bodenhausen, David Turner and Reinhard Niedermeyer (a visiting PhD student from the group of Dieter Leibfritz in Bremen) had to recode the instrument's control programme not only to control in real time the new pulse sequence required, but also to Fourier transform the free induction decays measured, transpose the resultant data matrix, and FT again, all within the limited 16 kilobyte footprint of the original programme. No compiler was available, so all the coding had to be done in 16-bit machine code, and the total number of data points in the resultant 2D spectrum was initially limited to 8192. Shortly afterwards a Diablo removable hard disc system with a 1 megabyte capacity was added, enabling much larger spectra to be processed. Figure 3 shows a short segment of the control programme for a pulse sequence, with the instruction addresses and codes in octal and handwritten annotations in assembly language.


2 measurements

90 – τ – 180 – τ – acq. Patch.

MOSTLY BASIC A pulse setting routine.

```
K*P1
K*S4731,5020,
 0,0
004731 011074 LDA PD(P)
004732 021075 LDB PD(P)+1
004733 002000 CALL
004734 011303 RELAX
004735 001704 ? "?"
004736 011413 LDA TT(P)
004737 001010 JAZ
004740 004752
004741 011113 LDA CT(P)
004742 004257 LRLA
004743 001104 JA<0
004744 004776
004745 100476 EXC PULSE
004746 103074 ONE TIMR
004747 001413 TT(P)
004750 002000 CALL
004751 011351 HANGON
              LDA DU(P)
004752 010305 LDB DU+1(P)
004753 020306
004754 002000 CALL
004755 011303 RELAX
004756 000725 "U"
004757 011522 LDA PF(P)
004760 001010 JAZ
004761 004771
004762 100476 EXC PUL
004763 103074 ONE TMR
004764 001522 PF(P)
004765 002000 CALL
004766 011351 HANGON
004767 005000 NOP
```

Patch in
to basic
PW is n
1st pulse
2nd —"—
Delay
Used twic
Stacked

Note
1. Only l
2. T_2 is
due to
3. Use c
(see R.F
Spm relax
Phys. Dyna

Results
For pyridi
fit T_2
carbon.
Suspect

Figure 3. Annotated octal machine language code from the control programme of the CFT-20 spectrometer, from the laboratory notebook of JK, *ca*. 1980.

Early experiments with 2D *J* spectroscopy showed the presence of extra, unwanted signals. These took the form of weak copies of the expected signals, slightly displaced in the 2D spectrum; the two families of attenuated peaks were christened ‘ghosts’ and ‘phantoms’. These artefacts arise because the 90° and 180° radiofrequency pulses used are necessarily imperfect, the radiofrequency field B_1 varying slightly across the sample. Fortunately, Geoffrey Bodenhausen had modified the CFT-20 transmitter channel to add the capability to generate phase shifts in multiples of 90°. This then allowed the artefact signals to be averaged to zero, while the wanted signals survived unchanged, by systematically cycling through 90° phase shifts of the refocusing pulse while alternately adding and subtracting FIDs (30). The method was given the name ‘EXORCYCLE’, in the light of its exorcism of unwanted apparitions. The technique of ‘phase cycling’ proved to be very general, and is now routinely used wherever multiple pulse experiments, such as in multidimensional NMR, are performed (Bodenhausen *et al.* 1984).

Implementing 2D processing on the CFT-20 both illuminated some of the practical implications of 2D methods, for example the natural ‘phase-twisted’ lineshape of a signal that is phase modulated in two independent time dimensions (28), and gave a solid foundation for the development of further 2D methods. Because the CFT-20 was limited to carbon-13 measurements, the next step was to investigate, in parallel with Ernst's group, heteronuclear correlation methods (32, 33, 36). These generate 2D spectra plotting carbon-13 chemical shift against proton chemical shift, in their most useful form generating a single peak for each directly-bonded C–H atom pair in a molecule. Because of the wide dispersion of ^{13}C chemical shifts, such methods offer extremely high resolution, circumventing the limitations imposed by the narrow range of proton chemical shifts. The heteronuclear correlation methods developed by the Freeman and Ernst groups were the prototypes for the highly sophisticated 2D and 3D NMR methods now used in structural biology to provide atomic resolution three-dimensional structures of proteins, DNA and RNA in solution.

An analysis of the sensitivity of heteronuclear correlation methods (for the DPhil thesis of GAM) showed that these benefit both from the greater Boltzmann polarisation of the proton at thermal equilibrium (the proton having four times the intrinsic magnetization of a ^{13}C nucleus), and from the more rapid spin-lattice relaxation of protons (again determined in part by its higher magnetogyric ratio). The same advantages can be obtained in a simple 1D NMR experiment by replacing the evolution period of a 2D heteronuclear correlation experiment with a fixed spin echo. An initial demonstration of the sensitivity enhancement of proton-coupled carbon-13 NMR (37) was carried out in the weeks between GAM completing his thesis and leaving for Canada. This required splicing a crude 90° phase shifter into the CFT-20 decoupler ^{1}H channel, using a switched delay line, while Ray was on holiday and out of contact; fortunately the instrument survived the operation unscathed. The basic experiment was given the name INEPT (Insensitive Nuclei Enhanced by Polarisation Transfer). This pulse sequence results in antiphase signals, so experiments were also carried out using a second spin echo to generate in-phase signals, but there was insufficient time to write these up. The 'refocused INEPT' experiment was subsequently published by the group of Richard Ernst (Burum & Ernst 1980). INEPT has since become a standard building block for transferring signals between different isotopes, in a range of applications from structural biology to quantum computing; the original paper has been cited over 2000 times.

A second paper (38) that had a large and lasting impact on the field of NMR arose from the undergraduate Part II research project of Malcolm Levitt (FRS 2007). Malcolm appeared in room 049 one afternoon and diffidently explained that by combining an imperfect 90° pulse, an imperfect phase-shifted 180° pulse, and a second imperfect 90° pulse, one could obtain an almost perfect spin inversion. The group were so impressed with this that they downed tools for the afternoon and took Malcolm out for afternoon tea (Levitt 2011). Over the years that followed, a forest of papers on what Ray christened 'composite pulses' grew from this small seed. They include many more from Ray's group (40, 44, 48, 59, 63, 64, 68, 140), and a seminal series of papers, first with AJ Shaka and then with Eriks Kupče, exploring the use of phase-permuted cycles of composite pulses to reduce greatly the amount of radiofrequency power needed to suppress heteronuclear scalar couplings (39, 47, 50-52, 55-58, 65-67, 69, 70, 90, 106, 110, 111, 113, 114). Such heteronuclear decoupling methods made it possible for the first time to acquire proton spectra with broadband ^{13}C and/or ^{15}N decoupling, are now routine in almost every laboratory that uses NMR, and have become essential tools in the use of NMR in structural biology.

Some years after the publication of his paper with Malcolm, Ray was touched to receive a postcard from Richard Ernst in Zürich in which the future Nobel laureate wrote that when he first saw the paper he thought it was merely cute, but that he now realised that this was a profound contribution to NMR. More public recognition of Ray's commanding stature in the field came in 1979 in the form of election to the Royal Society, a distinction that he valued greatly.

Shortly after Malcolm Levitt's inspired discovery – the first of many – another researcher joined the group who was also to become a dominant figure in NMR methodology (and for some years the world's most cited chemist). Ad Bax was a doctoral student of Toon Mehlkopf in Delft, but came to Ray's group as an academic visitor to broaden his horizons. One of Ad's first contributions was to collaborate with Stewart Kempsell, who had begun his research career laboriously synthesising ^{13}C-labelled molecules in order to determine carbon-carbon coupling constants. Because the natural abundance of ^{13}C is low (ca. 1.1%), the signals of di-^{13}C isotopologues are very difficult to detect at natural abundance as they are both very weak, and swamped by the much stronger signals of the mono-^{13}C species. The arrival in room 049 of a superconducting spectrometer, the XL200, greatly reduced the first problem, but the second remained. Figure 4 shows many of the group members from 1980; unfortunately Malcolm Levitt was away when the photograph was taken.

Figure 4. Group photograph from 1980 showing (centre) Gladys, who presided over refreshments for the Physical Chemistry Laboratory, and (rear from left) Ray, Ad Bax, Tom Mareci, GAM, Stewart Kempsell, Regina Schuck, JK and Tom Frenkiel. Photograph kindly provided by Professor T. Mareci.

Ad realised that the need for ^{13}C enrichment could be avoided if it were possible to suppress the signals of mono-^{13}C isotopologues, and proceeded to show that this could be achieved by restricting the spin systems observed to those in which forbidden double quantum transitions could be excited. Ad showed that it was possible to generate double quantum coherence with close to 100% efficiency by applying a 90° pulse at the end of a spin echo of appropriate duration, and that a further 90° pulse would then convert this double quantum coherence back into observable single quantum coherence. Careful design of phase cycling enabled excellent results to be obtained, with the interfering signals of mono-^{13}C species attenuated more than 1000-fold (41). This INADEQUATE (Incredible Natural Abundance DoublE QUAntum Transfer Experiment) transformed the measurement of carbon-carbon coupling constants, both one-bond (41) and long-range (42), from a niche specialty requiring weeks of bespoke chemical synthesis of costly enriched compounds to a routine measurement on unenriched material.

While the values of carbon-carbon coupling constants are of significant interest, for example in studies of structure and conformation, the lasting significance of the INADEQUATE experiment lies in its 2D analogue (45, 53, 54), which adds an evolution period t_1 between the penultimate and final 90° pulses. This yields a 2D spectrum which correlates the 1D spectra of di-^{13}C species with the frequencies of the double quantum coherences used. The signals of carbon atoms which are directly bonded appear at the same F_1 frequency (their average chemical shift), making it immediately obvious which carbon is bonded to which, in effect tracing out the carbon skeleton of a molecule. Where sample quantity permits, the 2D INADEQUATE experiment remains one of the most powerful structure elucidation methods currently available to chemists.

In three very highly-cited papers, Ray and Ad revisited Jean Jeener's original 2D NMR experiment, later christened 'COSY', that had been analysed in detail by Ernst (Aue *et al.* 1976) but that had up to that point been very little used. They showed first that the problem of distinguishing the signs of frequencies in F_1 could be solved by phase cycling (43), and second that the unfavourable broad absolute value lineshapes inherent in the basic COSY experiment could be corrected (46) by weighting the experimental data to enforce time-domain symmetry, thus cancelling the antisymmetric dispersion mode contributions to frequency-domain lineshapes. They went on to demonstrate the power and flexibility of the COSY experiment (49) using as an example a molecule, 9-hydroxytricyclodecan-2,5-dione, an intermediate in a projected synthesis of dodecahedrane. These developments, coupled with improvements in the data storage capabilities of commercial spectrometers, made COSY one of the most popular of the NMR experiments used by synthetic chemists, a position it retains over forty years later.

Ray's fourteen years in Oxford had a great and lasting impact on science. His intuitive and creative approach to the technical challenges and opportunities of NMR complemented the analytical and theory-based approach of Richard Ernst's group in Zürich, and together Ray and Richard made NMR spectroscopy the single most important and widely-used structural technique for chemists. Synthetic chemists nowadays expect and require instant access to NMR, routinely using a range of 1D and 2D methods to follow every stage of a synthesis. In the authors' departments, for example, synthetic chemists now run over a quarter of a million spectra every year, many of which use methods pioneered by Ray. Many of Ray's group members from this period went on to academic careers in magnetic resonance, including Geoffrey Bodenhausen, David Turner, Malcolm Levitt FRS, Ad Bax, Tom Mareci, Ole Sørensen, AJ Shaka, Steve Wimperis, Hartmut Oschkinat, Peter Barker and Peter Hore FRS, in addition to the authors.

In 1987, though, Ray was made an offer that was too good to turn down. Completely unexpectedly, he was offered the John Humphrey Plummer chair at the University of Cambridge, without even an interview. This was a research post with minimal teaching responsibilities, and although he had been promoted to become the Aldrichian Praelector in Chemistry in 1982 there was no prospect of a comparable position in Oxford. With four out of Ray and Anne-Marie's five children having left home this was a good time for a change, so they made the decision to move. For almost 30 years more, Ray's research would be based in the University of Cambridge and Jesus College.

CAMBRIDGE 1987–1999 AND RETIREMENT

The move to Cambridge was perhaps more disruptive than Ray had imagined it might be. After his long familiarity with the Oxford Physical Chemistry Laboratory there were new people and new ways of working to adapt to, and, most importantly, the ready supply of talented research students which the Oxford Part II system delivered had no parallel in Cambridge. Nevertheless, the freedom from onerous teaching duties was welcome, and this enabled Ray to focus on research with renewed intensity. He also become a Fellow of Jesus College, which he found to be a congenial second home, much as he had found Magdalen College, Oxford.

In Cambridge Ray continued to explore a wide range of new methods in NMR, sometimes in response to current topics in the literature and sometimes taking entirely new directions. It was during this period that that Ray accepted into his group a postdoctoral scientist, and native of Latvia, by the name of Ēriks Kupče. Ēriks was an organometallic chemist by training, but had developed a serious interest in NMR. This blossomed when he started working with Ray, initially on a one-month visit supported by a Humboldt Fellowship and subsequently with support from the Royal Society. Ēriks was a gifted experimentalist and endlessly interested in trying out new ideas and approaches. He and Ray worked exceptionally well together, their collaboration continuing beyond Ēriks' time in Cambridge and Ray's eventual retirement. Together they published over 60 papers.

Ray's works from this period can be grouped into a number of themes.

Selective pulses and their applications

A selective pulse is one which affects only a subset of the resonances in the spectrum. Earlier work in Oxford (60) had shown that a pulse whose amplitude is shaped to a smooth function, rather than having the abrupt on and off transitions of a traditional 'square' pulse, had significant advantages in terms of selectivity. Ray, working with Helen Geen (76, 78), developed this idea further by exploring more complex shapes based on Fourier series. Careful numerical optimization of the shape led to the 'BURP' (Band-selective, Uniform-Response, Pure-phase) pulses, which offered a significant improvement over simpler shapes such as the Gaussian or half-Gaussian. These new pulses, and variations on them, were used widely by Ray and his collaborators, and his second paper with Geen is the most cited of Ray's papers from his Cambridge period.

Further work in this area was motivated by the desire to be able to create an arbitrary excitation profile, for example one in which several different parts of the spectrum are excited. Ray and Ēriks approached this problem by applying interleaved DANTE sequences (25) in which the phase is steadily advanced from pulse to pulse in each separate sequence (88, 91, 93). This has the effect of creating a frequency shift in the excitation resulting from each individual sequence. Such an approach was possible because of the growing sophistication of the spectrometers available which, by this time, were capable of executing small phase shifts and very complex sequences of pulses.

With this new toolkit of effective and flexible selective pulses Ray and his collaborators went on to explore a wide range of applications. A key idea which was frequently used was the transfer of excitation from one spin to another in a very directed way by applying selective pulses to both spins. The excitation could be transferred to a third spin by the application of further pulses, and so on. This approach made it possible to examine the topology of a set of coupled spins in great detail, and to extract additional information such as the values of coupling constants. Typical of these kinds of approaches are the DAISY experiment and its variants (85-87), and the TSETSE experiment and its variants (96, 103, 107). The latter experiments identify pairs of coupled spins and can be used to simplify crowded spectra.

Measurement of coupling constants

The values of coupling constants are known to be useful indicators of molecular conformation, and indeed if sufficient values are known for a given molecule it may be possible to constrain the conformation to a significant degree. However, obtaining accurate values for coupling constants is notoriously difficult because of the overlap of resonances in complex spectra and the limitations imposed by their linewidths. These problems are often all the more difficult in two-dimensional spectra where the resolution can be lower and the presence of both positive and negative peaks can complicate the analysis.

Ray’s group addressed these issues in a variety of ways which used spectra generated by special pulse sequences combined with data processing to extract the values of the couplings. The data processing step typically involved either convoluting the spectrum with a trial function, as in the *J*-doubling procedure (82, 92, 95, 101), or attempting to remove the splitting by deconvolution (83, 97). In both cases the principal difficulty is to identify, in an automatic way, the best estimate for the coupling in question. Typically, this was done by examining the integral of the convoluted or deconvoluted spectrum, although this approach is not without its difficulties. Under favourable conditions these methods yield good estimates of coupling constants even for small couplings close to the limit of detectability imposed by the linewidth.

Adiabatic pulses and broadband decoupling

Ray’s work with Malcolm Levitt (47, 50) and AJ Shaka (56, 57) from the Oxford days had resulted in a dramatic improvement in the performance of broadband decoupling, in the sense that much lower power was needed to decouple a given range of resonances. However, with growing interest in the NMR spectra of ^{13}C labelled proteins there was a need to decouple the very wide range of shifts of this nucleus, a challenge made all the more difficult by the relentless move to ever higher magnetic fields. Despite the improvements that had been made, there was clearly a need for much more efficient broadband decoupling sequences.

Levitt’s work demonstrated that efficient decoupling sequences could be constructed from inversion pulses. Ray, working with Kupče, realised that inversion over a wide range of frequencies could be achieved by an adiabatic passage technique in which a radiofrequency field is swept through the resonances – a technique well-known from the days of CW NMR. With some careful optimization of the sweep rate and the amplitude envelope Kupče was able to create inversion pulses which worked over an unprecedented range. Their name, WURST pulses, reflected both the sausage-like shape of the pulse envelope and the folk wisdom that with sausages one should never enquire too closely as to what they contain. These pulses were then shown to provide the basis for broadband decoupling methods of much greater efficiency than had been achieved up to that point (106, 108, 110). These papers are amongst Ray's most cited from this period, and testify to the impact and wide adoption of WURST-based decoupling. One disadvantage with these broadband sequences is that they introduce 'cycling sidebands' into the spectrum, and can be adversely affected by the evolution of couplings during the relatively long sequences. These issues were addressed, and some remedies suggested, in a series of follow-up papers (113, 114, 116).

Pure shift spectra and data reduction

The removal of all the splittings due to proton-proton couplings from a proton NMR spectrum would result in an attractively simple spectrum, with just a single line for each chemically distinct proton. Finding a convenient way of generating what later came to be known as 'pure shift' spectra has long been a goal of NMR spectroscopists, indeed it might be described as something of a Holy Grail. Ray made a number of contributions to this quest, typically starting from a modified two-dimensional *J*-spectrum which was then subjected to special data processing to achieve the desired result (79, 81, 99, 102). A key part of the processing was the recognition of the particular symmetry that the two-dimensional multiplets possess, and then using this to identify the centre of the multiplet, which locates the desired chemical shift. A related approach was also used to process correlation spectra such as COSY so as to reduce the spectrum to single peaks (rather than multiplets) showing connectivities (105, 109, 118).

Alternatives approaches to multi-dimensional NMR

Two-dimensional NMR has without doubt greatly increased the range and complexity of structural problems that can be readily addressed by NMR techniques. The underlying idea can readily be extended to three or more dimensions; such experiments offer the possibility both of greater dispersion of the resonances, and also of identifying more complex networks of interacting nuclei. This idea has been exploited extensively in structural work on proteins and nucleic acids (Boelens & Kaptein 2007). However, a significant drawback of such methods is the long experiment times which are needed to map out, step by step, the evolution in each of the indirectly observed dimensions. Ray addressed this issue by exploring alternative ways of recording multi-dimensional spectra that avoid the need to map out the evolution in the indirect dimensions in such a complete way.

One particular promising approach to this problem is the use of Hadamard data processing, which Ray and Kupče explored in a series of papers (94, 125-128). In this method a spectrum is recorded using multiple selective pulses, simultaneously applied to different spectral regions. The experiment is repeated with different phases for the selective pulses and the resulting spectra are then recombined using an Hadamard transform in such a way as to generate separate spectra for each of the regions excited by the selective pulses. The Hadamard approach confers a multiplex advantage similar to that achieved by the Fourier transform, but without the need for complete sampling of the data space. The disadvantage is that the regions of interest to be excited by the selective pulses need to be selected in advance. However, given that there is almost always some prior knowledge of the spectrum this is not such a serious drawback. Ray's prior work on selective and polychromatic pulses, as described above, proved to be pivotal in implementing these methods.

Ray had always maintained an interest in the world of magnetic resonance imaging (MRI) and this led him to explore the possibility of using the projection-reconstruction method, originally developed for X-ray scanners and used in the early days of MRI, for generating two- and higher-dimensional NMR spectra. The sparse nature of many multi-dimensional spectra (particularly those from labelled proteins) means that only a relatively small number of projections is needed to reconstruct the spectrum, hence giving the possibility of a considerable saving in time. Ray and Kupče explored this approach in a series of papers with a particular focus on the experiments used in the NMR of labelled proteins (129-131). They also explored different processing methods, such as the direct and inverse Radon transforms, which are attractive alternatives to the conventional projection-reconstruction method (132, 134, 136).

Further spin-offs from these explorations included the idea of making a tilted projection of a three-dimensional spectrum (133, 135) to resolve ambiguities, and ‘hyperdimensional NMR’ (137). The intriguing possibility of constructing an entire two- or three-dimensional spectrum from a very small number of measurements was also explored (141, 142).

Exotica

Ray was always intrigued by new ideas in NMR and the possibilities opened up by innovations in instrumentation. In this vein he spent some time, in collaboration with his then colleague from the Department of Applied Mathematics and Theoretical Physics, Noah Linden, exploring how NMR experiments could be used as models for quantum computing (119, 121, 122, 123). The possibility of recording signals for several different nuclei at the same time led to the development of the PANSY experiment (138, 139), and further innovations connected with alternative methods for multi-dimensional NMR (143). Stochastic NMR (89), the advantages of over-sampling (100), the PASADENA effect (112), and the effects of radiation damping (120), all received attention from Ray over this period. It is interesting to note that when looking across his output of publications, Ray’s formal retirement in 1999 is barely perceptible and that he published more than 40 papers after this point.

Books

In 1987 Ray published his first book *A handbook of nuclear magnetic resonance*, a project which had been long in the making (71). This book comprised a series of one- or two-page essays on a wide range of topics in NMR, arranged alphabetically. Ray’s idea was that the book might be kept by the spectrometer so that the operator could conveniently reach for it and refresh their understanding or look up a new concept. The style of writing is typical of Ray: clear and concise, and sprinkled with a dry humour. The book features many of Ray’s beautifully drawn figures and some whimsical cartoons either adapted from his favourite cartoonists (such as Thelwell and Halbritter) or drawn especially for the text. No other single piece of work so effectively conveys Ray’s view that NMR can be simple if viewed from the right perspective and illustrates his stylish writing and his love of graphic art.

In 1998 Ray published *Spin choreography: basic steps in high resolution NMR* (115). This is a more didactic text than the *Handbook* and leads the reader through the various approaches which are used to describe and devise NMR experiments. It is less whimsical than the *Handbook*, but still features Ray’s characteristic style and illustrations, and emphasises throughout the utility of physical pictures. Ray followed this up in 2003 with *Magnetic resonance in chemistry and medicine* (124), which was more aimed at practitioners of MRI who wished to gain a wider understanding of magnetic resonance in chemistry, and *vice versa*.

RAY THE MAN

At this point anyone who actually knew Ray will be saying that all this dry history rather misses the point. There have been many great scientists, but few with Ray's warmth, creativity, dry wit, and powers of communication. His unique style of lecturing at conferences, often enlivened by his own adaptations of the work of famous cartoonists (a compilation of Ray's humorous slides has been made available here by the International Society of Magnetic Resonance), meant that he was in demand as a speaker well into his eighth decade. One of the keys to Ray's success was his egalitarian and collaborative approach to research. The most productive place in his Oxford years was not the laboratory, but the tearoom. The many hours spent there discussing ideas for new experiments over morning coffee, lunch and afternoon tea may have bemused his more dirigiste academic colleagues, but they paid great dividends in the creativity of his research group, with everyone contributing ideas and building their understanding. Ray led by example rather than precept; he very rarely told students what to do, but rather gently led them to work things out for themselves.

While science had great importance for Ray, family had even greater. His 64 years of marriage to Anne-Marie produced five children and were the foundation on which his other achievements rested. Away from work he was a great enthusiast for traditional jazz (indeed for some years he had the thankless task of being Senior Member - and carrying the can - for the Oxford University Jazz Club). A strong swimmer, he took up windsurfing in his fifties after trying it while attending a conference at a resort hotel in Sardinia.

In addition to over 300 journal articles, reviews, book chapters and books, Ray left a number of less formal articles describing his career and the influences on it. These are included in the materials accompanying this memoir, and are available online here. Ray's distinctive voice speaks clearly through these pieces, and the reader interested to go beyond this present pedestrian account of Ray's achievements is urged to enjoy them. It seems only fitting to give Ray the last word, so here to close are his thoughts on supervising PhD students:

I learned a great deal by simply observing Rex in action - teaching by osmosis. Rex clearly understood the importance of a "hands off" style of supervising research. A neophyte student was allowed the chance to shrug off the doctrine (inherited from the undergraduate courses) that there is always a correct, prescribed way to attack a scientific problem. For the very first time, one could use one's own initiative and perhaps discover new things for oneself. Trial and error, with a large dose of the latter. I suppose it was inevitable that, many years later, I adopted a similar laissez-faire approach to supervising my own students. As an analogy, I am reminded of an almost surreal episode recounted by our youngest daughter Louise. One day, on a visit to Magdalen College, she was passing the old squash courts when "it started to rain ducklings". Together with another girl, Louise tried to catch these fluffy little balls before they hit the hard ground. The ivy-covered walls of the squash courts must have been over 15 feet high, but Mama duck had decided that the time had come to ease the ducklings out of the nest so that they could find their own way to the river Cherwell and learn to fend for themselves. Darwin would have been very pleased. I found that my own research students seemed to fall neatly into two distinct groups (a) highly motivated ones who would have been *seriously hindered by any micro-management, and (b) others who were not really interested and who would soon graduate to careers outside of chemistry.*

MAJOR AWARDS

1978	Chemical Society Award in Theoretical Chemistry and Spectroscopy
1988	Honorary DSc, Durham University
1990	Leverhulme Medal, Royal Society
1999	Longstaff Medal, Royal Society of Chemistry
2002	Queen’s Medal, Royal Society
2006	Günther Laukien Prize
2008	Fellow of the International Society of Magnetic Resonance
2012	Russell Varian Prize

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AUTHOR PROFILES

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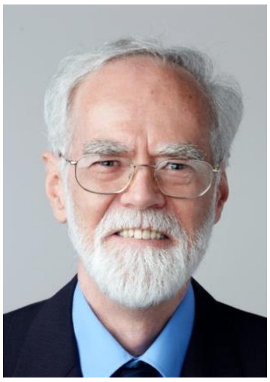

Gareth Morris is Professor of Physical Chemistry at the University of Manchester and continues to work on the development of novel techniques in liquid-state NMR and their application to problems in chemistry, biology and medicine. He was a Part II and D.Phil. student of Ray Freeman from 1975 to 1978, a Fellow by Examination of Magdalen College, Oxford from 1978 to 1981, and an Izaak Walton Killam Postodoctoral Fellow (on leave from Oxford) with Laurie Hall at the University of British Columbia 1978-79. From 1982 he was successively Lecturer, Reader and Professor at Manchester, and was elected FRS in 2014.

James Keeler

James Keeler is Professor of Chemistry in the Yusuf Hamied Department of Chemistry, University of Cambridge, and a Fellow of Selwyn College Cambridge. He was a Part II and D.Phil. student of Ray Freeman from 1979 to 1984. In 1984 he moved to Cambridge as a University Demonstrator in Chemistry under the New Blood scheme. As well as running a small research group in NMR (now defunct) he has been Admissions Tutor and Senior Tutor at Selwyn College, and Director of Undergraduate Teaching in the Department of Chemistry. He is presently Head of Department.

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