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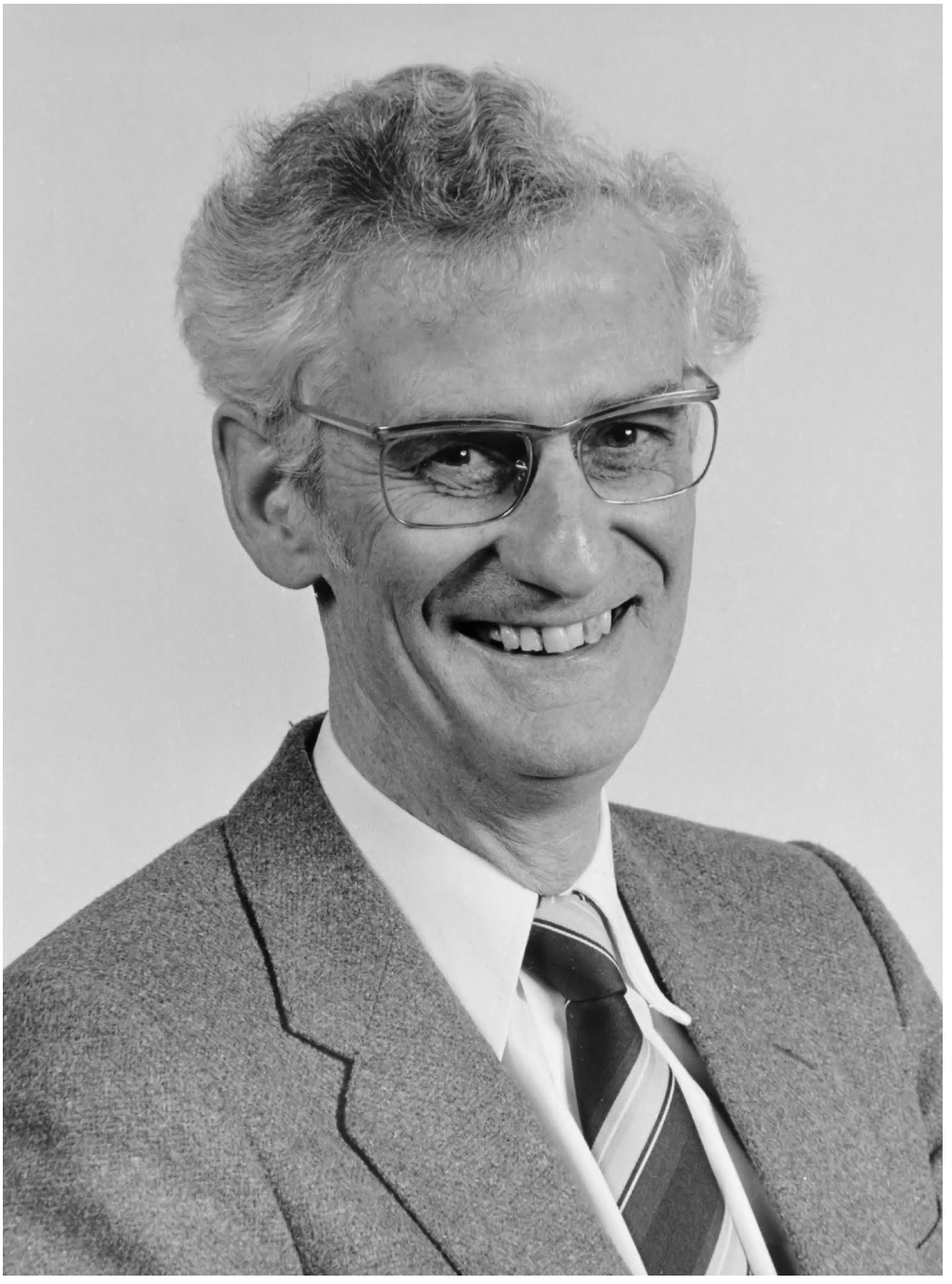

J. R. Angle

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Elected FRS 1978

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J. Rodney Quayle was an outstanding microbial biochemist whose early training in pure chemistry was coupled with rigorous enzymology and experience in the relatively new techniques of using radioactive ^{14}C compounds in the study of metabolic pathways. These he used to investigate and elucidate the pathways of carbon assimilation during microbial growth on compounds with a single carbon atom such as methane and methanol. When he started, little was known about these organisms (methylotrophs), which, largely as a result of his own work and the work inspired by him, have formed the subject of regular international symposia over a period of more than 40 years. After a short time working in Melvin Calvin's laboratory in California and a very fruitful period in Hans Krebs's Unit for Research in Cell Metabolism in the University of Oxford he moved for the next 20 years to the University of Sheffield, after which he became a highly successful and popular Vice-Chancellor at the University of Bath. His rigorous approach to his subject, his generosity and inspiration made him a much revered and much loved father figure to generations of microbial biochemists.

Early life

John Rodney Quayle (always known as 'Rod') was born on 18 November 1926, in Hoylake, a seaside town located at the northwestern corner of the Wirral Peninsula on Merseyside, England. He and his brother, Brian, lived with the family over his father's pharmacist shop. Brian was only 14 months older than Rod and they were very close. Brian also had a successful career, becoming an executive for IPC Magazines in London.

Rod's maternal grandfather was also a pharmacist with his own shop nearby in Hoylake. Rod has said that maybe his early exposure to a world of slender flasks filled with variously coloured liquids, measuring cylinders and chemical balances led to his later interest in chemistry.

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For reasons that Rod never really understood, his parents separated in 1931 and he, Brian and his mother moved in with his recently retired maternal grandparents at their holiday bungalow in Cilcain, a small farming village on the side of the Clwydian range of hills in a very rural setting about four miles from the market town of Mold in Flintshire, North Wales. Rod never did find out the reason why his father had left, or where he had gone. His father did not support the family financially, and his grandfather had to support them all out of the money he had saved for retirement; money was therefore always very short. Rod said that, although their lack of a father led to teasing at school, Cilcain was a wonderful place to live: he could wander about the countryside with none of the constraints that children are placed under today.

They attended the village (Church of England) primary school with about 30 pupils, mostly farmers' children. They were taught by three spinster schoolmistresses; all the infant classes were taken by one teacher in one room, and all of the other children were taught by the other two teachers in another room at the same time. At the age of 10 years Rod sat the entrance examination for the Alun Grammar School in Mold, achieving third place in an intake of about 50 entrants. Many of his schoolfellows were wartime evacuees from Merseyside.

In 1943 he gained a Higher School Certificate of the Central Welsh Board with a distinction in physics, a credit in chemistry and a pass in mathematics, leading to the award of a County Scholarship for university study. That summer he was not yet 17 years of age, and his headmaster and his admired and influential physics master (G. Roblin) advised him to go straight up to university and at least complete the first year before possible military service took over. So in September he entered University College of North Wales at Bangor, a coastal city between the Menai Strait and the mountainous Snowdonia National Park, providing an environment that fostered his love of mountain walking and rock climbing. He also become a member of the Bangor rowing team, an activity he continued when he moved to Cambridge, where he took it very seriously, in the 'Gentlemen's Rowing Team'.

After graduating with a BSc (honours) in chemistry in 1946, Rod stayed on at Bangor to take a PhD in physical organic chemistry. During this time he was awarded a University of Wales Post-graduate Studentship and was appointed Tutor at the Hall of Residence (Neuadd Reichel). His research was supervised by Professor E. D. Hughes (FRS 1949), a trailblazer in kinetics and mechanisms in organic chemistry; the title of Rod's thesis was 'The reactions of s-triphenylbenzene and derivatives with special reference to steric hindrance'. On the basis of this research he was awarded a University of Wales Fellowship, which persuaded Professor Alexander (later Lord) Todd FRS (PRS 1975–80) to accept him into his laboratory at the University of Cambridge to work on the structure and chemical synthesis of the blood pigments of aphids (Aphididae), which led to 10 publications, mainly in *Journal of the Chemical Society*. While there he entered St John's College as a research student, leading to the award of a second PhD degree (in 1952) with a thesis entitled 'Colouring matters of the Aphididae'. In 1951 he was awarded a Senior Research Award from the Department of Scientific and Industrial Research (DSIR) and in the same year he married Yvonne Sanderson, who had been a fellow student at Bangor.

Introduction to methylotrophy

After Cambridge, Rod's research changed direction towards enzymology and microbial biochemistry. This paragraph has therefore been inserted to place his subsequent contributions

into this context. Any account of his contribution to microbiology becomes a broad chronological survey of those bacteria and yeasts that grow at the expense of compounds containing a single carbon atom (C_1 compounds), including methane, methanol and methylamine. When he started this research, very few such microorganisms had been described but it is now known that there exists a huge diversity of these microbes having a correspondingly wide metabolic diversity. All living organisms are either autotrophs or heterotrophs. Autotrophs use carbon dioxide as their sole source of carbon for growth, whereas heterotrophs use organic carbon sources. The name 'methylotrophs' was coined to include the huge group of heterotrophs that are able to grow at the expense of reduced C_1 compounds. The groups of microbiologists with an interest in these previously unknown bacteria have expanded enormously over the years, so at the time of writing there have been 17 international symposia and conferences on this topic. For reviews of Rod's contribution to the study of methylotrophy see his reviews (3, 8, 10, 13)*, and for a more extensive account see Anthony (1982).

An admirable characteristic of Rod's research presentations was his concern to emphasize the importance of the contributions of his students and associates. Much of the work described here is based on these contributions; to achieve a clearer presentation, his colleagues are not always mentioned but can be identified in the complete list of publications (available as electronic supplementary material at http://dx.doi.org/10.1098/rsbm.2015.0008).

California

In 1953 Rod was awarded a Fulbright Travel Grant to work as a Research Fellow with Melvin Calvin (ForMemRS 1959) in the Department of Chemistry of the University of California at Berkeley, concentrating on the first enzyme-catalysed step in the assimilation of carbon dioxide by plants. It was here that he established a friendship with Hans (now Sir Hans) Kornberg (FRS 1965) that was to have important relevance later in his career.

Although he was not to know at the time, Rod's path to methylotrophy can be said to have started in the Calvin laboratory in Berkeley (1953–55). It was here that the Calvin–Benson ('C_3') cycle was established as the photosynthetic pathway for the assimilation of carbon dioxide in plants. Rod became the first author of a publication (1) still regarded as providing conclusive evidence for the existence of this cycle. It had been shown that plants fixed ^{14}C-labelled carbon dioxide initially by the carboxylation of ribulose 1,5-bisphosphate (RuBP) (first synthesized by Rod) to give an intermediary C_6 compound that was cleaved into two C_3 compounds. He showed that cell-free extracts of the green alga *Chlorella*, exposed to labelled CO_2 for only 1 minute, formed labelled phosphoglycerate when RuBP was also added, and that phosphoglycerate was not formed when alternative candidate sugar phosphates were used. The authors of this one-page communication (1) concluded: 'It is clear that the extracts contain an enzyme (or enzymes) capable of catalyzing the carboxylation of ribulose diphosphate, specifically, to form phosphoglyceric acid.' This was the first description of the activity of the enzyme now known as ribulose bisphosphate carboxylase (RuBisCo), the most abundant enzyme on Earth. It was in Berkeley that Rod first met Hans Kornberg, with whom he would later collaborate in Oxford. Rod impressed Calvin not only by his excellent science but, as mentioned in a reference posted to Professor Hans (later Sir Hans) Krebs FRS to support his

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

application to join the MRC Unit in Oxford, 'His stabilizing influence was felt throughout the lab, particularly by the graduate students as well as by his peers.'

Oxford

In 1955 Rod and Yvonne returned to England, where Rod had accepted a post as Senior Scientific Officer in the DSIR's Tropical Products Institute in London, to study the chemistry of the naturally occurring pyrethrin insecticides. He was not enthusiastic about the topic or the rigid constraints of work in a government laboratory, and within a year a chance meeting with Hans Kornberg at a London theatre led him to apply for a position with Hans Krebs in his MRC Unit for Research in Cell Metabolism at the University of Oxford. Here he enjoyed a fruitful collaboration with Kornberg on the newly proposed glyoxylate cycle for the growth of bacteria on C_2 compounds. This led to what became his main research area: the biochemistry and physiology of bacteria growing on the C_1 compounds formate, methane, methanol and methylamine. Although a member of a Research Unit within the precincts of Oxford University he was not part of the university until 1957, when he accepted a lectureship in biochemistry at Oriel College. With it came formal membership of the university, offering an opportunity to demonstrate his exceptional gifts as an inspiring and caring teacher and research supervisor.

Bacterial growth on C_2 compounds

Working in Krebs's MRC Unit, Hans Kornberg had addressed the question of how bacteria are able to grow on the C_2 compound acetate. The tricarboxylic acid (TCA) cycle (also known as the Krebs cycle) functions to *oxidize* acetate to CO_2, but acetate also has to be converted into C_3 and C_4 compounds for *assimilation* into cell material. To achieve this, supplementary enzymes are needed to replenish the cycle when intermediates are removed for biosynthesis. Kornberg & Krebs (1957) had recently proposed the existence of the glyoxylate cycle (or 'bypass'), comprising two key anaplerotic ('filling-up') enzymes—isocitrate lyase and malate synthase, previously described in the literature—and they showed both to be present in cell-free extracts of acetate-grown bacteria. It was still necessary to demonstrate that the cycle operated *in vivo*. Using the chromatographic techniques that had proved so successful in Berkeley for elucidating the Calvin–Benson cycle in photosynthesis, Rod and Hans Kornberg joined forces to isolate and characterize, by chemical degradation, intermediates formed from ^{14}C-labelled acetate and CO_2. The isotope distributions supported the simultaneous operation of the TCA and glyoxylate cycles (2). Such experiments became the key type subsequently used by Rod in his future work on methylotroph pathways.

After their initial collaboration Rod and Hans Kornberg made independent studies on the metabolism of C_2 compounds more highly oxidized than acetate. Rod was joined by an Australian visitor, Bruce Keech, to investigate the routes by which *Pseudomonas oxalaticus* grows on oxalate, the most oxidized C_2 compound. In a series of seven papers they described how oxalate was reduced to glyoxylate and then converted into glycerate (the precursor of other cell constituents) by the glycerate pathway. The glycerate pathway had been discovered by Kornberg and his student Tony Gotto working on the other side of their shared laboratory bench using glycollate-grown *Pseudomonas ovalis*; two of their key papers on bacterial growth on glycollate (Kornberg) and oxalate (Quayle) were published together in the same issue of *Nature* in 1959. Rod's last paper in this series showed that energy for growth comes

from the decarboxylation of oxalyl-coenzyme A to formate and thence to carbon dioxide. A key intermediate in this process is a tiny formyl group bonded to two large coenzymes, coenzyme A and thiamine pyrophosphate. A visitor to his laboratory at that time was met by Rod bubbling with excitement because of this intermediate 'which showed so much care being taken over one little carbon atom'.

Bacterial growth on C_1 compounds

Pseudomonas oxalaticus is also able to grow on formate as its sole source of carbon and energy, raising the question of how this C_1 compound is assimilated into cell material. The obvious route would be by way of the Calvin–Benson (photosynthetic) pathway. Again with Bruce Keech, Rod showed that this was indeed the case. The first intermediate in the assimilation of [^{14}C]formate or [^{14}C]bicarbonate was phosphoglycerate, the formate being oxidized to carbon dioxide before assimilation into cell material. Similar extensive experimentation, as he had performed in Calvin's laboratory using *Chlorella* extracts, confirmed the presence of the key enzyme ribulose bisphosphate carboxylase together with phosphoribulokinase during growth of *P. oxalaticus* on formate but not on oxalate. About 15 years later he showed that some methylotrophs (such as *Paracoccus denitrificans*) also grow on methanol by way of the ribulose bisphosphate pathway (the Calvin–Benson photosynthetic pathway).

Rod has pointed out that his study of methylotrophic microbes might have taken a different route had he started with *Paracoccus* instead of isolating his own organism, *Pseudomonas* AM1 (now *Methylobacterium extorquens* AM1). This organism was originally isolated on a methylamine medium in 1960 by his first research student, David Peel. After 50 years it is still the 'workhorse' of those working on the biochemistry, molecular biology and biotechnology of bacteria growing on methanol. Rod used the same experimental approaches that he had developed to confirm the operation of both the glyoxylate cycle during growth on acetate and the glycerate pathway for the assimilation of oxalate. With his students Peter Large and David Peel, in a series of elegant and rigorous studies (see (4) and (5)), he showed that methanol is assimilated in *Pseudomonas* AM1 (and in *Hyphomicrobium vulgare*) by a novel assimilatory pathway, the serine cycle, in which methanol is fixed at the oxidation level of formaldehyde into serine, and at the level of carbon dioxide into oxaloacetate. This model investigation involved the identification of early intermediates produced by incubating methanol-grown bacteria with either [^{14}C]methanol or [^{14}C]bicarbonate, the position of the isotope in the isolated labelled compounds (serine, glycine, aspartate, etc.) being determined by chemical degradation and analysis (figures 1 and 2). The pathway was then established by the discovery and detailed characterization of novel specific enzymes characteristic of the pathway, their importance being confirmed by studying their induction during methylotrophic growth and by their absence in mutants lacking the ability to grow on methanol. By the mid 1970s the serine cycle seemed to be complete, except for understanding how acetyl-coenzyme A is oxidized to glyoxylate. This essential step was not elucidated for another 30 years. After each International Conference on Microbial Growth on C_1 compounds in the intervening period, Rod would ask, 'Have they solved the serine cycle yet?' Sadly it was not until 2006, shortly after Rod had died, that a satisfactory description of the complete pathway arose from a presentation by George Fuchs and the Freiburg group at the Gordon Research Conference in Magdalen College, Oxford. For a description of the development and history of Rod's serine cycle see his influential 1972 review (8), and for a more extensive review of this cycle and its completion see Anthony (2011).

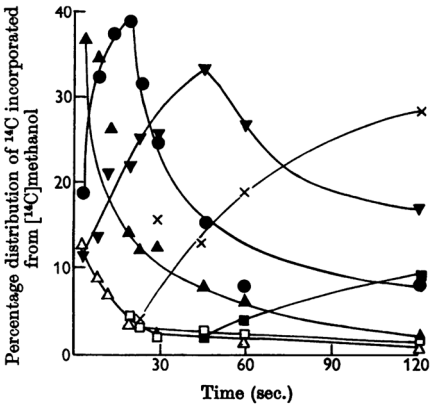

Fig. 2. Variation with time of the percentage distribution of ^{14}C incorporated from [^{14}C]methanol into the constituents of the ethanol-soluble fraction of *Pseudomonas* AM1, growing on methanol. ●, Malate; △, aspartate; ▲, serine; □, glycine; ■, glutamate; ▼, phosphorylated compounds; ×, trehalose.

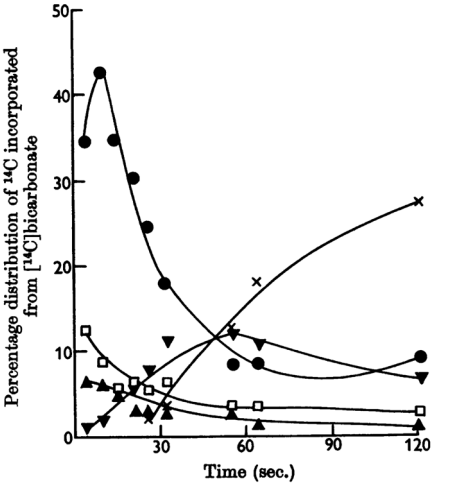

Fig. 3. Variation with time of the percentage distribution of ^{14}C incorporated from [^{14}C]bicarbonate into the constituents of the ethanol-soluble fraction of *Pseudomonas* AM1 growing on methanol. ●, Malate; ▲, serine; □, glycine; ▼, phosphorylated compounds; ×, trehalose.

Figure 1. Figures taken from the first paper published by Rod Quayle (with P. J. Large and D. Peel) on methanol assimilation by *Methylobacterium extorquens* AM1 (current name) (4). They show the result of experiments in which samples were taken every few seconds after the addition of radioactive substrate, after which the labelled metabolic intermediates were separated, identified and quantified. A key feature of these experiments is that it is not the total activity in each intermediate that is graphically recorded but the percentage of label in each compound. This decreases with time for an early intermediate in the pathway. (Reproduced with permission, from P. J. Large *et al.* (1961) *Biochem. J.* **81**, 470–480. Copyright © the Biochemical Society.)

Microbiology in Sheffield, 1963–83

Hans Krebs was the head of the Biochemistry Department in the University of Sheffield (1938–54), where he frequently used microorganisms in his research, appreciating their many advantages for studying cell metabolism. In 1948/49 he helped establish within the Bacteriology Department a Sub-Department of Microbiology, with Sidney Elsden as the Senior Lecturer-in-charge and one lecturer (Bernard Fry). The Department of Microbiology was formally established in 1952, and the Agricultural Research Council added a Unit of Microbiology with Elsden as its Honorary Director and three additional members of Agricultural Research Council (ARC) staff. Krebs was later involved in establishing the West Riding Chair of Microbiology for Sidney Elsden (1959–65), the title reflecting generous financial support from the West Riding County Council. During its first 13 years (1952–1965) the Department of Microbiology gained international recognition for research on the biochemistry of anaerobic and photosynthetic bacteria and the energetics of bacterial growth, and it ran a successful MSc course in Microbiology.

In 1954 Krebs moved with most of his staff from Sheffield, to take the Whitley Chair of Biochemistry at Oxford. His replacement, Professor Quentin Gibson (FRS 1969), with an extremely successful group of scientists quickly re-established the department's prestigious international reputation. Sadly, he left Sheffield with many of his colleagues to work in North America (1962/63), the Sheffield Biochemistry Chair being filled by Walter Bartley (1963–81). At about this time the future of the Oxford MRC Unit was becoming uncertain as a result

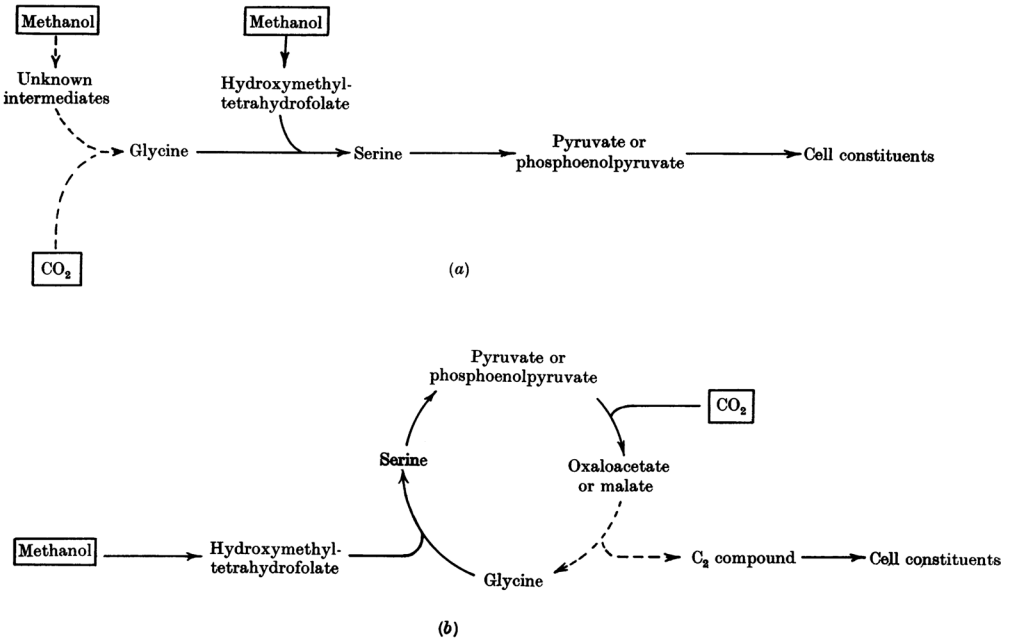

Fig. 1. Possible routes for synthesis of cell constituents from methanol by *Pseudomonas* AM1. The broken lines represent the hypothetical schemes for the crucial step in the biosynthesis, namely the net synthesis of glycine from C_1 units. (*a*), Direct synthesis of glycine; (*b*), cyclic synthesis of glycine.

Figure 2. Figure taken from the second paper published by Rod Quayle (with P. J. Large and D. Peel) on methanol assimilation by *Methylobacterium extorquens* AM1 (current name) (5). This shows an outline of the two possible pathways for methanol (and carbon dioxide) assimilation, based on the experiments illustrated in figure 1 together with analysis of the locations of the radioactive carbon atoms within the postulated intermediates. Rod eventually showed that the assimilation pathway is cyclic (the serine cycle). (Reproduced with permission, from P. J. Large *et al.* (1962) *Biochem. J.* **82**, 483–488. Copyright © the Biochemical Society.)

of Krebs's impending retirement, and Rod accepted an invitation to move with Bartley to the Sheffield Department as a Senior Lecturer.

Two years later Rod was appointed to the West Riding Chair of Microbiology and Head of the Microbiology Department (1965–83) after Elsden's move to Norwich as Director of the ARC Food Research Institute with the simultaneous departure of his ARC staff. Three lecturers (John Guest (FRS 1986), Margaret Attwood and Peter White) were soon appointed to replace the former ARC staff, and with Bernard Fry as Senior Lecturer they represented the entire research and teaching staff of the department for the next 10 years. They were joined later by Milton Wainwright (1975) and Ann Moir (1981), ultimately bringing the total staff to seven. When Rod accepted the Sheffield chair there were plans for the Departments of Microbiology and Genetics to occupy a new Biology Building, but these plans were soon revised in favour of another department. For the next seven years Microbiology was confined to the cramped conditions of the Elsden department, with no offices for staff and only four spaces to accommodate research students. There was a small office for the professor and secretary, and just four small laboratories surrounding the chimney of the university incinerator, one of which was infested by rodents entering from the local park and escaping from the adjacent animal house. John Guest remembers occupying two sides of an island bench in Rod's laboratory,

with his desk being next to a large fermenter growing bacteria on a possibly explosive methane–air mixture. Peter White was accommodated in a communal laboratory with a desk crushed into a closed doorway. Applying for research grants was a problem because there was no space for additional staff or equipment, and in other respects these were frustrating times because microbiology, including microbial genetics and molecular genetics, was expanding at an explosive rate, providing the materials and techniques for the genetic revolution and the emerging era of recombinant DNA. The Microbiology Department seemed to be the only department wanting to develop along these lines. Under Bartley the Biochemistry Department had grown in size but was little interested in molecular biology or in collaboration with other departments. In his obituary of Krebs (14), written in 1980, Rod wrote:

> Krebs appealed to Sheffield University in 1951 to provide him with more space, arguing that the scant space given to the Biochemistry Department ($\frac{1}{6}^{th}$ of the space available to Chemistry and $\frac{1}{3}^{rd}$ of that available each to Zoology and Botany) suggests that the general importance of Biochemistry as an academic subject has not been appreciated by the Sites and Building Committee.

Rod went on to write: 'Add 30 years on to 1951 and substitute Microbiology for Biochemistry, and you have a paragraph in current use by many Heads of British Microbiology Departments'. Eventually, in 1972, dedicated teaching space for microbiology and more space for research were acquired when another department was relocated to a new building.

Everyone in the Microbiology Department, including Rod, had a heavy teaching load. They continued to teach in the biochemistry degree course and in 1966 started a new dual honours degree in genetics and microbiology in the outlying Genetics Department. Then, from 1976, they offered a single honours degree in microbiology in addition to dual degrees with biochemistry, with genetics and ultimately with biotechnology. The courses included a wide range of topics reflecting the staff's expertise in microbial structure, function, physiology and metabolism, growth kinetics and energetics, environmental microbiology, bacterial and phage molecular biology and molecular genetics, genetic engineering and biotechnology.

Rod was an excellent head of department, always approachable and friendly to everyone. By regularly attending weekly seminars he kept aware of the research of all the members of staff and their students. Decisions were made democratically by common consent at informal meetings of the academic staff over lunch on Fridays during term, and in this way a harmonious and highly efficient department was maintained.

With so many constraints of time, space and university attitudes it is truly remarkable how much was achieved by this small department, not least the fact that two of the seven members of staff (Quayle and Guest) were elected Fellows of the Royal Society.

Bacterial growth on methane; the methanotrophs

After moving to Sheffield in 1963 Rod turned his attention to the methanotrophs—those bacterial methylotrophs that usually grow only on methane, but sometimes also on methanol. In their first paper on the serine cycle in methanol-utilizers, he had said 'It remains to be seen whether microbial growth on methane involves a metabolism broadly similar to that involved in growth on methanol' (5). This was particularly relevant to methanotrophs because it had previously been assumed that methane would be assimilated as carbon dioxide by the RuBP pathway of carbon dioxide fixation.

If Rod had chosen to study a different methanotroph he might have come to the obvious conclusion that all methylotrophs, including methanotrophs, would use the serine cycle for

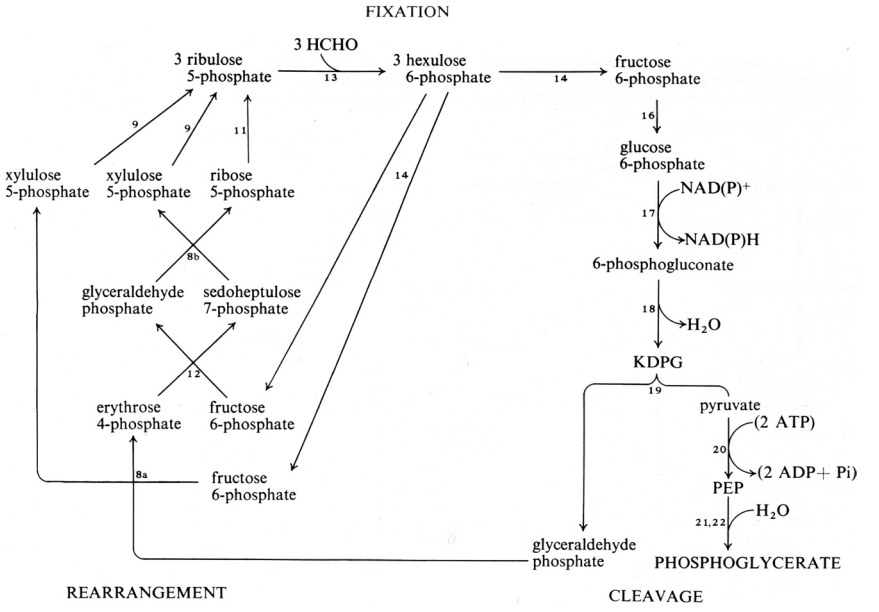

Figure 3. The ribulose monophosphate (RuMP) pathway of formaldehyde assimilation (2-keto, 3-deoxy, 6-phosphogluconate (KDGP) aldolase/transaldolase variant). This cyclic pathway achieves the conversion of three molecules of formaldehyde to one molecule of phosphoglycerate, which is the starting point for biosynthesis of all cell materials. The numbers refer to the enzymes catalysing the reactions: 8, transketolase; 9, pentose phosphate epimerase; 11, pentose phosphate isomerase; 12, transaldolase; 13, hexulose phosphate synthase; 14, hexulose phosphate isomerase; 16, glucose phosphate isomerase; 17, glucose phosphate dehydrogenase; 18, phosphogluconate dehydrase; 19, KDPG aldolase; 20, phosphoenolpyruvate (PEP) synthetase or equivalent enzyme(s); 21, enolase; 22, phosphoglyceromutase. (Figure reproduced from Anthony (1982), with permission.)

assimilating methane as well as methanol. But his first paper based on work at Sheffield (with Pat Johnson) showed that neither of the known pathways is operating (6). During growth on methane, ribulose bisphosphate carboxylase was absent from *Pseudomonas methanica* (now called *Methylomonas methanica*), and the ^{14}C-labelled compounds accumulating at early times during incubation with [^{14}C]methane or [^{14}C]methanol were neither phosphoglycerate nor serine but mainly glucose and fructose phosphates. Their demonstration of a novel formaldehyde-condensing enzyme in crude cell extracts indicated the presence of a pentose phosphate cycle for formaldehyde assimilation, analogous to the RuBP pathway for carbon dioxide assimilation. This was confirmed by a thorough examination of the labelling patterns and by characterizing (with his student Michael Kemp) the novel enzyme responsible for condensing formaldehyde with ribulose monophosphate to give a sugar phosphate. This sugar phosphate was later identified as a novel hexulose phosphate, D-arabino-3-hexulose phosphate (Kemp 1974). Rod eventually completed the pathway, now known as the ribulose monophosphate pathway (RuMP pathway) by purifying and characterizing a second novel enzyme, hexulose phosphate isomerase, and by demonstrating the presence of essential cleavage and rearrangement enzymes (for a review see (13)). In summary, three molecules of formaldehyde are condensed with RuBP to produce three molecules of hexulose phosphate, which then undergo a series of cleavage and rearrangement reactions to regenerate the acceptor ribulose monophosphate and to produce the C_3 phosphoglycerate for assimilation into cell material (figure 3).

After this first description of the RuMP pathway in methanotrophs growing on methane, it was shown to be the main route for methanol assimilation in many bacteria including *Methylophilus methylotrophus*, the bacterium used by Imperial Chemical Industries (ICI) for their single-cell protein (SCP) Pruteen project. This was significant because the RuMP pathway is energetically (and therefore commercially) more favourable than the serine cycle for bacterial growth on methanol. He also demonstrated that by having an extra enzyme (6-phosphogluconate dehydrogenase) in the pathway, some of these bacteria can oxidize formaldehyde to CO_2 by a cyclic route instead of the usual linear pathway. Rod showed that there are four possible variants of the RuMP pathway, depending on which rearrangement reactions are operating (13).

Although Rod showed that the RuMP pathway operates in some other methanotrophic species, he soon obtained evidence that at least one of them must use a different pathway. Short-term labelling experiments with *Methanomonas methanooxidans* identified serine and carboxylic acids as the early-labelled products, as had been observed for methanol assimilation in *Pseudomonas* AM1, and key enzymes of the serine cycle were present during growth on methane whereas those of the RuMP pathway were absent. This provided the first indication that there are two metabolically distinct groups of methanotrophic bacteria. In 1970 another of the great milestones in C_1 metabolism was reached when Roger Whittenbury, John Wilkinson and their colleagues transformed the field by their detailed study of elective culture of methanotrophs, which resulted in the isolation and characterization of more than 100 new strains (Whittenbury *et al*. 1970). These formed two distinct groups according to the arrangement of their internal membranes, and Rod quickly confirmed that bacteria in one group used the RuMP pathway, and the other used the serine cycle (7).

Methylotrophic yeasts

In the late 1970s Rod transferred his attention to some recently described methanol-utilizing methylotrophic yeasts (13). In 1977 Hans van Dijken from the University of Gröningen was spending a year in Sheffield and Rod, together with other colleagues from Gröningen and Sheffield, decided to carefully examine the literature suggesting that *Candida* uses the RuMP pathway during growth on methanol (11). They repeated the labelling experiments with [^{14}C]methanol, using *Hansenula polymorpha* in place of *Candida*, and obtained identical results for the two yeasts. However, cell-free extracts of methanol-grown *H. polymorpha* and *Candida boidinii* lacked the two key enzymes of the RuMP pathway, namely hexulose monophosphate synthase and hexulose phosphate isomerase, which were investigated using the authentic substrates and sensitive spectrophotometric assays that Rod had developed for the bacterial enzymes. Thus, although the ^{14}C labelling experiments and the presence in cell-free extracts of an enzyme system capable of catalysing a pentose phosphate-dependent fixation of formaldehyde pointed towards a yeast equivalent of a bacterial RuMP pathway, the absence of essential key enzymes showed that this is not the case. Roger Cox, a postdoctoral colleague, then drew their attention to the possibility that a pentose phosphate-dependent fixation of formaldehyde in crude extracts might be catalysed by transketolase, using xylulose 5-phosphate as the ketol donor, and formaldehyde as acceptor, a reaction that he had considered with Len Zatman during their investigation of the growth of *Bacterium* 2B2 on trimethylamine (Cox & Zatman 1974). On the basis of such a condensation reaction, Rod and his colleagues proposed another novel assimilatory cycle, the dihydroxyacetone cycle for formaldehyde

fixation, in which dihydroxyacetone would be the primary product formed from formaldehyde (11). Higher activities of a dihydroxyacetone kinase and fructose-1,6-bisphosphatase would be required during growth on methanol than during growth on multi-carbon substrates, and this was confirmed in methylotrophic *Hansenula* and *Candida* species. It was then shown by Mary O'Connor (now Mary Lidstrom), a visitor from the USA, that mutants of *H. polymorpha* and *C. boidinii* lacking dihydroxyacetone kinase were unable to grow on methanol (12). In one respect at least, Mary was typical of visitors to Rod's lab, gaining techniques, experimental approaches and inspiration, and then over 35 years continuing to be an inspiration and leading light in the hugely expanded field of methylotroph genetics.

Some further key questions answered

The timely identification of key questions was a common feature of Rod's approach, sometimes leading to extensive studies, as in the assimilation pathways in bacteria and yeasts, but sometimes involving a short successful foray into a related field. A good example of this is his work on methane oxidation with Dr John Higgins. Methane is rather inert chemically, and it had been proposed that the first oxidative step in its metabolism would be catalysed by a monooxygenase, with energy being put into the reaction by the reductant NADH. This was very difficult to confirm with conventional biochemical techniques, but Rod saw an opportunity to solve the problem by using 'heavy oxygen' (^{18}O), both as the gas and as a constituent of water. In 1970 with Higgins he showed unequivocally that the initial reaction must be catalysed by a monooxygenase, incorporating ^{18}O into methanol from $^{18}O_2$ but not from $H_2{}^{18}O$.

Rod spent a sabbatical year as a visiting professor in Göttingen (1973–74), working with Professor Gerhard Gottschalk, Professor Norbert Pfennig and Professor Hans Schlegel at the famous Institut für Mikrobiologie in the Georg-August-Universität. Norbert Pfennig had shown that some members of the photosynthetic bacteria (the Rhodospirillaceae) are able to use methanol instead of carbon dioxide as their carbon source during anaerobic photosynthesis. During his visit Rod found a better way of isolating these bacteria and showed that it was likely (as has now been confirmed) that they assimilate methanol carbon after first oxidizing it to carbon dioxide. Returning home, he collaborated with a visitor from Germany, Hermann Sahm, and with Roger Cox to confirm that the RuBP pathway is indeed used for growth on methanol after its initial oxidation to carbon dioxide. During this process, methanol is oxidized by the NAD^+-independent quinoprotein methanol dehydrogenase, which passes on its electrons to a special cytochrome *c* and thence, in aerobic conditions, to oxygen. However, Rod's measurements of growth yields during anaerobic photosynthesis on methanol (9) showed that the dehydrogenase is also responsible for the reduction of NAD^+ to NADH, essential for assimilation of the carbon dioxide produced by methanol oxidation. This process must involve oxidation of the cytochrome *c* by a cytochrome bc_1 complex, ubiquinone and NADH dehydrogenase. It is thus a rare example of 'reversed electron transport' from methanol in bacteria, the energy being provided by the light reactions of photosynthesis (see Anthony 1982).

Industrial links and conferences

In the late 1960s the discovery of the North Sea oil and gas fields led oil and chemical companies to realize that they had a new and cheap chemical and biological feedstock on their doorsteps. Accordingly in 1967 the Institute of Petroleum organized a Symposium

Figure 4. The ICI 'Pruteen' plant at Billingham on Teesside, UK. The specially developed airlift fermenter is the middle tower; the others are for the production of growth medium and for cooling.

in London on Hydrocarbon Microbiology. Both Rod and Douglas Ribbons had included methane microbiology in their talks, and after the symposium Rod was approached by two chemists, P. P. King and D. Watchorn, from the Agricultural Division of ICI at Billingham, Cleveland, UK, who felt that ICI might be interested in the possibility of very-large-scale microbial conversion of methane to bacterial protein for use as an animal foodstuff. They invited Rod to Billingham, where in discussion he persuaded them that methanol would be a far more suitable substrate than methane. King recalls this 'as a Eureka situation', adding, 'if there is one thing we can do it is to make methanol out of natural gas very efficiently.' Out of these beginnings the ICI Pruteen project was born. Within the astonishingly short time of 13 years from the first discussions, the world's largest fermenter was constructed for the fast-growing *Methylophilus methylotrophus*, and full production was achieved on Teesside in 1980. The Pruteen output from the 50 m-high (1.5 million litre) airlift fermenter (figure 4) was 50 000 tonnes per annum. Sadly this pioneering ICI project, which cost well in excess of £100 million, had to be abandoned because of falling prices of competing products such as soybean protein. Although nutritionally excellent, Pruteen was just too expensive to produce. However, thanks to Rod's initial relationship with ICI, this company was for many years a very welcome sponsor of research by many academic microbiologists in the UK engaged in fundamental work on methylotrophic bacteria. This quest for inexpensive SCP was a worldwide phenomenon: once industrial giants such as ICI, BP and Shell had become interested in methane and methanol microbiology, large research funds began to flow and the study of methylotrophs rapidly gathered pace in Europe and the USA, with research groups forming in Sittingbourne, Canterbury, London, Hull, Grangemouth, Göttingen, Madison, Dallas, Puschino, Kiev, Tokyo, Kyoto and Haren, in addition to those already active in Sheffield, Edinburgh and Reading.

By 1973 there was sufficient interest for Rod, together with John Wilkinson and Roger Whittenbury, to raise financial support from BP, ICI and Shell to organize in Edinburgh what must be considered as the first authentic C_1 symposium. There were 50 participants and it lasted 2½ days. The first 'official' International Symposium on the Microbial Growth on C_1 Compounds was held a year later in Tokyo, and this was followed every three years by

wonderful symposia, in Puschino, Sheffield, Minneapolis, Haren, Göttingen and Warwick. The eighth of these was held in San Diego in 1995; from 1998 onwards they have continued every two years under the auspices of the Gordon Research Conferences, the most recent being in 2014. It was at these meetings that Rod's influence was most personally experienced. His authority coupled with his modesty and helpfulness made his contributions eagerly anticipated. His lecturing style was rather formal, often speaking from a typescript, whereas his informal contributions often took the form of elegant hilarious anecdotes often aimed at the pompous or self-important. He will be remembered by those who knew him at these conferences as the voice of reason, a serious intellect, generous in his advice and help, bringing a compassionate almost genteel understanding of anyone's problems, personal or scientific. His valedictory lecture at the 1995 Symposium on Microbial Growth on C_1 Compounds in San Diego was typical of the man: he highlighted all the achievements since the first symposium 22 years earlier and paid scant attention to his own discoveries even though these had influenced nearly every facet of C_1 metabolism for more than 30 years.

Other aspects of his time in Sheffield

In 1974 it became Rod's turn to serve as Dean of the Faculty of Science (1974–76), during which he was able to award the first Krebs Prize for Biochemistry on degree day. He had established this prize by generously using the royalties accruing from a book of essays by former colleagues of Krebs and dedicated to Krebs on his 70th birthday. He also established the Boehringer Prize for the best microbiology graduate. In this case the original fund came from a substantial sum of money received by the Microbiology Department from the Boehringer Chemical Company as a discount based on their huge consumption of coenzymes and other fine chemicals. The money was intended to be used to buy further Boehringer chemicals, but Rod asked for it to be used to create a prize in Boehringer's name and the company agreed.

Rod's extraordinarily fruitful exploration of the biochemistry of the highly diverse range of microbes growing on C_1 compounds during his time in Oxford and this period in Sheffield led in 1978 to the award of the CIBA Medal and Prize of the Biochemical Society (13), and to his election as a Fellow of the Royal Society. If he had 'merely' elucidated a single novel pathway for microbial carbon assimilation, that pathway would probably have become the 'Quayle cycle'. This could not happen because he had described three novel pathways: the serine cycle, the ribulose monophosphate pathway (and its four variants) and the dihydroxyacetone pathway.

His time in Sheffield was shared with his wife, Yvonne, and their two children, Susan and Rupert. When Rod organized a highly successful C_1 symposium (1980) in which about 25 nations were represented, Yvonne organized the social activities for accompanying wives. She often joined him on his visits to the C_1 symposia, lightening and leavening the social aspects of the science community. She became an accomplished painter and an active member of the University Wives' Club and remembers their Sheffield period as a great time of entertaining. With three friends Yvonne produced an excellent cookery book—'Cooking by degrees'—containing recipes born of Rod's enthusiasm for bread-making: 'Quayle bread' and 'Rod's whole meal bread'.

Rod was always very much a family man, enthusiastically wrapped up in his two children and family activities. His leisure activities were pretty simple, a major relaxation being walking in the Peak District, right on his doorstep.

Figure 5. J. Rod Quayle with his portrait painted by Dr June Mendoza in 1992, the year in which Rod retired as Vice-Chancellor of the University of Bath. (Photograph by the university photographer; reproduced with permission.)

Bath, 1983–92

Twenty years after moving from Oxford to Sheffield, Rod felt he had achieved as much as he could in the areas in which he was interested, and after considering several other options he moved to the University of Bath as Vice-Chancellor (figure 5), where it is likely that his various experiences at Sheffield had an important influence in his attitudes and approaches to university organization.

This was a time of significant change in the restructuring of higher education management and performance in the UK, so Rod had to adapt to the role of businessman and chief executive. He had those qualities of making things happen, making people understand and follow his objectives, while at the same time getting on and steering the ship. Sometime after the Jarratt Report of 1985 he was charged by the University Council to implement, within three years, changes in the university's organization. This he achieved so successfully that within one year the University of Bath was transformed from a highly centralized managed university to one with management and executive authority devolved to heads of departments. During the nine years under his leadership, Bath University rose to be an outstanding research university with 11 of the 14 schools of study ranked within the top grade for UK universities in the Research Assessment Exercises.

During his time at the University of Bath, Rod vigorously championed this relatively young university as a centre for both pure and applied research, in the conviction that there is only one Science: 'Science applied to useful ends' and 'Science waiting to be so applied'. The remarkable growth in size, scope and influence of the University of Bath owes much to Rod's vision, leadership and enthusiasm for science. In spite of his involvement in all aspects of the life of the university, Rod maintained his enthusiastic interest in the research of all those within his own field of interest—the microbial metabolism of C_1 compounds. Even when unable to attend the international conferences, he was always eager to hear reports of recent advances and was always available to accept visitors who knew that time spent with him would revitalize their own enthusiasm. Here follows a personal anecdote: a visitor (Wolfgang Babel) to Southampton from the then repressive East Germany asked me if it would be possible to meet his hero and inspiration. After one telephone call, a visit was set up for the very next day. It was spent in very animated discussion and debate, almost leaving my visitor in tears and saying 'I hope you in the UK appreciate what a sensible system you have that gives power and influence to such a great, wise and generous man as Professor Quayle.' A measure of the personal respect, admiration and affection in which Rod was held by all those working on methylotrophs can be found in the preface to *The biochemistry of methylotrophs* (Anthony 1982) dedicated to J. Rod Quayle, 'The Godfather of Methylotrophy'.

Rod's relationship with students was quite special. He had a way of talking and always listening to students' needs. Typically he assumed that it was his place to offer lifts in his car to students who waited at the bottom of the long hill leading from the town to the campus. Although trying to avoid it, he sometimes had to admit that he was the Vice-Chancellor, but their shocked response was so great he eventually gave up the practice as being unkind.

His continuing work with the Royal Society brought about one of the coups of the time by transferring the National Cataloguing Unit for Archives of Contemporary Scientists to its location in the University of Bath. He was also influential and involved in bringing together the combined strengths of the universities of Bristol, the West of England and Bath, in the planning and initial strategy for a major science park. Working on the national scene, he was elected chair of the UK National Committee for Microbiology (1985–90), advising the UK government on all microbial matters, and he served as President of the Society for General Microbiology from 1990 to 1993. He continued to work in various capacities in the Royal Society until a few months before he died.

While working on behalf of the University of Bath, Rod also played a part in the local community and in national and international affairs, both academic and social. These included the reformation of the Bath Royal Literary and Scientific Institution, whose aim was the 'Promotion and Advancement of Science, Literature and Art'. He was a member of the Council of the Bath Institute of Medical Engineering, which 'Uses the multidisciplinary approach of medicine, engineering and science to identify needs of disabled people and hospital patients not being met elsewhere and to provide solutions'. He was a member of the Board of the Bristol Exploratory, a hands-on Museum of Science founded by Richard Gregory (FRS 1992). He also made a significant contribution to one of Yvonne's and his great loves in the world of music and the arts, by inspiring the management of the world-famous Bath Festival, which provided a happy, relaxed reward for them when dutifully meeting the performers and attending great concerts.

Retirement (1992–2006) and family

The first thing that bothered Rod in retirement was that he would no longer have a secretary, so he had to learn how to use a computer. At first he was very busy as President of the Society for General Microbiology. He also wrote biographical memoirs for Fellows of the Royal Society for W. Charles Evans (15), who had been a Professor of Biochemistry at Bangor, and Leonard Rotherham (16), an engineer who had been a previous Vice-Chancellor of the University of Bath.

During retirement, in the small Somerset village of Compton Dando, Rod continued with many of those activities he had enjoyed as Vice-Chancellor at Bath, including walking, swimming and going to concerts and the theatre in Bristol and Bath. He also had more time for cooking, baking bread and gardening.

Yvonne and Rod's daughter, Susan, went to Durham University to read law, qualified as a solicitor and now works in Bath as the in-house lawyer for a publishing company with various overseas offices. Their son, Rupert, did four years' training at Grimsby Nautical College and has since enjoyed a career as a captain in the Merchant Navy. Susan has three children and Rupert has two. Rod always played an active role in looking after the five grandchildren: taking them for days out, to swimming lessons, sometimes picking the local ones up from school, and watching school plays. All the grandchildren are very fond of each other—and they too were very fond of Rod. He loved small children and they loved him. As well as being a born raconteur, Rod also had an infectious sense of humour which is still remembered by everyone who knew him.

Honours

As mentioned in context above, in 1978 Rod was awarded the CIBA Medal and Prize of the Biochemical Society in honour of his outstanding contribution to biochemistry (13). In the same year he was elected a Fellow of the Royal Society, in which he served as chair of one of the Sectional Committees and also as a member of Council (1982–84). From 1990 to 1993 he was President of the Society for General Microbiology. During a three-month visit as visiting professor of microbiology in the University of Washington at Seattle he received the Walker–Ames medal. He was awarded honorary doctorates from the universities of Göttingen (1989), Bath (1992) and Sheffield (1992), and had an Honorary Fellowship conferred on him by Bangor University in 1996.

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The frontispiece photograph was taken while Rod was at the University of Sheffield (photographer unknown) and is reproduced with permission from the University of Sheffield.

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