

SIR HOWARD DALTON

8 February 1944 — 12 January 2008

INTERMEDIATE PROOF



Howard Dalton



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Elected FRS 1993

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Howard Dalton was an outstanding microbiologist who, after his remarkably productive DPhil work in the Nitrogen Fixation Laboratory at the University of Sussex, and a short period in the USA, spent his research career at the University of Warwick. He devoted himself to the elucidation of the process of methane oxidation by bacteria that use this relatively inert gas as their sole source of carbon and energy. He discovered two completely novel multicomponent monooxygenase enzymes responsible for the initial oxidation of methane to methanol. He then continued to elucidate their functions, mechanisms, regulation and structures. Their wide substrate specificity led to his interest in using these and related enzymes for biocatalysis, biological transformations and bioremediation. While remaining at Warwick University he also acted as a highly appreciated Chief Scientific Advisor to the UK Government at the Department for the Environment and Rural Affairs (Defra). Howard was a highly effective scientist, a down-to-earth, self-effacing man, outgoing and witty, an inspirational colleague who above all else made science fun.

EARLY LIFE

Howard Dalton was born in New Malden, Surrey, the son of Leslie Alfred Dalton, a lorry driver, and Florence Gertrude Dalton (*née* Evans). He was highly intelligent, with an enquiring mind, and his early interest in science was evident from his many exploits with cocktails of chemicals, which often had explosive consequences. In his late teens, a laboratory experiment

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Figure 1. Howard the teenager.

culminated in a blast that singed his hair and eyebrows, as shown for the next decade in the passport photograph taken shortly afterwards. Dalton also showed early entrepreneurial flair, buying an old-fashioned printing press at the age of 14 years and developing a lucrative sideline, producing circulars and wedding and party invitations, which were particularly popular as he slightly undercut established printing firms in the area (figure 1). His ambitious mother was the guiding influence of his childhood and she was enormously proud when he passed the 11-plus examination to gain a place at Raynes Park Grammar School. Despite his father's attempts to make him leave school at 14 years of age to take up a trade like his brother (David), who became a skilled carpenter, Howard was eager to continue his academic studies. Thanks to his mother's support, he became the first member of his family to go to university when he won a place at Queen Elizabeth College at London University. He graduated in 1965 with a BSc in Microbiology.

NITROGEN FIXATION

Howard's research career started when he undertook a DPhil with Professor John Postgate (FRS 1977) at the world-renowned ARC Unit of Nitrogen Fixation, Sussex University, where he worked on nitrogen fixation in the aerobic soil bacterium *Azotobacter*; this work led to the award of DPhil in 1968. During bacterial nitrogen fixation, atmospheric nitrogen gas is reduced to ammonia in a reaction catalysed by the nitrogenase complex, which consists of two proteins containing the metals iron and molybdenum. This enzyme is famously extremely sensitive to oxygen, raising the question that formed the basis of Howard's DPhil work: How does the oxygen-sensitive nitrogenase function in bacteria in a highly aerobic environment? His approach provides an excellent example of the use of continuous culture to sort out a puzzling problem of bacterial physiology. His extensive, imaginative study showed convincingly that this problem is solved by two mechanisms: first, respiratory protection in which respiration is



Figure 2. Howard embracing American culture. (Online version in colour.)

used to scavenge oxygen down to safe levels, and second, conformational protection in which changes in the conformation of the enzyme protect the oxygen-sensitive sites (1, 2)*.

Appreciating that a better understanding of nitrogenase would be based on a physico-chemical approach, Howard moved in 1968 to the USA to work for two years as a postdoctoral fellow with Professor Len Mortensen at Purdue University, Indiana, on the biochemistry of nitrogenase in the anaerobic bacterium *Clostridium*. These studies extended his expertise in protein purification, spectrophotometric analysis and electron paramagnetic resonance (EPR) spectroscopy of metal enzymes in complex multiprotein systems, all of which supported his subsequent work on methane oxidation.

A lively, outgoing man, he embraced American culture with gusto, frequently hosting convivial gatherings such as Superbowl parties for his colleagues (figure 2). He was also active in the anti-Vietnam War protest movement, and it was through this that he met his future wife, Kira Rostislavavna De Armitt Rozdestvensky, the Russian–American daughter of Rostislav Sergevich Rozdestvensky, a college professor; she was later an employment counsellor and management consultant. She advised him that he risked being drafted into the armed services, and suggested an unusual way to avoid this—by becoming a priest, one of the categories exempt from military service. Howard discovered a little-known religious group called the Universal Life Church of California which for \$25 would ‘ordain’ anyone. He duly sent off a cheque and within days was delighted to learn that he was now a *bona fide* Minister of Religion. It became a running joke, and his friends frequently addressed letters to the Reverend Howard Dalton; as a life-long atheist, he particularly relished the irony of his new title.

Recognizing that EPR spectroscopic techniques were going to be of great importance in the study of metalloproteins, Howard returned to the University of Sussex in 1970 to work with Dr Bob Bray in the Department of Chemistry on two molybdenum-containing enzymes, nitrate reductase from *Aspergillus nidulans* and xanthine dehydrogenase from *Veillonella*

* Numbers in this form refer to the bibliography at the end of the text.

alcalescens. He used EPR to study the chemical environment of their molybdenum cofactors, and their flavin and iron–sulfur centres, providing insights into the enzyme mechanism and the partitioning of electrons between the cofactors in the enzyme.

In October 1971 Howard and Kira were married.

WARWICK AND THE OXIDATION OF METHANE

In the early 1970s Derek Burke had just set up a Department of Biological Sciences at Warwick University and had appointed Roger Whittenbury to a chair to initiate microbiology there in 1972. Roger recalls that Warwick in those days was hardly a magnet for microbiologists, offering only an abandoned chemistry laboratory containing just two pieces of equipment, a broken piano and a dartboard! A year later, after a brief chat about his background and a promise that he would work on Roger’s beloved methane-oxidizing bacteria, Howard was appointed to a lectureship in the department to strengthen its microbial biochemistry and physiology in 1973, and he and Kira settled in the village of Radford Semele near Leamington Spa. This led to a long and highly successful tenure at the University of Warwick, during which his research brought him a much-deserved international reputation, yielded many seminal publications in a career generating more than 200 scientific papers and opened up whole new research fields in the microbiology of one-carbon (C₁) compounds. Howard was awarded a personal chair at Warwick in 1983.

The oxidation of methane

Methylootrophs are microbes able to grow on reduced carbon compounds containing one or more carbon atoms but containing no carbon–carbon bonds; examples are methane, methanol, methylamine and trimethylamine (Anthony 1982; Trotsenko & Murrell 2008). The end product of all anaerobic microbial degradation of organic material is methane; some of this reaches the atmosphere, where it is a powerful greenhouse gas. The methanotrophs are a major group of methylootrophs, able to use methane and so are clearly important in the carbon cycle, diminishing the amount of methane liberated into the atmosphere. They have become of considerable importance because they can be exploited in biotransformation and bioremediation processes. The methanotrophs are divided into Type I and Type II methanotrophs (Whittenbury *et al.* 1970); this was initially based on their internal membrane systems but the types also differ in their carbon assimilation pathways, genetic systems, phylogeny and so on.

Howard built up a large and vibrant research group at Warwick and pioneered work on the extremely complex process by which methane is oxidized to methanol. This is the essential first step for subsequent energy production and for the assimilation of carbon into new cells. All of the energy used for growth of methanotrophs is obtained by oxidation of methane to carbon dioxide:



In 1973 the first step in this process was very poorly understood, and Dalton set out to solve it using the expertise in multicomponent metal-containing enzyme systems that he had acquired during his work on nitrogenase and related enzymes. This was achieved together with his research students and postdoctoral researchers, most importantly John Colby and David Stirling. Work from many laboratories using a variety of methanotrophs had led to the

Methane oxidation

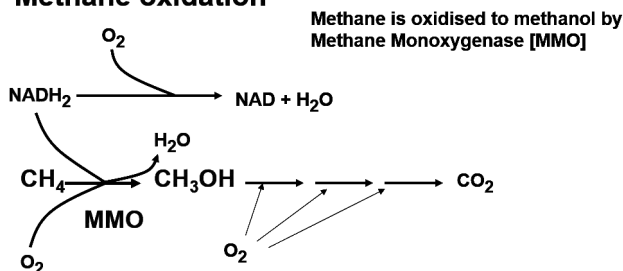
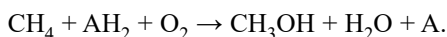


Figure 3. Methane oxidation by methane monooxygenase in methanotrophs. Assay of MMOs is made difficult by alternative routes for oxidation of NADH, consumption of oxygen, and metabolism of the product, methanol. (Figure taken from Anthony (2008).)

general conclusion that the first step in methane oxidation is catalysed by a mixed-function monooxygenase system. This is now called methane monooxygenase (MMO); it hydroxylates methane to methanol by using molecular oxygen and a reductant (AH_2):



The reductant was assumed to be the usual metabolic reductant, NADH or NADPH, but there was considerable confusion and disagreement about results in the earlier studies that was often due to the use of different bacteria, different membrane preparations, different enzyme assays and so on. The obvious assay systems would involve spectrophotometric measurement of NADH disappearance, or the methane-dependent and NADH-dependent consumption of oxygen. However, most cell-free preparations used membrane fractions containing NADH oxidase, which also consumes NADH and oxygen, and the product methanol may also be further metabolized (figure 3).

An essential first step in Dalton's solution of the problem was the development of reliable, unambiguous assay systems; these systems are still in use today. They did not use the obvious substrate, methane, but were based on the use of alternative alkanes whose oxidation by MMO depended on its exceptionally wide substrate specificity (3). These methods included the oxidation of bromomethane, whose disappearance was measured by gas-liquid chromatography (GLC), and the oxidation of ethylene or propylene, the epoxy products also being measured by GLC.

Discovery of the methane monooxygenases

Application of these methods led to a definitive description of MMO, using the enzyme purified from soluble extracts of the Type I methanotroph *Methylococcus capsulatus* strain Bath, originally isolated by Roger Whittenbury from the hot springs at the Roman Baths in Bath. This soluble MMO (sMMO) was subsequently shown to be present in several, but not all, methanotrophs. It catalyses the hydroxylation of methane to methanol, with NAD(P)H as the reductant. It is made up of three components and, as with nitrogenase, sMMO contains metal ions. Resolution of this enzyme into its component proteins was a considerable achievement because only one of the components could be assayed independently of the other two. This was component C, now known as the reductase, a flavoprotein containing FAD and an iron sulfide centre as found in spinach ferredoxin and putidaredoxin. Component A is the hydroxylase and contains non-haem iron. Component B, a coupling protein, is a small colourless protein.

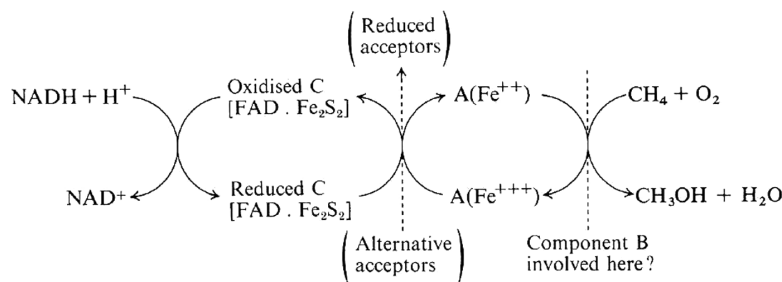


Figure 4. The pathway of electron transfer between the components of soluble MMO during the oxidation of methane to methanol by oxygen with NADH as reductant. This requires the participation of three proteins, A, B and C. (Figure taken, with permission, from the published proceedings of the 3rd International Symposium on Microbial Growth on C₁ Compounds (5).)

Component C transfers electrons from the donor NADH to the hydroxylase, which catalyses the methane substrate with the use of molecular oxygen (figure 4).

At about this time a three-component MMO was partly purified by John Higgins and colleagues (Tonge *et al.* 1977) from the membranes of a Type II methanotroph, *Methylosinus trichosporium*; the electron donor was NADH in crude extracts but it was necessary to use ascorbate or cytochrome *c* in purified preparations. The enzyme was relatively unstable and some results were not always easy to reproduce. It therefore seemed that there might be two different kinds of MMO or that there might be a single membrane-bound MMO in both types of methanotroph but that it might be more readily released from its normal association with membranes to produce the sMMO.

This confusion was eventually resolved by Dalton's group in an elegant study using continuous culture, reminiscent of his work on respiratory protection of nitrogenase. It was shown that there are two completely different enzymes in *Methylococcus capsulatus*, the sMMO and also a membrane (or particulate) MMO (pMMO). Which enzyme is produced depends on the availability of copper: pMMO is produced when the copper:biomass ratio is high, whereas sMMO is produced when the copper:biomass ratio is low (6). In batch culture both MMOs may be produced, because the copper:biomass ratio cannot be as well controlled or defined (for a recent review of the role of copper in methanotrophs see Semrau *et al.* (2010)). Dalton's group subsequently developed reproducible solubilization and purification methods and showed that the membrane-bound enzyme, pMMO, also has three components and that the two types of MMO are present in other methanotrophs, regardless of the membrane type. Some methanotrophs synthesize only a single type of MMO and in that case it is most often the membrane enzyme that is produced. Remarkably, the two families of MMO share no detectable similarity in amino acid sequence or three-dimensional structure.

The substrate specificity of methane monooxygenases

A remarkable feature of the MMOs, possibly related to their normal small, unfunctionalized methane substrate, is their extraordinarily wide substrate specificity, sMMO having a wider range of substrates than pMMO. Substrates for sMMO include n-alkanes, n-alkenes, chloromethane, bromomethane, trichloromethane, nitromethane, methanol, carbon monoxide, dimethyl ether, benzene, styrene and pyridine (3). Remarkably, this enzyme is also able to oxidize ammonia,

whose structure is clearly analogous to that of methane. When whole cells are used, a source of reducing equivalents must also be provided (such as methanol or formate) in addition to the potential substrate. When this is required, the oxidation of the potential substrate is referred to as co-oxidation. Dalton showed that because methanotrophs can co-oxidize a range of hydrocarbons and chlorinated pollutants they have a biotechnological interest that extends far beyond their ability to oxidize methane to methanol (7). Important examples include the industrial production of methanol from methane, the co-oxidation of propene to epoxypropane, the bioremediation of chlorinated hydrocarbons and the production of valuable recombinant proteins with the use of methane as the starting material. This interest in biotransformations stimulated his later interest in biofuels. He was a consultant for the New Jersey company Celanese and then joined the Scientific Advisory Board for the spin-out biotechnology company Celgene, which gave him considerable insight into chemical and industrial aspects of microbiology that he used to good effect in his biotransformation research.

Exploration of oxidizing enzymes for use in biotransformations

The wide substrate specificity of the methane monooxygenases made them obvious candidates as tools for the catalysis of difficult chemical reactions that might lead to useful materials.

Although Howard Dalton's earlier work at Warwick was largely based on methane monooxygenases, after 1986 his research interests increasingly involved other types of oxidoreductases. In this he was encouraged by Derek Boyd at Queen's University Belfast. They established a highly productive microbiology–chemistry collaboration that lasted about 20 years. The Warwick–Belfast link resulted in joint awards from UK Research Councils, European Union programmes and industry that funded projects on enzyme-catalysed chemistry in Warwick and Belfast resulting in 42 joint publications and 3 patents (7). At the outset of the collaboration (1986) they decided that, because demand was increasing for chiral synthons in both academic and industrial contexts, important objectives of the programme should include (i) the development of reliable methods for the assignment of structure and stereochemistry of metabolites, (ii) the discovery of new types of *cis* and *trans* dihydrodiol metabolites, (iii) the investigation of potentially competing toluene dioxygenase-catalysed reactions, and (iv) the evaluation of new applications of chiral metabolites in chemical synthesis including chiral ligands. Most of the biotransformations were conducted and analysed in Warwick before being transported to Belfast for chemical analysis on an almost weekly basis.

Derek Boyd recalls that Howard was a fearless individual who was willing to travel regularly to Belfast at times when many other academics were very reluctant to visit. Although 'the troubles in Northern Ireland' were no longer at their worst, over the years 1986–98 until the Belfast Agreement was signed, there was still an average of almost 100 terrorist-related killings annually. He recalls Howard's first lecture in Belfast 'when he tried to emphasise the wide range of substrates and reactions catalysed by a dioxygenase by stating "I would regard these dioxygenase enzymes as being really catholic in their taste"—that certainly took courage in front of a "mixed" audience!'

As a result of the Warwick–Belfast link, and of Howard's being able to demonstrate by example that it was now relatively safe to cross the Irish Sea again, several people transferred their expertise from Howard's laboratory at the University of Warwick to Queen's University Belfast; Howard's legacy, initiated in 1986 by the dioxygenase-catalysed chemistry link between Warwick and Belfast, is still continuing at the time of writing (2016).

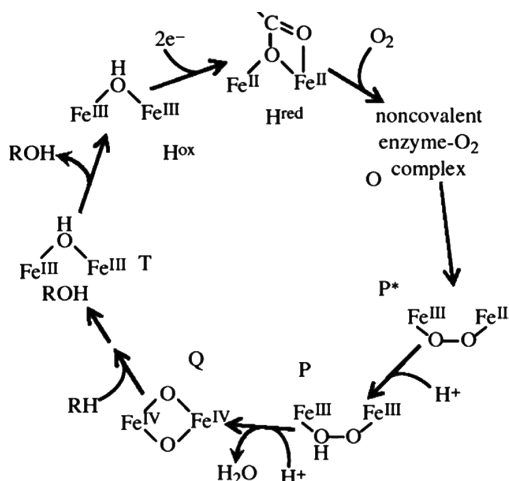


Figure 5. Principal intermediates during the sMMO catalytic cycle. This figure is based mainly on the work of the groups of Dalton, Lippard and Lipscomb; it is taken from Dalton's Leeuwenhoek Lecture 2000 (7), in which the significance of the intermediates is fully discussed.

The structure and function of methane monooxygenases

Further development of Howard's research on the methane monooxygenases was necessarily done in collaboration or was handed over to others in his group. After the purification and characterization of the two main types of methane monooxygenase, a major challenge was the molecular biology of their synthesis and regulation; this was taken up and developed in Howard's department by Colin Murrell (reviewed in Murrell *et al.* 2000).

The other major challenge was to elucidate their mechanisms and three-dimensional structures. Figure 5 shows the catalytic cycle of the soluble methane monooxygenase as determined mainly by the groups of Dalton, Lippard and Lipscomb and as described in Dalton's Leeuwenhoek Lecture in 2000 (7). The structure of the soluble enzyme was mainly determined by Lippard's group (see, for example, Rosenzweig *et al.* 1993). Howard's contribution to our understanding of the structure of the membrane enzymes was achieved by a fruitful collaboration with colleagues in Manchester and competition in the USA. Figure 6 shows the beautiful structure of one of these enzymes.

CONTRIBUTIONS TO LIFE IN AND AROUND THE UNIVERSITY OF WARWICK

Howard held many positions in the university, dealing with academic matters and other areas of university life. He was extremely generous of his time, with well over 100 PhD students and postdoctoral researchers; he was a great mentor and subsequently loyal colleague for many of his researchers who remained in the field of C_1 metabolism. He led a large and vibrant research laboratory in which training in microbial physiology and biochemistry was outstanding. While working with Howard, science was fun and there were many social gatherings at which successes such as the award of a PhD were celebrated. His 'Thanksgiving parties' at his house were also highly appreciated by all who attended, especially for some

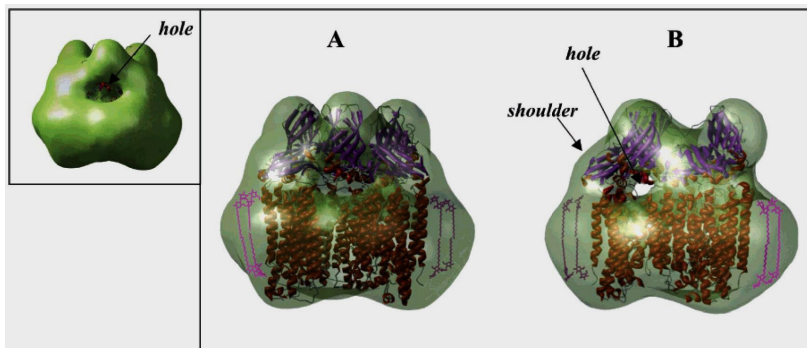


Figure 6. The structure of a membrane methane monooxygenase. Top left, the structure determined by electron microscopy and single-particle analysis at 23 Å resolution from one of Howard's last publications (8). In A and B it is shown superimposed on the crystal structure determined by Lieberman & Rosenzweig (2005). For a recent review of the structure and function of these enzymes see Sirajuddin & Rosenzweig (2015). (Taken with permission from A. Kitmitto *et al.*, *Biochemistry* **44**, 10954–10965 (2005). Copyright © 2005 American Chemical Society.) (Online version in colour.)

PhD students who were in need of a square meal. Howard was a very popular teacher at the undergraduate level, and his witty and relaxed style inspired many undergraduates to study microbiology and to pursue microbiology-related careers after graduating. In 1983 the School of Biological Sciences launched a Microbiology and Microbial Technology degree and Howard, together with his former PhD student Colin Murrell, who rejoined the department that year as a lecturer, were instrumental in developing this innovative course, one of the first of its kind in the UK. Its popularity increased over the next 10 years or so, ensuring a new generation of microbiologists who were very familiar with the use of microbes (especially methanotrophs!) in biotechnology. Throughout the 1980s and 1990s Howard led and gradually built up the Microbiology Research Group in Biological Sciences at Warwick until it was one of the biggest of its type in the UK, embracing multidisciplinary research in microbiology, often with an applied flavour. On Roger Whittenbury's retirement, Howard became Chair of the Department of Biological Sciences in 1999 and was an effective and popular leader there until he was seconded to Defra in 2002.

In 1973 a series of hugely influential International Symposia on Microbial Growth on C_1 compounds was initiated by Roger Whittenbury and Rod Quayle (FRS 1978), and these have been held every two or three years up to the present time. In 1980 the Symposium was hosted by Rod Quayle and colleagues in Sheffield, the book of proceedings being edited by Howard (4), who 12 years later was responsible, with his excellent departmental colleagues, for the 7th Symposium held in the University of Warwick (Murrell & Kelly 1993). Howard had a great influence at these symposia by his direct scientific contributions and even more perhaps by his personality. He was excellent at chairing scientific sessions in a relaxed way that encouraged participation by students and the less experienced researchers. He energetically browsed his way through most of the posters, providing entertainment and encouragement (figure 7).

Howard was a down-to-earth, self-effacing man, outgoing and witty and in the 1980s was a 'leading light' at gatherings of the staff of Biological Sciences at Warwick in weekly socials at local pubs (code-named 'Choir-Practice'!). He also enjoyed the occasional 'poker night'



Figure 7. Howard in typical happy enthusiastic conference mode. (a) With the authors (Chris Anthony and Colin Murrell) at the 8th International Symposium on Microbial Growth on C_1 Compounds in San Diego in 1995. (b) Howard at a Gordon Conference on the Molecular Basis of Microbial One-Carbon Metabolism in Oxford in 2006, chatting with his colleagues Colin Murrell (left) and Tom Smith. (Online versions in colour.)

with selected colleagues who invariably relieved him of his hard-earned cash. Howard's enthusiasm for, and extensive knowledge of, Japanese gardens was also brought into play on campus, resulting in the creation of two fine gardens at Warwick.

He was a fanatical supporter of Tottenham Hotspur Football Club (Spurs) and a highly competitive member of the Biological Sciences football team, aptly named 'Biohazard'. In the 1970s Howard performed with distinction in the 'Biohazard' team that played a friendly match with the Saudi Arabia national team, thereby adding to his illustrious international career. He also loved village cricket, turning out for a variety of local sides as a wayward but explosive fast bowler. Once, representing the nearby village of Rowington against admittedly inferior opposition, he took eight wickets for a miserly 15 runs, the highlight of his cricket career.

A great passion was real tennis and he was a member of Leamington Real Tennis Club, where his competitive spirit, guile and ability won him many tournaments. It was here, while playing in a friendly doubles tournament, that he tragically collapsed and died on 12 January 2008.

CHIEF SCIENTIFIC ADVISER TO THE DEPARTMENT FOR ENVIRONMENT, FOOD AND RURAL AFFAIRS

Howard served as the Chief Scientific Adviser at Defra from March 2002 to September 2007. He was the first departmental Chief Scientific Adviser to be appointed by Sir David King FRS, who was then Chief Scientific Adviser to the Prime Minister. The newly created Defra had risen from the ashes of the beleaguered Ministry of Agriculture, Fisheries and Food, which was widely criticized for its handling of the bovine spongiform encephalopathy crisis and the 2001 outbreak of foot-and-mouth disease. Howard did not enter an easy atmosphere. 'It was a very inward-looking department that didn't make use of scientific resources outside', Sir David recalled. Over the next five years, Howard transformed Defra's use of science, seeking to instil scientific rigour into policy-making decisions based on sound scientific evidence. Howard led the scientific advisory team generating the UK's contingency plan for dealing

with avian influenza virus and was instrumental in raising the profile of climate change as a significant threat, delivering lectures on this and other topics such as biofuels and genetically modified crops at many national and international meetings.

The following section has been kindly provided by Dame Helen Frances Ghosh, DCB, former Permanent Secretary, Defra.

SCIENCE AT THE HEART OF GOVERNMENT

By Dame Helen Ghosh DCB, former Permanent Secretary, Defra. A contribution to the Tribute to Celebrate the life of Professor Sir Howard Dalton FRS held at the University of Warwick in May 2008

As Permanent Secretary at Defra between 2005 and 2010, I had the privilege of working with Howard for almost two years. Defra is a department whose work is grounded profoundly in science, in its broadest sense: global climate to local conservation, farming and food, waste and pollution and, probably most famously, natural and sometimes man-made disasters such as flooding and animal diseases. All of these involve the most fascinating range of science, and though politicians might sometimes have found it challenging, science had to underpin all the policy that we made. Howard's work with us gave us a sure and secure—and in many areas world renowned—basis for those decisions.

No sooner had I arrived than Howard disappeared—to Antarctica. So the first image of Howard that is imprinted on my mind is a photograph of him at the bottom of a crevasse in Antarctica, reporting back to us and the public via his wonderful blog. Howard was an engaging and energizing communicator within Defra and outside, of the excitement of science and what it could do for us.

Howard was the first of Sir David King's new wave of Departmental Chief Scientific Advisors, whom he hired to be independent, authoritative and, as their title suggests, challenging.

These pioneers were asked to focus their attention on evidence-based policy making, and on ensuring that evidence was comprehensive and rigorous but above all used. Dave King also gave them the commission—when not fire-fighting on the day to day—to make space for horizon scanning.

The programme that Howard set up on his arrival focused on all these things—making sure we were doing the right science through horizon scanning, developing a science strategy, making sure we were commissioning sound and relevant evidence, and then making sure we were using it. Howard's decision to set up a Science Advisory Council to support us on all this was inspired. Initially its membership was predominantly focused on animal disease issues, which had provided the impetus for his role—and indeed the creation of Defra—in the first place. But over time its focus has expanded to the whole range of Defra science—including social science. And it has played a vital role in quality ensuring our science as a whole and also giving us immediate access—particularly in an emergency—to a range of the most distinguished scientists in their field. It was the envy of other government departments, and several followed our example.

From this concept of what his job was about, Howard pulled together a first systematic account of the science that Defra should do—the Science and Innovation Strategy—which we called 'Delivering the Evidence'. Miles Parker, our Director of Science, has reported

to me that at the end of the long day of the launch of this strategy, Howard referred to it serendipitously as ‘delivering the elephants’. Defra of course does have to deliver elephants, but not quite as Howard meant. That first strategy was followed a few years later by a second, ground-breaking, Evidence and Innovation Strategy.

By then it was clear that public spending constraints meant that there was no question of just carrying on with established patterns of science spend in the Defra budget, however beloved those might be with particular lobby groups, customers or—dare I say it—elements of the scientific establishment. Howard bravely argued that our spend needed to be refocused towards the issues of the day: to climate change and protecting the natural environment against the worst that humans could throw at it. That legacy lives on.

So far, so dignified and strategic, but of course what Defra gets most coverage for—however distinguished our achievements across the range of our responsibilities—is dealing with emergencies. And Howard was always there when we needed him. Howard provided a major support to the Chief Veterinary Officer (CVO) on a range of animal disease issues where his virology background and networks were used to great effect. He and CVO Debby Reynolds—particularly during the first few outbreaks of avian influenza in this country—would spend long hours closeted with Dave King and sometimes in Number 10 Downing Street, discussing the detailed science of the viruses with which we were dealing. Bovine tuberculosis was another subject for these scientific conclaves.

But Howard also had to turn his hand to the other kind of emergencies with which Defra—which we sometimes felt should be called the Department for Plague and Pestilence—had to deal. So plant disease, radioactive waste, the Buncefield fire, oil pollution and shellfish poisoning all got his attention and the benefit of his scientific experience and habits of mind. If he did not know the answer himself he generally knew a woman or man who did. When these emergencies break out, the support of the whole departmental team is vital. If my first memory of Howard will be the picture of him in Antarctica, probably my last mental image of him will be as he stood next to me at one of our early morning ‘bird tables’ in our National Disease Control centre in Page Street, in the early days of the outbreak of foot-and-mouth disease in 2007.

He and his wife had been in Africa when it broke out, but without a moment’s apparent hesitation he came back, because of luggage delays more or less only in the clothes he stood up in. He rapidly became an expert in the Civil Service’s complex rules for financing the purchase of new clothes in these circumstances, so that he could have another shirt to wear while he got his own washed! But he was still his normal optimistic, enquiring and energizing self, and made a real contribution to the emotional resilience of a team under a great deal of pressure.

Miles Parker, who probably knew him better than any of us, has commented to me, perhaps euphemistically, that ‘Howard was not the most enthusiastic bureaucrat.’ Despite more than 25 years as a civil servant, I think that is a real accolade.

What Howard brought was not just a new confidence and seriousness to Defra science, but also an infectious and vivid way of communicating his passions. The Antarctica blog was, I think, a first for any Whitehall scientist, and really caught the public imagination.

When Howard decided to retire from his Defra role in 2007 and return to his work at Warwick on a more full-time basis, it was a challenge for all of us. But by then and thanks to Howard, we knew what good looked like, and we were lucky—no, not just lucky, because I benefited from Howard’s wise advice in the process—to be able to attract a worthy successor

in Professor Bob [now Sir Robert] Watson [FRS 2011]. Howard left Bob a great legacy, which was epitomized in the excellent review of Defra science carried out by Dave King and the Office of Science and Technology shortly before the end of Howard's term with us.

Before I left Defra, I established a new award at our sports day, in the memorializing tradition of my (all-male) predecessors. Rather than call it the Helen Ghosh Cup, I decided that it should be the Howard Dalton Trophy, for the person who was the best overall performer on the day.

Howard will have lots of memorials—here in the UK and in The Gambia—but I thought that this would be one that would entertain and please him. I can just imagine him smiling—perhaps slightly embarrassed—at the idea.

In 2010 the inaugural event for the annual Howard Dalton Lecture was launched by Defra. This not only commemorates Defra's late Chief Scientific Adviser, Professor Sir Howard Dalton FRS, but also serves to acknowledge and celebrate excellence in science and policy.

But the greatest memorial to Howard's work in government is the legacy he gave us of sound science, and science at the heart of policy making. The best tribute we can pay him is to defend and protect that legacy and continue to work within the principles to which he was committed. We are very grateful to Howard for all he did for us in Defra and in government, and to the University of Warwick and to his family for lending him to us.

HOWARD'S SUPPORT FOR THE WORK OF LADY KIRA DALTON IN THE GAMBIA

Kira says that when she decided in 2000 to give up her work as a self-employed management consultant she went to The Gambia 'looking for a project'. After meeting the headmistress of a village school at Niumi Lamin on the north bank of the Gambia river she set out to raise money in the UK for various school renovations, including fencing, toilets, roofing and furniture. During the next few years she visited for two to four weeks a year, while raising money in the UK. Howard became very interested after he visited for the first time in about 2004 and subsequently they bought a small bungalow where he set up an observatory and viewing positions for his latest hobbies, astronomy and bird-watching. At about this time James Holden had become interested in starting some charitable work in Africa and realized that he needed someone on the ground who could be trusted to deliver on whatever he decided to do. As he says, 'the very person was to cross my path in the most unlikely of places—the Leamington Tennis Court Club'. Although the club was limited to male players, Howard had persuaded them to permit Kira to put on a series of talks at the club on Leamington's history, with all proceeds going towards her school in The Gambia. This led to an invitation to James to visit, which he did in November 2004, escorted by Kira and Howard to Niumi Lamin, bringing much-needed cash that he had raised in his church in Claverdon, near Leamington, together with a large quantity of medicines. When he returned to Warwickshire he decided to start a formal charity to support the work in The Gambia. Kira had appreciated by this time that it would be sensible to start a registered charity for the sake of Gift Aid and better credibility. Thus was born the charity the African Oyster Trust (<http://www.africanoystertrust.co.uk>). Kira says that because the administration involved did not really appeal, it was very fortunate that James Holden had the resources and the patience to do the painstaking procedures involved in all that side of it while her interest was always with the hands-on interaction in The Gambia—especially with the young children.



Figure 8. Lady Kira Dalton at the Howard Dalton Clinic established by Kira and Howard in Jappineh, The Gambia.
(Online version in colour.)

Although Howard was very busy with Defra he loved coming out to The Gambia for a rest, staying at their bungalow. During this time he sponsored his own football team of village youngsters, whose side rejoiced in the title Brufut Hotspur, in tribute to his north London heroes Spurs. In 2007 Howard was asked to provide advice regarding Gambian water policy through a contact at Defra, Pa Ousman Jarjue, who is now Secretary of State for the Environment in The Gambia. Howard was still in the process of doing this when he died.

The other project that caught Howard's interest was the creation of a health centre up-country in Jappineh, where a nursery school had already been established. A Dutch charity had begun some building work before running out of funds. They had not got around to finishing or furnishing the place with equipment, medicines or staff. Through speaking to various contacts in the UK and America Howard was able to obtain large donations to complete that project; it is now fully established as the Howard Dalton Clinic (figure 8), supported by generous donations made in his memory after his untimely death.

FAMILY MATTERS

Howard was always supported by his happy family: Kira and their children, Amber and Jed. Kira continues to live in Warwickshire in the summer while spending much of her time working with the African Oyster Trust in The Gambia. Amber lives in Peckham with her husband and two children, Huxley Howard and Inez; she is a magazine editor and restaurant critic as well as organizing food and wine-tasting events. Jed lives in Esher with his wife and



Figure 9. Howard with his family after receiving his knighthood. (Online version in colour.)

their children, Rosie, Henry and Aja; he runs a company that provides software consultancy to energy companies. He also enjoys playing real tennis at Hampton Court in his spare time.

THE SOCIETY FOR GENERAL MICROBIOLOGY

Howard was an enthusiastic supporter of the Society for General Microbiology (SGM) (now the Microbiological Society) in the UK; he served on the Council of the Society from 1985 to 1989 and became its President, serving from 1997 to 2000. The Council of the Society decided that it would use a bequest from Howard to support attendance at an SGM meeting by a microbiology student from The Gambia, where Sir Howard and Lady Kira were involved in educational activities. Council also decided to rename the Young Microbiologist of the Year Competition, which fosters science communication in early career microbiologists, in honour of Sir Howard, the prize now being the Sir Howard Dalton Prize and Fellowship.

HONOURS

In 1993 Howard was elected a Fellow of the Royal Society and, in 2000, was awarded the Society's Leeuwenhoek Medal and Lecture, which was established to award excellence in microbiology; his lecture was entitled 'The natural and unnatural history of methane-oxidising bacteria' (7). He served as President of the Marine Biological Association from 2007 to 2008 and as President of the Society for General Microbiology from 1997 to 2000. He was named a Knight Bachelor in the 2007 New Year's Honours list for his services to science (figure 9).

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We should like to thank Derek Boyd, Howard's collaborator in Belfast, for his help, Dame Helen Ghosh for her contribution about Howard's time at Defra, and Lady Kira Dalton, Amber and Jed for their enthusiastic encouragement in the production of this memoir.

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AUTHOR PROFILES

Professor Christopher Anthony



Christopher Anthony worked for his PhD in the Microbiology Department of the University of Reading, UK, then spent most of his professional life at the University of Southampton, UK, where he is now Emeritus Professor of Biochemistry. While there he was personal tutor to the co-author of this memoir, Colin Murrell, with whom he also played string quartets. His main interests are the biochemistry of methylotrophs during growth on C_1 and C_2 compounds. He is the author of the main textbook on these bacteria, *The biochemistry of methylotrophs*. He first discovered their unusual enzyme for oxidation of methanol (methanol dehydrogenase) and its novel prosthetic group (PQQ). He subsequently concentrated on this quinoprotein, and related quinoproteins with their associated electron transport chains, using the techniques of continuous culture, spectrophotometry, X-ray crystallography and molecular genetics.

Professor Colin Murrell



Colin Murrell studied physiology and biochemistry at the University of Southampton, where his Personal Tutor, Chris Anthony, suggested he study for a PhD with Howard Dalton. After obtaining his PhD on nitrogen metabolism in methane-oxidizing bacteria at the University of Warwick under the guidance of Howard Dalton, he spent two years as a postdoctoral researcher in Mary Lidstrom's laboratory at the University of Washington. Murrell then returned to Warwick, spending 28 years as a lecturer, senior lecturer and professor and working alongside Howard Dalton until he was seconded to Defra. In 2012 Murrell moved from Warwick to the University of East Anglia to take up the position of Director of the Earth and Life Systems Alliance. Murrell and Dalton enjoyed several fruitful collaborations and co-authored 15 papers on the biochemistry and molecular biology of methane oxidation and biotransformations using microbial enzymes. Jointly they edited a book entitled *The methane and methanol utilizers* and co-organized the Seventh International Symposium on Microbial Growth on C_1 Compounds at Warwick in 1992.

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