BIOGRAPHICAL MEMOIRS

Dudley Howard Williams. 25 May 1937 — 3 November 2010

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Elected FRS 1983

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Dudley Williams was a pioneer in using nuclear magnetic resonance (NMR) spectroscopy and mass spectrometry (MS) to solve important structural problems in Chemistry and Biology. His 35-year quest to understand the structure and mode of action of the vancomycin antibiotics led him to fundamental thinking about the nature and thermodynamics of molecular recognition, in particular the roles of solvation, flexibility, entropy, enthalpy and cooperativity. He was always keen that his expertise be used for practical benefit through his academic research and industrial consulting. His legacy also includes a set of textbooks that transformed the use of spectroscopic methods in organic chemistry, and a school of former PhD students and postdoctoral colleagues who have themselves made major contributions across a broad swathe of science.

EARLY YEARS

Dudley Howard Williams was born on 25 May 1937 in Farsley, near Pudsey, Yorkshire, the only child of Lawrence Williams (1906–90) and Evelyn, née Hudson (1907–82). His family background and environment were traditional working class, both parents leaving school to start work at 13, but they were relatively comfortable as his father had progressed from office boy to a minor managerial position in an engineering firm. Dudley remembered his childhood...
as being one of warmth, neighbourliness and complete security, despite the problems of the war years.

With no siblings, no television, and the only reading material in the house being the *Daily Express*, Dudley had to entertain himself. As an 11-plus scholarship boy at Pudsey Grammar School, his interests included playing football and cricket, as well as physics and chemistry. At home he reassembled battery-operated radios, built a chemical laboratory in the garden shed where he made gunpowder and prepared ‘dangerous’ oxides of chlorine, and kept bees. He once tried to prepare metallic sodium by electrolysis of molten sodium hydroxide, using his bicycle dynamo as the electricity source, only realizing afterwards that a dynamo produces alternating current so his efforts were doomed to failure. He recalled that his main inspiration at school was his physics and mathematics teacher, Mr Shuttleworth, who passed on his enthusiasm for nuclear physics and quantum theory. Dudley also captained the school’s 1st cricket team, was excited to sit behind (Sir) Len Hutton at the local cinema, and many years later played for the Churchill College Fellows team.

In the pre-television era, the piano played a major role in family life; Dudley’s father was an accomplished pianist of popular music, entertaining friends and family, and so Dudley learned to play at an early age. Later, he too became an accomplished pianist, with a broad repertoire from Chopin to jazz, and he maintained his love of playing throughout this life.

At Leeds University he obtained a first-class BSc in Chemistry (1958) and completed a PhD in 1961 on the synthesis of vitamin D and related compounds such as tachysterol, under the supervision of Basil Lythgoe (FRS 1958). His PhD work was completed without the benefit of either nuclear magnetic resonance (NMR) spectroscopy or mass spectrometry (MS): his thesis contained hand-plotted UV spectra and IR spectra, and he once said that, had he had NMR and MS available, he could have repeated the entire thesis work in a few weeks.

STANFORD AND MARRIAGE

In 1961 Dudley moved to Stanford University in California, where he spent three astonishingly productive postdoctoral years working with Carl Djerassi (ForMemRS 2010) exploring the application of MS in organic chemistry. Meanwhile, in the evenings he was investigating the use of NMR spectroscopy on a 100 MHz instrument with Norman Bhacca at Varian Associates in Palo Alto; at the same time Ray Freeman (FRS 1979) and Richard Ernst (ForMemRS 1993) were making pioneering technological advances at Varian. As described below, Dudley had access to Djerassi’s extensive steroid collection, which he used essentially as a physical database to study systematically the influence of structure and functional group on fragmentation patterns in mass spectra and on chemical shifts and coupling constants in NMR. The papers, reviews and books that Djerassi, Dudley and their colleagues published during that period provided powerful new tools for the determination of molecular structure and so transformed the way in which organic chemists worked. The early studies at Stanford of solvent effects on chemical shifts initiated Dudley’s career-long interest in intermolecular interactions and molecular recognition.

Meanwhile, while back in England, on 9 March 1963 Dudley married Lorna Patricia Phyllis (always known as Pat) Bedford (b. 1942), daughter of Anthony and Lorna Bedford, of Harrogate. Dudley and Pat had met at Leeds University when she started working as a secretary in the Chemistry Department in 1960. Gradually during the following year they got to know each other, going out together on occasions. The growing friendship resulted
in Pat typing his thesis in her spare time, but Dudley had already been awarded a Fulbright Scholarship and soon he left for Stanford. They wrote weekly (telephone calls in those days meant booking an international call in advance) and in December 1962 Djerassi gave Dudley three months’ leave to return home and marry. Pat and Dudley enjoyed exploring California, climbing, camping and hiking with friends, and later in life they travelled the world for scientific events (Figure 1). In California they had no piano at home, but Dudley had no qualms about playing in the bar at the Ahwahnee Hotel in Yosemite or the Top of the Fairmont Hotel in San Francisco. Throughout his life, he would write gently mocking but always affectionate poems about colleagues, frequently setting them to music to be played and sung at parties.

CAMBRIDGE

In 1964 Dudley was appointed by Lord Todd (PRS 1975–80) to a junior position in Organic Chemistry at Cambridge. He made it a condition of his appointment that the department became competitive by purchasing a Varian 100 MHz NMR spectrometer and an AEI MS9 mass spectrometer. He remained in Cambridge until his retirement in 2004, despite offers from Switzerland and California that greatly tempted him. In 1964 he also became a fellow of Churchill College, a relationship that was important to him for the rest of his life. The pioneering textbook *Spectroscopic methods in organic chemistry*, which he co-authored with
Ian Fleming (5), was first published in 1966 and went on to five further editions by 2008; it was translated into seven languages including Chinese, Indian, Japanese and Malaysian.

After moving to Cambridge, Pat and Dudley had two sons, Mark (b. 1966) and Simon (b. 1968), and in 1969 they moved to a fine house in Fulbourn, a few miles outside Cambridge, with a large garden that Dudley and Pat tended carefully, something they shared throughout their married life. When he had time, Dudley loved playing cricket and badminton with Mark and Simon in the garden, and snooker in the dining room, and he took them skiing as soon as they were old enough, at around four years old. In their teenage years the boys enjoyed playing squash with one another and with Dudley. He also loved playing squash with colleagues at lunchtime.

Cambridge was very parsimonious in giving recognition through promotion during most of Dudley’s time there. Scientists were not considered seriously for personal readerships until they had been nominated for Royal Society election; promotion to a personal professorship had to wait at least until election as a Fellow, and across the whole university there were usually just two ‘ad hominem’ promotions to professor each year. When Dudley was elected FRS in 1983 there were just five professors in Chemistry, and he had to wait for 13 years until 1996 for promotion; he chose the title Professor of Biological Chemistry.

**SCIENTIFIC CONTRIBUTIONS**

The different areas of Dudley’s science overlapped, intertwined and evolved so it is not easy to separate them out for discussion. We first summarize his work developing NMR and MS as useful techniques, before moving on to explore his work in determining the structures and modes of action of the vancomycin family of antibiotics and his associated studies on the fundamentals of molecular recognition. Finally, we briefly explore his thoughts on evolution.

*NMR spectroscopy*

In the early 1960s the application of NMR spectroscopy to organic chemistry was in its infancy. The first commercial instruments had been marketed by Varian Associates in the 1950s, but they were relatively primitive and insensitive. Most organic chemists had neither access to NMR nor any idea of its potential. By 1963, Varian had a flourishing business and research laboratory in Palo Alto, just a short drive from Stanford’s Chemistry Department, and Dudley was able to work there with Norman Bhacca, a Varian applications scientist. Combining good use of Djerassi’s steroid collection with Dudley’s chemical skills to make deuterated and other derivatives and Bhacca’s NMR expertise, they discovered useful new geometrical and electronic effects of structure on chemical shifts and coupling constants. They also showed that aromatic solvents such as benzene could form transient complexes with steroid molecules in solution, shifting the NMR responses of the steroid in a way that could remove accidental coincidences of signals and generate useful structural information. These discoveries were reported in several high-profile papers, for example (4)*, and summarized in an influential book (1).

Setting up independently in Cambridge, Dudley initiated the mass spectrometric work described below and continued his studies of solvent effects on chemical shifts. Careful

* Numbers in this form refer to the bibliography at the end of the text.
analysis of the complexation of steroids with aromatic solvent molecules led him to some understanding of the geometry and strength of intermolecular interactions, an area that was to underpin much of the science he pursued from the 1970s onwards.

In early 1969 Dudley told J.K.M.S. during a pre-PhD interview that NMR had ‘reached a boring plateau’ and that the future was in MS. However, later that year, when J.K.M.S. was moving to Cambridge to begin his PhD, Dudley noticed a paper describing the use of a lanthanide shift reagent to dramatically alter the NMR spectrum of cholesterol (Hinckley, 1969). He realized from the way that the paper was written that Hinckley had little experience of steroids and that there was great potential that was conceptually similar to solvent shifts but hugely more powerful. Within weeks, J.K.M.S. had vindicated and exceeded Dudley’s predictions by revealing all the normally hidden signals of \( n \)-hexanol. Dudley’s instant reaction – ‘We’ve hit a goldmine!’ – was confirmed when the first communication, published in early 1970 (6), received hundreds of citations and prompted many other groups to follow suit. More papers followed in the next two years, and later Dudley used a shift reagent in combination with mass spectrometry to provide a revised structure for the antibiotic echinomycin (8), but characteristically he persuaded J.K.M.S. to stop working on shift reagents as we had already scoped out the major uses and limitations, and could leave other groups to fill in the details.

Dudley then shifted the focus of his NMR research and usage to the elucidation of the structure and mode of action of the vancomycin family antibiotics, as described below.

**Mass spectrometry**

When Dudley arrived in Stanford in 1961, commercial mass spectrometers were becoming available. Volatile organic compounds could be vaporized into a vacuum, and subjected to bombardment by a beam of energetic electrons which ionized and fragmented them. The resulting fragments were then sent to a detector through a magnetic field which sorted them by mass. In principle, inspection of the fragment masses allowed a kind of molecular archaeology, mentally reassembling the intact molecule, but there was little understanding of the relationship between structure and fragmentation. Djerassi and his group, including Dudley, used his extensive collection of steroids containing various functional groups to explore this relationship, where necessary clarifying the fragmentation pathways by substituting deuterium into specific places so as to identify which parts of the molecules contributed to which fragment. Again, there was a series of papers summarized in book form (2, 3).

Studies into fragmentation pathways were initiated in Cambridge and continued for some years, but the new MS9 instrument also provided other opportunities: it achieved high resolution by placing an electrostatic analyser between the ion source and the magnet. Just before the magnet was a ‘field free region’: when ions of mass \( m_1 \) fragmented in this region to a mass \( m_2 \), they appeared in the final spectrum as broad ‘metastable ions’ at mass \( m_2/m_1 \). Dudley realized that the intensity and shapes of these peaks gave valuable information about the mechanisms of these slow unimolecular gas phase reactions and he spent several years exploring fundamental aspects of this chemistry using simple organic molecules. In particular, he and his group discovered that some symmetry-forbidden pericyclic reactions were easy to detect and study. This profound work was summarized in outstanding reviews (9, 10) but it did not receive much attention or recognition from conventional chemists interested in solution state reactions. So, when new gentle methods of ionization became available, making more
polar and biologically relevant molecules susceptible to study by MS, Dudley abandoned the study of small molecules.

He was always keen that his expertise be used for practical benefit, partly through long-term consultancies at Kratos (for mass spectrometry) and at Smith Kline & French (later SKB), Napp, Upjohn and Xenova (in the pharmaceutical area), but also through his academic science. In the early 1970s, he and his postdoc Howard Morris (FRS 1998) collaborated with Egon Kodicek to unravel the pathway of vitamin D activation. C1-tritium-labelled vitamin D was fed to rats with induced rickets and a few micrograms of the metabolites were isolated; the MS fragmentations shown in Figure 2, together with loss of radioactive label at C1, showed how the inactive form of vitamin D that we eat is hydroxylated first in the liver and then in the kidney to the 1,25-dihydroxy form (7). This metabolite acts as the human hormone responsible for calcium absorption into the bloodstream, and thus is necessary for the formation of healthy bones; this work led to life-saving therapies for patients with kidney failure.

In her PhD interview with Dudley in 1979, C.V.R. was told that mass spectrometry had become routine and that most of the important discoveries had taken place. We had not predicted the transformative discoveries of fast-atom-bombardment (FAB) MS reported in 1980 by Michael Barber at UMIST. Once the potential was established, Dudley was quick to capitalize on these discoveries, collecting a prototype source from AEI and driving back over the Pennines with it in the boot of his BMW. At that stage almost everything that we tried worked beyond our wildest imagination, including polar antibiotics, nucleoside phosphates and underivatized peptides; these discoveries led to a landmark paper which was to become one of Dudley’s most highly cited (11). FABMS was particularly valuable in sequencing biologically active peptides that are blocked at the N-terminus (12) or are derivatized in an unusual way (16) or phosphorylated (14) and therefore cannot be sequenced by classical means. Dudley was particularly proud of the discovery and structure determination of antibiotic cyclic peptides found on the skin of the toad *Xenopus laevis* (13). But it was not long before he was pushing the boundaries further: with high mass-to-charge magnets he began sequencing large peptides (gastrin and insulin) as well as small proteins, and he established productive collaborations with neuroscientists and biochemists at the MRC Laboratory of Molecular Biology and the University Biochemistry Department in Cambridge.

In the early 1990s FAB gave way to a further transformative development in mass spectrometry, that of electrospray ionization. Dudley was quick to realize that this could provide answers to some of his long-term questions concerning cooperativity on binding. Using hydrogen–deuterium exchange labelling of free and bound proteins he showed how
‘structural tightening’ took place upon binding. This research led to one of his last scientific papers (19), in which he considered how enhanced packing could account for remarkably high-affinity binding of proteins and ligands.

**Vancomycin antibiotics and molecular recognition**

In 1969 Dudley took on a new problem: determining the molecular structure of vancomycin, a powerful natural antibiotic first isolated from a bacterium found in Borneo and active against Gram-positive bacteria. Vancomycin was known to inhibit peptidoglycan formation but little was known about its structure or mode of binding; at the time it was obscure and thought to be too toxic for clinical use, but determining the structure was a challenge that Dudley expected to complete in six months, using a combination of chemical degradation, NMR and MS.

Those six months turned into almost four decades of science, initially difficult and frustrating, with some thin PhD theses, because vancomycin does not belong to a readily recognizable structural family. It turns out to be derived from a linear peptide but rigidified by condensation of several aromatic rings and decorated with sugars to give a multi-ring species that is not susceptible to ready analysis by MS or to straightforward degradation (Figure 3). Nevertheless, this was ultimately a successful venture, NMR, MS, thermodynamics, crystallography, synthesis and molecular biology being combined to bring understanding not only of the structure of vancomycin and a whole family of closely related molecules, but also of the interactions leading to molecular recognition and antibiotic activity. Dudley provided a detailed overview of the chemistry, biology and clinical use of the vancomycin family of antibiotics, and his contribution to this area in (17). We provide only a brief summary here.

Gram-positive bacteria generally possess a thick outer peptidoglycan protective layer. This consists of polysaccharide chains (shown in Figure 4 as ellipses) which are cross-linked through short peptide chains. Cross-linking is achieved by displacement of a terminal d-Ala residue by a lysine-NH$_2$ belonging to an adjacent peptide chain.

Using the nuclear Overhauser effect, an NMR technique for identifying which atom is spatially close to another, Dudley and his group were able to determine precisely the covalent structures and shapes of vancomycin and its analogues (correcting errors in earlier work), and how they use a pattern of hydrogen bonds to bind to peptides terminating in d-Ala-d-Ala. The group then discovered that peptide binding encourages dimerization of the antibiotic and strengthens binding. This triggered an enduring interest in enthalpy, entropy and cooperativity, and also helped to design a next generation of semi-synthetic antibiotics. This work was a major contribution to the clinical success of this class of antibiotic, which became a key weapon in the fight against MRSA ‘superbugs’, saved thousands of lives annually and generated sales in 2007 of approximately one billion dollars.

Throughout those decades Dudley also used vancomycin and related structures as vehicles for fundamental thinking about molecular shape and flexibility, and about the thermodynamics of solvation, binding, non-covalent interactions, molecular recognition and cooperativity (18).

**Evolution**

Exploring the closely related structures of the vancomycin family also led Dudley to think extensively about evolution. He argued powerfully that ‘natural products’ such as the alkaloids found in many plant species that have no known function must have a vital but unknown role
Figure 3. The structure of vancomycin.

Figure 4. Biosynthesis of peptidoglycan by cross-linking. This is inhibited by vancomycin, which is shown schematically as a box enfolding a terminal D-Ala-D-Ala.
in order to justify the evolutionary effort and energy expenditure in maintaining their presence through many cycles of natural selection (15).

**PERSONALITY AND LEGACY**

Dudley was a compulsive scholar: his conversation, whether in a research meeting, a dull committee or the pub, would always turn to philosophy, entropy, evolution and the meaning of life. Boltzmann was a particular hero, making a surprising number of appearances both in casual conversation and in formal meetings. Dudley never had any interest in administration or management, either in themselves or as career vehicles for himself, but when J.K.M.S. was head of department, Dudley could be relied on to be a sympathetic and constructive listener. During his 40 years in the Chemistry Department, he did sit on a variety of internal and external committees; notably, in 1997, he was chairman of a new development committee which was highly successful in raising funds, particularly for the Unilever Building.

After 1964, most of Dudley’s experimental results were inevitably obtained by his students and postdocs. The relationship between supervisor and research group is perhaps one of the greatest pleasures of academic life, and Dudley showed us that we are privileged to have an academic family as well as a biological family. The influence, teaching and learning flow
in both directions in a way that is hugely enriching and rewarding. Dudley gave his students scientific freedom, while also ensuring that everything we did was worth doing. He challenged our sloppy thinking and lazy responses. He encouraged us to think laterally and imaginatively, to confront orthodox thinking and to have the courage to work in new areas. He always stressed the importance of asking and addressing important questions. His early students in Cambridge were often encouraged to work simultaneously on separate NMR and MS projects to give them variety and breadth. He insisted that having provocative and testable ideas that might turn out to be wrong was more important than pursuing boring details. He trained us to combine the highest standards of experimental rigour and data analysis with unconventional thinking and unconstrained imagination, preferably in the context of a team approach to problem solving. Occam’s Razor was frequently and ruthlessly applied to fanciful explanations. One corollary of this view of science was his disapproval of extremely large research groups, his own only occasionally approaching 20 members.

Dudley was never afraid to challenge conventional wisdom and to think the unthinkable. Some of his potential achievements were thwarted by others: many years ago he submitted to SERC a proposal on what we would now call combinatorial chemistry, but it was years ahead of its time and was not funded.

He was immensely proud of the successful careers of former members of his research group, above all perhaps of those who went on to be elected Fellows of the Royal Society: Howard Morris (FRS 1998), Jeremy Sanders (FRS 1995), Anne Dell (FRS 2002) and Carol
Robinson (FRS 2004). Amongst the undergraduates he taught at Churchill was Chris Hunter (FRS 2008), with whom he enjoyed sparring about entropy and molecular recognition many years later (see Figure 5).

Weekly group seminars took place in the evening after an early dinner. For students making presentations about topics they didn’t understand or with poor diagrams, they could be intimidating, in the face of forensic questioning. But they also covered the whole of science when Dudley invited friends from other departments: particularly memorable were an early talk on stem cells by (now Sir) Martin Evans (FRS 1993) when he was still a genetics lecturer in Cambridge, and a practical demonstration by Herbert Huppert (FRS 1987) of how volcanic eruptions occur, using mixtures of solutions. A recurring theme was ‘There is no such thing as a stupid question’. These evenings were followed by sessions in the Panton Arms, where the philosophy, jokes and anecdotes flowed as freely as the beer, although many group members remember that, with surprising frequency, Dudley’s wallet was missing or empty.

In his younger days, Dudley liked to captain the group football team, the rivalry with the Battersby group team being particularly strong. His garden parties and social events often included sporting events with a competitive edge. Cricket, badminton and squash tournaments on the lawn were played to win, but always in good spirit. Until his 60s, when both hip joints were replaced, Dudley remained an enthusiastic and competitive squash player. Group Christmas parties in the early days were also legendary, with impromptu piano recitals.

Dudley’s 60th birthday fell on a Bank Holiday Monday. Pat, Mark and Simon secretly invited ex-members of the group to a party, and on the morning of the party Dudley was sent out with one of his sons on some concocted errand. When they returned, over 50 current
and former members of the group, and their families, together with lab friends and colleagues, were gathered in the garden, enjoying glorious late spring weather, some having flown in from Asia, America and Australia. A memorable series of photos captured Dudley with his group, decade by decade (Figure 6).

Dudley retired in 2004. The present authors organized a retirement symposium and dinner, and collected together reminiscences and photos from former group members and colleagues to create an Academic Family Album. In addition to some of the points made above, we note
the following lessons from working with Dudley (courtesy of John de Maggio):

- Argument is the highest form of intellectual exchange and education.
- Optimism about science is fully compatible with cynicism about scientists and especially politicians.
- Bizarre unexpected results can be good.
- Bizarre unexpected people can be good.
- Anything is a legitimate subject for humour.
- Find the time to laugh at yourself and your colleagues.
- As the world becomes more specialized and narrow, a broad perspective remains valuable.
- Two months in the lab can save two hours of thinking about the experiment, especially if the thinking is done in the pub.
- Everything, absolutely everything, is related to evolution.

After retiring, Dudley devoted much time to enjoying his family (Figure 7), especially his three grand-daughters, and to his garden, playing the piano and completing a book that he had started in the mid-1980s. This book is aimed at the lay reader interested in science and sets out his own perspectives on science, evolution and human behaviour and his personal, firmly atheist, philosophical views. Over many years during his career, he was only able to work on this book in any spare time so consequently it underwent many changes and it was not until his retirement that he could spend more time writing. He finished it, except for the index, in hospital just before he died. Testing truths was published posthumously in 2013 (20).

In the summer of 2010, following several months of general ill health, Dudley was diagnosed with an aggressive carcinoma of the liver and he died soon afterwards in Arthur Rank House, a hospice in Cambridge, on 3 November. He faced his last few, painful weeks with honesty and courage, analysing the personalities and behaviour of those around him until almost the end. Figure 8 is one of the last photos of Dudley, taken while walking in the Lake District.

RECOGNITION AND AWARDS

1966 Meldola Medal, Royal Institute of Chemistry
1968 Corday–Morgan Medal, The Chemical Society
1983 Fellow of the Royal Society
Tilden Medal, Royal Society of Chemistry
1984 Structural Chemistry Award, Royal Society of Chemistry
1990 Academia Europaea
1991 Bader Award, Royal Society of Chemistry
1996 Leo Friend Award, American Chemical Society

ACKNOWLEDGEMENTS

We are grateful to Pat, Mark and Simon Williams and Chris Hunter, for their help in illuminating Dudley’s life, and to the family for the photographs in Figures 1, 7, and 8. Figure 5 is © Nathan Pitt, University of Cambridge. The frontispiece was taken by Godfrey Argent in 1983 and is © Godfrey Argent Studio.
Jeremy Sanders studied for his BSc in Chemistry at Imperial College, London. His final year dissertation on the determination of stereochemistry from NMR spin–spin coupling constants inspired him to move to Cambridge in 1969 to study for his PhD with Dudley Williams. After a postdoctoral year at Stanford working on protein NMR, he was appointed to a junior academic position in Chemistry in Cambridge. He was promoted through the ranks, becoming a professor in 1996, and was Head of Chemistry from 2000 to 2006. He led the University’s 800th anniversary year-long celebrations in 2009, was Head of the School of Physical Sciences 2009–2011, and then Pro-Vice-Chancellor for Institutional Affairs until his formal retirement in 2015. His initial scientific interests in the development and application of NMR methods in chemistry and biology evolved into extensive interests in molecular recognition and supramolecular and dynamic combinatorial chemistry. He is currently Editor-in-Chief of Royal Society Open Science and a member of the Editorial Board of Biographical Memoirs.

Carol Robinson (née Bradley) studied for her Graduate of the Royal Society of Chemistry Degree while an employee of Pfizer Ltd. She obtained her PhD under the supervision of Dudley Williams in 1982, after just two years in his research group. After an eight-year career break she returned to full-time research at the University of Oxford in 1992 and received a Royal Society University Research Fellowship (1995) to undertake her independent research. In 2000 she moved back to Cambridge and was later awarded a Royal Society Research Professorship. In 2009 she became the Dr Lee’s Professor of Physical Chemistry at the University of Oxford, a post she still holds.

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The following publications are those referred directly in the text. A full bibliography is available as electronic supplementary material via http://dx.doi.org/10.1098/rsbm.2017.0009 or via https://doi.org/10.6084/m9.figshare.c.3784685.

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