IAIN DONALD CAMPBELL
24 April 1941 — 5 March 2014
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Elected FRS 1995

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Iain Campbell defined the study of proteins by nuclear magnetic resonance spectroscopy (NMR) in the UK, and was a towering international figure in biophysics and structural cell biology. His scientific career spanned nearly 50 years, almost entirely spent at the University of Oxford. As a PhD student he recorded electron spin resonance spectra, then later became a pioneer in the application of NMR methodology to whole cells, determining the world’s second and UK’s first protein structure by NMR. He ended his career as one of the leading scientific lights in integrin adhesion and focal cell assembly. His scientific contributions are characterized by intellectual rigour and a desire to solve the problem by applying the most appropriate tools. All who knew Iain noted his incredible work ethic, his precision and in particular his wry humour. The co-workers trained by Iain form the backbone of protein NMR internationally today, a tribute to his mentorship. His loss was deeply felt by colleagues across the world and of course most of all by his loving family.

EARLY LIFE AND EDUCATION

Iain was born in Blackford, a village outside Perth, Scotland, on 24 April 1941 to Daniel and Catherine Campbell. Iain’s sister Lorna came along a little while later.

Iain’s father left school at 14 and was a First World War veteran who had fought, been wounded and captured on the Western Front. On return to Perthshire, Daniel worked on the railways until retirement. Catherine, who also left school at 14, worked as a telephonist until

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Iain’s birth. His early life was spent in a loving but very poor home; the house had no electricity until his seventh birthday and heating came from a single traditional cooking stove. A small inheritance allowed the family to move to Perth and buy a house. In turn, this allowed Iain to attend Perth Academy, one of the many outstanding state schools that built Scotland’s reputation for educational excellence. In addition to academic work, in which he excelled, Iain learned to dance and made friends with similar ambitions, the classic ‘lad o’ pairts’ (a Scottish phrase denoting a promising youth from a humble background).

Iain entered St Andrews University, Scotland’s first and the English-speaking world’s third university, in the autumn of 1959 to study physics, then known as natural philosophy. Entrance to a Scottish university in 1959 was extraordinarily competitive. Iain was clearly identified as an exceptionally talented pupil. In today’s world, where inequality of life opportunities is a very topical concern, it is worth noting that a pathway to university existed for exceptionally bright kids from families that lacked both financial capital and what we today call social capital. While insisting there was nothing special about himself, Iain voiced his concern in several talks (a concern shared by others whose life followed similar journeys) that these pathways for children whose families lack capital are atrophying if not outright vanishing. Iain’s concern was not a call to turn the clock back to a mythical golden age when extremely small numbers went to university, rather it was to point out that we need to invest real money to nurture and support talent right across society. A system that requires parental wealth or a social network to enter the top universities is closing itself off to a large share of the future talent pool.

When Iain studied physics at St Andrews, the department was housed in a grand stone building on the Scores, on the sea cliffs where it overlooked the North Sea, the West Sands and the famous Old Course; ‘the golf’ has provided a competing attraction for students’ attentions for hundreds of years. The stone building remains in use by the university today, but with moral rather than natural philosophy taught in its rooms.

After four years, Iain graduated with an upper second class degree in 1963. Both St Andrews University and the town, then as now, are much smaller than other UK universities and its location by the sea in rural Fife means it feels slightly removed from the wider world. This gives rise to a uniquely intimate atmosphere that its students greatly value; Iain described it as a special place of peace and serenity where he could learn about scholarship and life. Iain attributed his upper second degree, as opposed to gaining a first, to his greatly improved golf handicap, a testament to the pull of ‘the golf’.

With no fixed plan, Iain decided to remain in St Andrews and to undertake a PhD, joining the group of Dr Dirk Bijl. He set to work building electron spin resonance (ESR) spectrometers with disused Second World War radar equipment in a wooden hut in the gardens of the grand old house on the Scores (figure 1). During his PhD he came into regular contact with the inspirational Professor John ‘Jack’ Allen (FRS 1949), the then head of the Physics Department. While at St Andrews, Iain managed to record an electron paramagnetic resonance (EPR) spectrum of the photoexcited triplet state of triphenylene at X-band. These states are extremely short lived, and it was only by building a resonance cavity that could be held at liquid helium temperatures and pumped with light that such an experiment was possible. For a PhD student to build this device in such a primitive laboratory was a clear signal of his talent, perseverance and work ethic.
After defending his PhD, Iain and his wife Karin moved to Bradford with Bijl, who had just accepted a departmental chair there. Iain, by his own description, was drifting and, at Karin’s urging, in 1967 he applied for a post in the lab of Rex Richards (FRS 1959), the Dr Lee’s Professor of Chemistry at Oxford.

Oxford, stage I 1967–1979

Setting up NMR

When Iain arrived at Oxford in October 1967, nuclear magnetic resonance (NMR) was in its infancy. There were immense practical hurdles to overcome with these machines, and commercial reliable software was non-existent, so setting up a new machine was a laborious, complex task requiring sophisticated pen and paper calculations and adjustment of components. Yet, Iain describes this environment as a revelation and the turning point in his scientific career, as suddenly there were ambitious successful scientists with important problems who had vague ideas about what biophysics might do.

His first paper on NMR was published in Nature in 1970 (1)* and dealt with the biological polymer collagen. Little was known about collagen at this time: it was a fibre composed of peptides and it had some regularity in its structure, but there were several competing models of how the peptide bonds were arranged relative to the fibre axis and thus how the underlying

* Numbers in this form refer to the bibliography at the end of the text.
structure was organized. Iain’s paper sets out how the splitting pattern of the unpaired spins of the deuterium nucleus (spin 1) is sensitive to the surrounding electronic charge distribution.

Iain and his colleagues tested their idea first on a known α-helical structure, poly-γ-benzyl-L-glutamate. The coordinates of this helix were known, and theory predicted that a splitting of 289.4 kHz would arise in the NMR spectra. Despite the challenges of the experiment, since the NMR probes were far from perfect at that time, they measured a splitting of 288.3 kHz. Having performed the control experiment, they moved to collagen. The literature had three favoured models for collagen, known as II, the Ramachandran two-bonded and IIa. Each model has a different proportion of three defined hydrogen-bonding arrangements. The type A arrangement has a typical (short) helical hydrogen bond, type B has a long hydrogen bond and type C has no hydrogen bond. Thus each of the three models of collagen produces a different predicted set of splittings with a range of line broadenings allowing Iain and colleagues to make inferences about the natural material.

Early applications on enzymes and proteins

The work of Daniel Koshland and others had shown that enzyme activity could be regulated by ligands that were bound separately to the substrates (Monod et al. 1965; Koshland et al. 1966). This is known as allosteric regulation and is particularly important in metabolism. In the early 1970s there was essentially no experimental structural or molecular insight as to how a ligand at the allosteric site influenced enzyme activity. Although protein crystallography had begun to resolve atomic structures by this point, it was a slow process and still unclear how it would unravel complex regulatory events. Glycogen phosphorylase is central to energy metabolism in animals; the enzyme breaks down the glucose storage polymer glycogen, releasing glucose-1-phosphate. Adenosine monophosphate (AMP) was known to activate the enzyme by binding distant to the active site where adenosine triphosphate (ATP) and glycogen were bound. Prior work had established that AMP binding changed the structure of the protein in some way, but few details of the change were known (Birkett et al. 1971).

Iain and colleagues demonstrated an approach that could begin to quantify the conformational changes that AMP induces in glycogen phosphorylase $b$ (2). The approach built on a known physical phenomenon, that the unpaired electron spin of a metal, in this case the paramagnetic Mn$^{2+}$ ion, which is bound to the enzyme, will broaden the linewidth of protons in a $^1$H NMR spectrum. The extent of broadening is a function of distance and the correlation time, which is dependent on the motion of the ion (as well as other physical parameters, which can be determined).

A second related approach is to use the single unpaired electron of nitroxide to broaden the line width, thus providing distance measurements. The ESR signal of nitroxide can also be influenced by the paramagnetic Mn$^{2+}$ ion in a distance-dependent manner, providing an orthogonal technique to mapping distance, presumably the electron spin approach benefited from Iain’s postgraduate work.

The final technique relied on knowledge that the metal ion quenches the fluorescence generated by chromophores. With well characterized model systems to hand this allowed the quenching effect to be correlated to distance. Thus in a series of experiments in one paper, Iain and colleagues studied the changes in linewidths of the $^1$H NMR spectra of both AMP and glucose-1-phosphate, the influence of Mn$^{2+}$ on the ESR spectrum of nitroxide-labelled protein and fluorescence quenching. Integrating these approaches produced a metric model of the allosteric and catalytic sites. In detail, the model has not stood the test of time, yet some
of its conclusions were prescient. AMP does sit at the interface between subunits and effects structural changes through this interface that drive allostery.

To a modern audience, these experiments seem crude, but the depth and rigour of the analysis behind them remain impressive. It was clear from Iain and others that NMR could have important things to say about protein structure and biology. Yet, as the collagen study and glycogen analysis show, the NMR of this era was low resolution and imprecise.

At this time, even contemplating using NMR to determine the structure and composition of a protein seemed an impossible dream, but one believed by the Oxford group, of which Iain was a key part. In 1973, they published a paper that contemplated determining the structure of lysozyme using NMR methods (3), and although these methods never produced the molecular structures, the paper served as a signpost and enunciated a grand challenge. Perhaps the most fundamental obstacle to realizing this dream was that the resonances from common regions (aromatic, aliphatic residue side chains) appeared as broad peaks and were overlapped. Since individual resonances could not be identified, even as the hardware had improved, the task looked hopeless. However, this paper on lysozyme contemplated the use of two methods that held promise in reducing overlap (4). The first method was a calculation based technique they termed convolution difference. In this approach the free induction decay is multiplied by an exponential and convolved with a second exponential. The end result is that the NMR line width is significantly reduced at the expense of signal strength. The spectra of lysozyme in figure 2 demonstrate the transformation in the spectrum that results from this approach.

The second approach they developed was to use paramagnetic ions; these broaden the resonances of nuclei to which they are close. Subtracting the spectrum in the presence of the paramagnet from the spectrum in the absence of the paramagnet leaves only the resonances close to the paramagnet. This greatly simplifies the spectra and, when the binding site is known, can help in the assignment of residues. The effect on the resonances from methyl

Figure 2. The aromatic regions of lysozyme are much sharper and more dispersed using a convolution difference approach. (From (4), used with permission from Elsevier.)
groups, predicted to be Val 109 and Ala 110, is shown in figure 3. Using this approach, the Oxford group began to assign the $^1$H NMR spectrum of lysozyme (9).

Iain, now recognized as an international authority in NMR, published over 30 papers on methods and applications. This was a golden period during which the marriage between Oxford biochemists and Iain demonstrated that NMR rigorously applied gave valuable insights into protein structure–function relationships.

Hindsight is both clarifying and distorting; since protein NMR is well established today, it is hard to avoid seeing the field as one that was always predestined to succeed. However, it is worth considering to what extent other techniques were explored but vanished over time. Were they doomed to fail, or did they lack the right people at the right time with enough vision, tenacity and talent? NMR in Oxford in the 1970s certainly had the right people, in fact there was a unique combination of extraordinary individuals. The far-sighted polymath R. J. P. (Bob) Williams (FRS 1972) was by then already a leading international figure in chemistry and biochemistry, and the two biochemists Raymond Dwek (FRS 1998) and Chris Dobson (FRS 1996) were on their way to becoming towering figures in glycobiology and protein folding respectively. Contributing to some of these papers was the chemist George Radda (FRS 1980), who had developed novel fluorescent probe molecules as a means to study biological metabolism and was now applying NMR. Iain completed the group, bringing a
rigorous physicist’s eye to biological spectroscopy. Together in various combinations and separately, the papers of this group transformed what spectroscopy, especially NMR, could do in biology. It does not seem unreasonable to suppose that without this cast of characters all together at this time, the entire field of NMR would look different today. In what is now known as ‘industrial impact’, Iain, with the assistance of Rex Richards, began a lifelong engagement with the makers of NMR machines, notably Oxford Instruments, then led by Martin (later Sir Martin) Wood (FRS 1987). Iain was never satisfied with current technology, an impatience that remained intact throughout his career, and worked synergistically with the engineers at Oxford Instruments to develop a series of cutting-edge machines.

If we look back across Iain’s work with a modern lens, we can identify some of the crucial steps on the way to develop NMR as a tool for biology (5–11, 13, 15, 16). What stands out in Iain’s contributions is the demolition of technical and scientific obstacles by new approaches. Even in this early stage of his career, it is striking how Iain’s hard-won methodological contributions were anchored to significant biochemical problems.

Oxford, stage 2 1977–1985

Cells, going big

Iain continued to work on questions of enzyme mechanism and to refine NMR approaches, but this period also marked his foray into whole-cell NMR. The boldness to move to such a complex challenge was very much in Iain’s character: push to find limits of a technology. George Radda, who remained an important colleague, had by this time demonstrated that it was possible to study metabolites in tissue by NMR (Hoult et al. 1974). The first of Iain’s papers appeared in 1977 (14). In this study, red blood cells were washed with D₂O, depleting them of glucose and lactate and removing the intense signal from water. The cells were then incubated with glucose, allowing the production of lactate to be followed. The study is a significant demonstration of the power of the spin echo pulse sequence that Iain and his colleagues had previously reported (8, 12), to greatly simplify NMR spectra. In addition, the paper notes the assignment of resonances for individual metabolites.

Building on these results, ¹H NMR was used to study the flow of metabolites across the cell membrane (17). Iain’s approach relied on magnetic susceptibility differences between the inside and outside of cells, which in a spin echo experiment results in an increase in a molecule’s signal intensity as it enters the cell. The approach was demonstrated for two compounds, alanine and lactate, crossing red blood cell membranes. They also observed that the difference in magnetic susceptibility in red blood cell suspensions, and therefore the increase in signal intensity, depended on the level of haemoglobin oxygenation. It is this phenomenon that is exploited in the blood oxygen level dependent (BOLD) effect, which is the basis of magnetic resonance imaging of brain function. Iain and colleagues continued to expand the approach, and used measurements of isotope exchange in deuterium-labelled compounds to study the kinetic properties of individual enzymes in cells (19–22).

The technique also showed promise to interrogate metabolism in cancer cells (18). In 1987 Iain’s first PhD student, Kevin Brindle (FRS 2020), now a professor at Cambridge, and Iain published a review of work (24) from the preceding decade, which they summarized had shown that:
NMR studies of cells and tissues can give unique and detailed information about the kinetic properties of specific enzymes in vivo.

They concluded:

In cases where the observed flux is catalysed by several enzymes, application of genetic methods to determine the contribution of a single enzyme seems to be an attractive area for further exploitation.

Oxford, stage 3 1986–1995

A return to proteins

Always his own harshest critic, Iain, in classically taciturn Scottish phrasing, described the insights from whole-cell NMR as ‘limited’. A more accurate, less self-critical statement was that, with the limitations of technology available to him, Iain had indeed taken the technique to its limits, leaving, in his phrase, ‘dotting i’s and crossing t’s’. Subsequent advances in NMR machines, in part inspired by Iain’s early work, have made cell NMR an extremely important area of biomedical research (Luchinat & Banci 2017). In fact, one of the most significant figures in this work is Kevin Brindle, who most recently used hyperpolarized $^{13}$C NMR to characterize tumours in breast cancer patients by studying the same enzyme reaction that they had studied in red cells in the 1980s (Gallagher et al. 2020). The paper is a striking demonstration that the hopes embodied in the 1987 review have come to fruition.

During the early 1980s, while Iain laboured in whole cells, the lab of Kurt Wüthrich (ForMemRS 2010 and Nobel Laureate 2002) had clearly taken the lead in applying NMR to protein structures, and in the 1980s this group published a series of new methods that culminated with the first solution structure of a protein determined by NMR (Williamson et al. 1985). Inspired by this landmark, Iain and colleagues began work on determining the structure of epidermal growth factor (EGF) (23). The protein is a powerful biological agent; when it binds to its receptor on cells, it stimulates them to grow and also to differentiate. The therapeutic potential of EGF had meant that its structure was of considerable interest. In what is now called an industrial impact activity, but was previously known as collaboration, scientists from the pharmaceutical division of Imperial Chemical Industries, part of the forerunner of AstraZeneca, worked with Iain’s group. As the paper’s reference list shows, the methods of Wüthrich were key to this solution, yet it was only the second complete de novo NMR protein structure and the first in the UK (25). Their analysis of the protein structure suggested how the compact module was folded up and identified the structural determinants for interaction with the receptor.

The significance of the paper was appreciated at the time. Here was the evidence that Wüthrich’s methods were indeed robust, powerful and generally applicable. Although protein crystallography was just beginning its explosive growth, Wüthrich’s studies followed by Iain’s showed that there existed a route for structure determination of proteins that did not crystallize. The work vindicated the long push by Iain and his colleagues to equip Oxford with both the machines, which they helped bring into existence, and the people to study proteins with NMR. This far-sighted decision meant that Oxford was going to be a key part of the explosion in protein NMR. Perhaps not fully appreciated at the time was the legend to Figure 3b in the manuscript:
Extrapolation of the features in [the structure of the EGF protein] to the first EGF-like region of Factor IX (residues 47–84) and Factor X (residues 46–83).

Unpacked, the legend was pointing out that the structure of EGF in this paper gives a good model of the domains within a larger protein that contain a similar sequence. This insight, that by determining the structure of a smaller domain by NMR one could learn about much larger proteins, prefigured Iain’s dissection of proteins into discrete domains that could be characterized by NMR. This approach became the signature by which Iain’s laboratory came to worldwide attention in structural biology.

**Modules: to divide is to conquer**

The breakthrough of protein structure determination by NMR came as the molecular biology revolution took hold. This transformed structural biology: macromolecules for which it had taken months of work to painstakingly isolate small amounts of material from natural sources could be expressed in *Escherichia coli* in a couple of days and purified in hours. This revolution also transformed protein crystallography, which by the mid 1980s was determining an increasing number of new structures. There was a light-hearted rivalry between NMR spectroscopists and protein crystallographers, although both recognized that their ‘technique’ had limitations that the other could address. These technique labels for scientists were out of date even as they were coined, for already the leaders of the field, such as Iain, had begun to define themselves by the biology they addressed and not the technique they used. This was just as well, since today the resolution revolution in the technique of single particle electron cryomicroscopy has swept all before it.

A limitation of NMR was that, with the hardware of the 1980s and 1990s, solving the structures of proteins with monomeric weights much above 30 kDa was intractable. Following their work on EGF, Iain started to determine the structure of EGF domains within larger molecules, for example in Factor IX (27). In this way, rather than focusing on ‘small’ problems, Iain brought NMR to bear on biological challenges. Iain made explicit the intellectual underpinning for this approach in an important 1990 paper (26), where he reported the structure of the type I fibronectin domain:

... the identification of ‘mosaic’ proteins. These proteins have evolved by duplication, insertion and deletion of a common pool of structural units or modules, yet their biological functions are diverse. They are involved in cell adhesion and migration, embryogenesis and the pathways of blood clotting, fibrinolysis and complement.

The structure was revealed to be composed by two β-sheets cross-linked by two disulfide bonds. The N and C termini are found at opposite ends of the structure, and, as the authors recognized, this facilitated the connection of such molecules as a chain. Right from the outset Iain grounded the module approach that his lab was taking in an understanding of biology (26):

... determining the structures of other types of module, which will allow models of many mosaic proteins to be constructed. ... Models of mosaic proteins will aid the understanding of the structure/function relationships and the design and interpretation of module swapping and site-specific mutagenesis experiments.

Guided by this road map, the lab reported the structure of the type III fibronectin domain (28). The larger type III domain is also composed of two β-sheets, but lacks the disulfides
of the type I domain. The paper showed that the loop with the Arg-Gly-Asp (RGD) motif is flexible (figure 4), something that was uncertain at this point. The RGD motif is commonly found in extracellular proteins and is bound by integrins; it is thus central to a wide range of cell biology. The lab continued to determine module structures, including that of SH3 (29) and part of the P17 protein from the human immunodeficiency virus (HIV) (30).

Oxford, stage 4 1996–2014

A physicist turns immunologist

With a dazzling reputation safely made and with his mentees appointed to head their own NMR groups in the UK and worldwide, Iain could have chosen to run a productive lab focused on determining the structure of modules in proteins. Throughout his professional career, when an easier, less demanding route opened to him that could allow some rest upon hard-won laurels, Iain sought out the more demanding route. It is difficult not to see in this work ethic a strain of Calvinism that at one time marked strands of Scottish culture.
Through his studies on the structure of protein modules, Iain was exposed to adhesion and integrin assembly. Iain, in what he described as the most rewarding phase of his career, brought all his mastered techniques to bear on this aspect of immunology. He did not enter the work as the physicist with a stellar career demanding to be heard, but rather he turned himself into an immunologist, making his contributions to the field on this basis.

Adhesion, getting stuck into a new field

Evidence that Iain was moving beyond reporting NMR structures can be seen in his work on integrin activation by talin (38). Talin is a cytoskeleton protein that binds to integrins in the final step of switching integrins from an ‘off state’ to an ‘on state’. The activation of integrins is important in increasing adhesion, a process at the heart of many biological events, including platelet aggregation and extracellular matrix assembly. In this paper, the authors focus on the F3 domain of talin, which had previously been identified to bind to integrin by recognizing a peptide found in the integrin tail. Using NMR, they studied the kinetics of binding of various peptides to the talin domain. This approach identified those residues that were most perturbed (determined by monitoring their NMR signal) by peptide binding. The technique relies on the fact that residues that come into close contact during formation of a complex undergo a shift in their NMR signal, so monitoring perturbation is a means to identify what regions form the complex interface. They next determined a complex that confirmed and extended insights from a previous crystal structure (figure 5a). Notably, they identified additional interactions between the membrane-proximal portion of the peptide and the talin. The talin structure is rigid and the study identified the peptide regions most involved in binding. Structural data were supported by extensive site-directed mutagenesis of both the peptide and talin that were evaluated in a cell-based assay. These studies singled out the MP region as critical to the conformational activation. In the conclusion of the paper, drawing on the impressive biophysical and cell biology observations, a model for activation is proposed (figure 5b). Briefly, the talin first binds to and orders the integrin tail and triggers binding to the membrane-proximal portion. This interaction with the integrin peptide breaks the dimeric integrin dimer and thus activates
integrin. Iain continued along this line of research with multiple papers and reviews that added deeper insights into this vital process (36, 39, 42, 43), bringing new researchers into his quest.

Adhesion led Iain to study collagen binding by fibronectin and more generally to an interest in the extracellular matrix (ECM). He made many contributions to this field, starting with individual domains and building up into more complex pictures (31–34, 40). In a review (37), Iain and his co-author outlined his vision and challenges for the field:

increasing attention to extraction procedures, new structural tools and an ability to express a variety of defined recombinant molecules can lead to a much better understanding of how the network of large, cross-linked molecules are laid down in the insoluble ECM by a series of precise association events.

In among this focus on immunology and adhesion, Iain managed to produce an elegant mathematical model of cell differentiation in *Bacillus subtilis* (35). This was one of the early papers in what became known as systems biology. The significance of the paper is not just the mathematics, but also the careful experimental verification of the model. Once again, Iain finding a partner, in this case Michael Yudkin, an expert in *B. subtilis* sporulation, was able to bring Iain’s analytical rigour to bear on a field, and by doing so set a new standard.

**A MENTOR AND TEACHER**

On Iain’s death generous tributes were paid by colleagues, former students, co-workers, institutions and organizations. The tributes of Professor Christina Redford and Professor Mark Sansom in the scientific literature (Redfield 2014; Sansom 2014), when read alongside obituaries in UK newspapers (*The Daily Telegraph*, *The Guardian*, *Oxford Mail* and Perth’s *The Courier*), convey the breadth of Iain’s influence and the high regard in which he was held.

His scientific legacy rests not only in his papers and the new approaches he devised, but also in a truly global network of Campbell lab alumni; Iain was very proud to have played a part in the careers of so many talented NMR spectroscopists and structural biologists. In addition to his papers, Iain wrote multiple books, and these are now standard texts in biological science; no serious structural biology student will not have come across his books or papers. His lecture notes as well as the books still form the basis of some of the courses taken by undergraduates in Oxford. His last book, a thorough and comprehensive undergraduate textbook, *Biophysical techniques* (41), completed during his final illness, is a distillation of 40 years of tutorial delivery and lecturing experience and is a masterful treasure trove of information and challenging problems (with solutions!). As one, straight to the point, reviewer says on the Amazon website: ‘Must have if you are into biophysics.’

For five years, starting in 2008, Iain was director of teaching for the Oxford four-year undergraduate course in molecular and cellular biochemistry (ca 100 students per year group). As would be expected, this was a role he took extremely seriously, expending significant effort, and where once again he had a lasting impact.

Beyond NMR, Iain was a generous mentor across biochemistry and structural biology. Famously direct, he would give an unsentimental and unsparing account of the weaknesses in an idea. Having done so, he then rolled up his sleeves to help fix the weaknesses. In his moving personal tribute, Mark Sansom, until recently the head of the Biochemistry Department at Oxford, recalls just such an incident when Iain turned round a manuscript in under an hour, greatly improving it (Sansom 2014). At the same time as poking holes, Iain never failed to
be generous in his praise for what he found to be good in the work of others; he was entirely free from petty jealousies and a ‘not invented by me’ approach. This collegiality, honesty and fairness endeared to him to generations of colleagues. Elspeth Garman, now a biophysics professor at Oxford, but back in late 1980s a newly arrived from a post-doc in nuclear physics, remembers how Iain could be relied on to side with and support the junior faculty whatever their field. He asked for nothing in return from any of the people or organizations that he did so much to assist over the years.

**FAMILY AND OTHER INTERESTS**

While a student in St Andrews, Iain met and subsequently married Karin Wehle, a German citizen, who was in Scotland as part of her teacher training. Iain’s dancing skills and quiet determination persuaded her to take an interest in the physicist. They went on to have three children, Louisa, Fiona and Andrew, who in their turn have had six children.

Iain always said that only two things really mattered to him: his family and his work. Their home in Oxford has many lovely photographs of Iain and Karin as parents and as grandparents that testify to his love of family. It was through Karin that Iain grew to enjoy and appreciate both art and classical music. The families of driven scientists often have to share them, perhaps unequally, with their work, something that Iain frankly acknowledged in the dedication to his last book. Yet, everyone who knew Iain knew that love for and by Karin and their family was the rock upon which he built his life. When Iain died on 5 March 2014, he and Karin were days short of their forty-seventh wedding anniversary.

At St John’s College Oxford, Iain greatly appreciated the intellectual cross-pollination that the best of such institutions can provide. He used his position in the college to help others and create opportunities for his colleagues. It is worth noting that, among the huge number of cards and tributes that came from across the world after his death, were ones from the domestic college staff. They knew him simply as ‘Iain’, the friendly approachable Scot who talked and listened to them on their terms. In more than one of these cards, people remarked that they had no idea he was ‘such a famous person’. Those who knew Iain would suspect that he would have taken as much pride in having succeeded to have ‘no airs or graces’ as he would have done in the tributes on his scientific accomplishments.

Iain was great company, the master of the deadpan throwaway delivered with a twinkle in his eyes (figure 6a). The seriousness of work was always mixed with laughter. I, like so many others, benefited from his wisdom, generosity and support in many ways over the years. If Iain had thought something over and you disagreed with the analysis, it was a safe bet he was right. In fact, I can find only one example of a statement made by Iain that not only has proven wrong over time but was wrong from the moment he made it. In the notes he left to the Royal Society, he remarked: ‘I don’t believe anyone would find my story interesting enough to spend time over.’ Iain’s contributions have changed science, but how he made these contributions, his enthusiasm, integrity, humility and compassion are not only interesting, they are inspirational.

**CLOSING THOUGHTS**

I had ‘grown up’ in the structural biology community, and knew and admired Iain as one of its guiding lights. As a fellow Scot from not too dissimilar a background, I felt an affinity with
Iain, who, to me, embodied some of the virtues and character traits that Scotland likes to think of as particularly Scottish.

I had the privilege to give the laureation address for Iain when he was given an honorary DSc by St Andrews University in 2012, and it was a pleasure to get to know Karin, who came along too. Iain was clearly delighted to be recognized by his alma mater and spoke movingly from the stage of his affection for St Andrews (see figure 6b) and the importance of learning. Of course, in his typically modest way, Iain was also discomforted at being the centre of so much attention and praise. He was very ill with cancer and weakened by the treatment, but was in remission when he came back to St Andrews. At his request the seriousness of the illness remained a fact known only to very few.

**AWARDS AND HONOURS**

The following are some examples of the awards that Iain received for his work.

- 1982  Education in Partnership with Industry
- 1990  The British Drug House Medal of the Biochemical Society
- 1990  Member of European Molecular Biology Organisation
- 1995  Fellow of the Royal Society
- 2000  DSc (Honorary) University of Portsmouth
- 2000  DTech (Honorary) University of Lund
- 2003  Novartis Medal, Biochemical Society
- 2006  Royal Society Croonian Lecture
- 2012  DSc (Honorary) University of St Andrews

Figure 6. (a) The author and Iain sharing a joke. (b) Iain speaking from the podium immediately following his honorary graduation from St Andrews in 2012. The photographs are used with the permission of the University of St Andrews and at the request of the Campbell family. (Online version in colour.)
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The frontispiece portrait photograph was taken in 1995 by Prudence Cuming Associates and is © the Royal Society.

AUTHOR PROFILE

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James Naismith FRS FRSE FMedSci is currently director of the Rosalind Franklin Institute and is also professor of structural biology at the University of Oxford. He graduated from Edinburgh as a chemist and went to Manchester to study for a PhD in structural biochemistry with Bill Hunter, John Helliwell and Dave Garner (FRS 1997). After a two year post-doc with Steve Sprang in structural biology, he took up a lectureship at St Andrews University, where he remained until 2017, when he moved to Oxford. His research interests are in the fields of structural biology and enzymatic chemistry.

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