Obituary

Obituary - Edward Charles Slater (1917-2016)

With the death of E.C. Slater, Bill for insiders, the Biochemical Society loses an honorary member, and biochemistry at large loses one of the giants of the field of bioenergetics. Slater was not only an excellent biochemist, but also an outstanding mentor and a gifted administrator who turned Biocchimica et Biophysica Acta (BBA) into the largest and one of the most influential biochemical journals of the 1960s and 1970s and who contributed to the governance of numerous organizations, such as the International Union of Biochemistry and Molecular Biology (IUBMB).

Slater has meticulously recorded his life in science in an autobiographic review, “An Australian Biochemist in Four Countries”, published in Comprehensive Biochemistry, 40 (1997) 69-203. He grew up in Melbourne, Australia, where he studied chemistry. When World War 2 broke out, chemists were not allowed to enlist in the army as they were so scarce, but were put to good use to optimize soldier’s rations or in the defense industry. Slater worked briefly on war gases and this brought him in contact with British Anti–Lewisite (BAL) or dimercaptopropanol, a treatment for heavy metal poisoning and an important tool in his later biochemical research. For most of the war period Slater determined vitamin concentrations in food, scientifically not his most interesting work. As Slater says in a 1992 interview with Brian Beechev: “a silly job, totally useless”. However, in a curious historic coincidence, he used the thiocchrome method for thiamine determination developed by B.C.P. Jansen, the man he would succeed 15 years later as Biochemistry Chair in Amsterdam.

In 1946 Slater and his wife Marion went to Cambridge, England, where Slater started his PhD research with David Keilin who had become famous by discovering the cytochromes of the mitochondrial respiratory chain. The choice of Keilin’s lab was a fortunate one. Keilin started as a parasitologist and his wide knowledge of biology complemented that of chemist Slater. Keilin also proved to be an excellent mentor who took time to discuss experiments and to teach his gifted pupil the biochemical knowledge that Slater still missed.

Keilin’s lab studied the respiratory chain using the Keilin and Hartree heart-muscle preparation, now known to contain fragments of the mitochondrial inner membrane. Slater started his biochemical research by looking at the oxidation of succinate and this led to his first discovery. Following reports that succinate dehydrogenase is inhibited by glutathione disulphide (GSSG), Slater found that reduced glutathione inhibits oxidation of succinate even better than GSSG and that BAL worked best. However, BAL did not inhibit succinate dehydrogenase itself, as reported, but the respiratory chain at an unknown component, the BAL-labile factor, later dubbed “Slater Factor”. Much later Rieske and others would show that the Slater Factor was an iron–sulphide protein.

After his initial publication of the BAL-labile Factor, Slater spent the next two years on a detailed study of the oxidation of succinate and NADH by the respiratory chain. This work was presented at Biochemical Society Meetings and in a series of articles in the Biochemical Journal. Later, when Slater was building up his department in Amsterdam, he would still send his students over to Britain to present their work at Biochemical Society Meetings. When we complained that we could not present our wonderful experiments in a 10-minute talk, Slater would invariably answer that he had heard Fred Sanger present his Nobel-prize winning work on insulin in 10 minutes. If Sanger could do it, we should be able to manage as well.

After 3 years in Cambridge, Slater moved to New York, USA, where he worked as a post-doc in the lab of Severo Ochoa. This introduced Slater to oxidative phosphorylation, the field that would become his main research interest in later life. After N.Y., Slater applied in vain to jobs in Australia. He wanted to do basic research, but there were mainly applied jobs on offer. Fortunately, Keilin found a fellowship, allowing Slater to return to Cambridge in an independent position in Keilin’s Molteno Institute.

In the highly productive period that followed, Slater set up collaborations with several of the excellent staff members of the Molteno Institute, on enzyme kinetics with Bonner, on oxidative phosphorylation in insect mitochondria with Lewis and on the P.O ratio in different steps of the respiratory chain in animal mitochondria with his student Holton. Studies with dinitrophenol, an uncoupler of oxidative phosphorylation, led Slater to formulate a theory for the coupling of oxidation to phosphorylation that became known as the chemical theory of oxidative phosphorylation, to contrast it with the chemi-osmotic theory formulated in 1961 by Peter Mitchell. The competition between these two theories would dominate bioenergetics in the 1960s and eventually Mitchell would prevail and receive the Nobel prize.

The clash between Slater and Mitchell was not only a matter of biochemical theories, but also of personalities. Mitchell had brilliant insights, but was not always precise with facts. Slater was meticulous, critical, analytical, systematic and his reviews were models of clarity and precision. Nevertheless, the Slater-Mitchell controversy was scientifically productive and their intensive and friendly correspondence testifies to that. The persistence of Slater in pointing out loopholes and inconsistencies in the chemi-osmotic theory probably led Mitchell to a more complete version of his theory.

Slater would search in vain for the chemical high-energy intermediates postulated by the chemical theory of oxidative phosphorylation. However, together with Rosing and Berden, eventually he would find tightly-bound ATP and ADP in the highly purified F1-complex. Slater then realized that the high-energy intermediate might be a high-energy state of this complex. A complete form of this conformational hypothesis for ATP synthesis was formulated by Boyer, who received the Nobel prize for his work.

In the mid-50’s Slater had become one of the most visible and productive scientists in the bioenergetics field and with his obvious drive and ambition he looked like an ideal chairman for a biochemistry department. No offer came forth from Britain or Australia, however, and in 1955 Slater accepted the chair in Physiological Chemistry of the medical faculty in Amsterdam. The department was in poor
shape, but Slater was undeterred. He rapidly attracted a cast of foreign colleagues coming for sabbaticals and of foreign post-docs and within a year the first cohort of graduate students was recruited. Eventually, the Amsterdam biochemistry department would grow out into a super-department, serving 4 (sub)faculties – Medicine, Chemistry, Biology and Dentistry –, housed in 3 different locations in the city, but all under the coordinating chairmanship of master Slater, supported by 7 (associate)-professors, mostly recruited from the ranks of his pupils. As biochemistry was expanding in the 1960s and 1970s, other Slater pupils were exported to chairs in many other Dutch universities. The Amsterdam lab became the start for many outstanding careers elsewhere, with alumni, such as Richard Flavell, FRS, Sir Alec Jeffreys, FRS, Titia de Lange, Jan Hoeijmakers, to mention just a few.

In the hectic early days in Amsterdam Slater also had to learn Dutch. Already 1 year after his arrival he was fluent enough to teach medical students in Dutch. His Dutch would never become perfect, however. For instance, he would mix up the Dutch word "schoorsteen", which means chimney, with "goootsteen", which means sink in Dutch. We always relished the moment when Slater decided that an experiment was no good and that the results could be thrown down the chimney, rather than the sink.

Eventually Slater would become the most influential biochemical scientist in the Netherlands and the dominant force in shaping Dutch biochemistry in the second half of the 20th century. This was not only due to his exceptional talents as a scientist and organizer, but also to his ability to attract the best students, post-docs and colleagues on sabbatical and to inspire and educate them. He was indeed the ideal role model with his high standards, his devotion to well-planned research, his fantastic knowledge of the literature and his superb way of organizing and running a department. Slater never owned a car and anybody who saw Slater cycle through Amsterdam, would not easily guess that this typical Dutchman was born in Australia and retained his Australian nationality. Slater was not a man claiming privileges. "Public money should be spent on research, not on taxis", he used to say.

From his base in Amsterdam, Slater increasingly contributed to the organization of biochemistry in the world. He was secretary of the Committee on Biochemical Nomenclature of IUPAC (1959–1964) and he contributed in many ways to the running of EMBO and the EMBL. He chaired the EMBO Fund Committee (1974–1978); he was the president of the EMBL Council; he was the chairman of the Search Committee that selected Lennart Philipson as the new director-general of EMBL to succeed John Kendrew; and he was the (almost eternal) auditor of EMBO.

Slater liked the excitement and camaraderie of scientific meetings and was one of the few biochemists in the world who could claim to have attended every single International Congress of Biochemistry organized by the IUB(MB) up to 1994. Hence, it is not surprising that a person of Slater's scientific stature and managerial qualities would be recruited by the IUBMB for help. In 1964 he became a Council member, for 8 years (1971–1979) he acted as Treasurer of IUB, in 1985 he became President-elect and from 1988 to 1991 he served as President. He became Treasurer for a second time from 1999 to 2000.

To many biochemists Slater was known as Mr BBA. He became involved with the journal in 1957 when, still at the fledgling stage, it started publishing Preliminary Notes and Short Communications. Slater was recruited as Managing Editor for this section and by combining fast with competent reviewing, he made a success of it. After the early death of Westenbrink, then the Managing Editor for the whole of BBA, Slater took over. This was an ideal job for Slater. Running a rapidly growing journal, required enormous energy, deep knowledge of biochemistry and biophysics, a vision on the future of the field and tact and tenacity to deal with Elsevier, not only interested in scientific quality, but also in profit. Under his leadership BBA grew out to become the largest scientific journal in the world and it would long remain one of the best. Slater continued running BBA until 1982, often together with former pupils and close international colleagues. He remained Honorary Executive Editor and continued doing editorial work for BBA until well in his eighties.

Slater's retirement from the university in 1985 did not end his involvement with science and teaching. He moved to Lymington in the South of Britain, became an honorary professor at the University of Southampton where he contributed to the teaching of biochemistry and to the difficult task of distributing scarce money. Slater was uniquely qualified for this demanding task, as an outsider, a meticulous administrator and a tactful but forceful committee chairman. The University of Southampton thanked him for his important contributions with an honorary doctorate. He also received an honorary doctorate from the University of Bari, Italy, in recognition of his contributions to the highly successful Bari-Amsterdam Symposia on Bioenergetics, the first truly European biochemical symposia. Slater received many other honours during his professional life, such as the honorary membership of the British Biochemical Society and four other biochemical societies around the world. He was a Fellow of the British Royal Society, a member of the Royal Netherlands Academy of Arts and Sciences and a foreign member of the Academies of Science of Argentina, Australia, Belgium and Sweden. In the Netherlands he received the Royal Dutch Shell Prize and the Dutch queen made him Knight in the Order of the Dutch Lion, one of the highest distinctions bestowed on scientists in the Netherlands.

Slater was blessed with excellent health and he retained this until well in his nineties. He skied from his second home in Switzerland until 80; he sailed single-handedly on the North Sea until 90; he continued writing lucid and interesting overviews of the history of the development of biochemistry; and he kept up a lively correspondence with colleagues and former pupils. His last years were difficult, because he lost his only daughter to cancer and his wife Marion, who survives him at the age of 100, lost hearing and vision. He is mourned by his 3 grandchildren, his son-in-law, and a wide circle of former colleagues and pupils, as an outstanding biochemist, an unforgettable mentor and a warm friend.

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1. "A life of research in mitochondrial energy metabolism" is recorded on DVD and obtainable from the Biochemical Society Archive.