CSIRO PUBLISHING

Historical Records of Australian Science
https://doi.org/10.1071/HR19016

David Roderick Curtis 1927–2017

Stephen J. Redman[A,C] *and Robert Porter*[B]

[A]Australian National University, 62 Kensington Rd, Bolwarra, NSW 2320, Australia.
[B]Emeritus Professor, Monash University and ANU.
[C]Corresponding author. Email: steve.redman@anu.edu.au

David Curtis was a pioneer in the identification of excitatory and inhibitory transmitters released at synapses in the central nervous system. He made major contributions to the identification of gamma-amino butyric acid (GABA) and glycine as inhibitory transmitters released at inhibitory synapses. His work laid the foundation for the subsequent acceptance that L-glutamate was the major excitatory transmitter. David's scientific work led to him receiving many accolades and honours, including Fellowships of the Australian Academy of Sciences, the Royal Society and a Companion of the Order of Australia.

Published online 3 June 2020

Introduction

As David Curtis indicated in his own published autobiography,[1] a memoir of his life and work is also an historical account of the origins and development of the field of experimental neuroscience in Australia. He pioneered the elucidation of transmitter functions in the mammalian nervous system. He did this by developing multi-barrelled glass microelectrodes for use in electrophoretic techniques to examine the effects of potential synaptic transmitters and compounds that blocked or enhanced transmission at excitatory or inhibitory synapses. These studies were all conducted in the central nervous system of living animals beginning at a time when the 'Soup *versus* Sparks' controversy of nerve action had only just been resolved (see below).[2]

Curtis was an initiator of the society of scientists and clinicians that developed into the flourishing Australian (now Australasian) Neuroscience Society. He spent his entire scientific life at the Australian National University (ANU) having been appointed in the early years of this institution and progressed from PhD scholar to Fellow and, through the introduction of the discipline of neuropharmacology, professor and eventually director of the John Curtin School of Medical Research (JCSMR) and Howard Florey Professor of Medical Research. Accordingly, his life also covered the whole development and evolution of the ANU itself from its beginnings.

His election to the Australian Academy of Science in 1965 led him to a range of major engagements in support of Australian science through the academy and its committees and also with major national organisations like the National Health and Medical Research Council (NH&MRC). He was made a fellow of the Royal Society in 1974, the Royal Australian College of Physicians in 1987 and he was elected president of the Academy of Science in 1986. He was made a Companion of the Order of Australia in 1992 and received a Centenary Medal in 2003.

Throughout his career, his scientific work received the highest international recognition and made him one of the foremost neurophysiologists in the world.

Early life and education

David Roderick Curtis was born on 3 June 1927 in Melbourne, and died in Canberra on 11 December 2017. He was the elder of two children in the family, both boys. Born at the beginning of the Depression, as he indicates in his autobiography, his family circumstances were 'not particularly affluent'. Fortunately, his father, Edward David Curtis (1900–73), the son of a building contractor, had a public service position with a regular income, albeit reduced by the government of the day. David writes that his father 'had joined the Postmaster General's Department (PMG) when he left school at 16', had obtained engineering qualifications through night school and in-service training and 'by the time of his retirement in 1963 had become Head of the PMG Engineering Division of Victoria'. He participated in the replacement of Morse code instruments by teleprinters, in the transition from manual to automatic telephone exchanges, and in the introduction of national radio and later television.

Both David's mother, Edna (née Brown), and his father came from very large families with backgrounds in building construction. His home environment was one in which scientific enquiry, making electrical and mechanical equipment, and constructing radio receivers and audio amplifiers in his father's and grandfather's workshops were encouraged. David pursued these activities to the stage of constructing, with war surplus thermionic valves, a single channel ink-recording electrocardiograph—an important introduction to electronics and an interest that would be very useful later in his career. David's mother encouraged him to take piano and tennis lessons, and these remained important pastimes for David throughout his life.

Education in physics and chemistry was stressed in his family. From primary education at the local state school in Ormond, he spent two years at Tooronga Road Central School in Malvern, where he 'first came in contact with science'. He did well academically and was awarded a Junior Government Scholarship to attend the selective Melbourne Boys' High School where he had

[1] Curtis (2006). Throughout the memoir there are frequent citations from this source.
[2] Valentine (2005).

excellent teachers in pure and applied mathematics, physics and chemistry. In the state-wide matriculation examinations of 1944, he gained honours in both maths subjects and the State Exhibition in physics. This provided him with a Senior Government and Gowrie Scholarship to attend the University of Melbourne in medicine or engineering. He chose medicine: 'a decision I have never regretted'.

Medical education and training

David studied medicine at the University of Melbourne, 1945–50. His interest in the nervous system was encouraged by Professor Roy D. (Pansy) Wright,[3] one of the most influential proponents of the establishment of the Australian National University (that included the John Curtin School of Medical Research), and a long-time member of its council, and Sydney Sunderland, an outstanding neuroanatomist and a foundation fellow of the Australian Academy of Science. On graduation, Curtis worked as a junior (1951) and then a senior resident medical officer (1952) at the Royal Melbourne Hospital. He reports that he had only one week off during those years and that was in August 1951 when he married Lauri (née Sewell). During those two years he spent terms in the neurology/neurosurgery ward where he benefitted from the experience of Dr E. Graeme Robertson (neurologist), Mr Reginald Hooper (neurosurgeon) and his assistant Mr John B. Curtis.

His third year residency in 1953 was as neurological registrar at the Alfred Hospital where he came under the influence of Leonard B. Cox and John A. Game. David always felt that the excellent clinical background and experience provided by these leading neurologists and neurosurgeons was of great benefit to him. He remained personally in touch with all of the Melbourne clinicians throughout his career and he attended meetings of the Australian Association of Neurologists and the Neurosurgical Society of Australia, becoming an honorary member of each body. However, his own interests continued to be centred in laboratory-based research relevant to the neurological disorders that he had encountered as a clinician. On the advice of Pansy Wright, he wrote to John Eccles, who had been recently appointed to the Foundation Chair of Physiology in the JCSMR.

Eccles had commenced work in temporary buildings at the ANU in 1953. He offered David a three year research scholarship to commence in February 1954 and the ANU provided a house for him and his family. In his personal autobiography, David recounts:

> My wife and I, and our 16 month old son, Christopher Mark, arrived in Canberra on February 16th. Our daughter Belinda Jane was born later that year in October. We had some difficulty in accepting that this rather small town was destined to be the nation's capital. February 16th, 1954 is a very significant date in the history of science in Australia, because on that day Queen Elizabeth II in person founded the Australian Academy of Science by presenting its Charter to several Petitioners, which included 10 Fellows of the Royal Society of London then resident in Australia. This was only the second time that a reigning monarch had presented a Charter to such a body since 1662, when King Charles II had presented his Charter to the Royal Society of London. Eccles (FRS 1941) was one of the Petitioners, served on the Academy's inaugural Council and was its second President (1957–61).

Scientific life

David's scientific life began in Canberra in the stimulating environment of Eccles' laboratories. These were housed in the 'huts' at ANU that accommodated the electrically-shielded rooms, the electronics/mechanical workshop, photographic darkroom and the specialised equipment that was then necessary for the electrophysiological studies Eccles and his colleagues were engaged upon. Eccles had only recently abandoned his electrical ('Sparks') hypothesis of central nervous excitation and inhibition and accepted that these processes were chemical in nature ('Soup'). His approach was to use glass microelectrodes, drawn out to tips of one micron diameter, and filled with 3M KCl solution, to record the potentials across the membranes of individual nerve cells in the living animal's spinal cord. These potentials were amplified using a special cathode follower input stage, designed by Jack Coombs, who had come from Dunedin with Eccles. All equipment had to be purpose built. David relished the need to have hands-on involvement in the design, manufacture and development of mechanical and electronic equipment required to pursue the experimental objectives. He also had to dextrously perform complicated dissection of peripheral nerves in the hindlimb, and delicate surgical exposure of the living spinal cord. A great deal of international expertise was available to be shared because of the presence of large numbers of collaborators who flocked to this centre of excellence; Paul Fatt and Sven Landgren were among those who were available to advise David in the early days.

In his published autobiography, he described his own contributions and their significance in meticulous detail, covering more than thirty pages of print, the progress of his scientific thinking from its origins in the Canberra laboratories to his retirement from active hands-on experimentation in 1995.[4] It cites all his major discoveries and provides references for each. We have no doubt that he meant this account to be read as definitive. It indicates the enormity of his contributions, gives credit to his many collaborators and students, and provides some insights into the conditions under which experimental work was conducted with the primitive, purpose-built equipment then available. Not only were the electronic devices of the time poor by modern standards, but there was a need to devise new and better methods of drawing out fine capillary microelectrodes and to invent multi-barrelled micropipettes.[5] These multi-barrelled electrodes allowed simultaneous recording of potentials via one barrel and ejection of chemical agents from the others. Electrode assemblies with up to seven barrels allowed six different drugs to be tested on a single neuron from which a recording was being made. This required the construction of a more sophisticated gravity and solenoid driven 'puller' for the formation of the glass pipettes. Glass-blower technicians in the laboratory were very important contributors to the production of these electrodes. As David reports, it was possible to mimic, enhance and antagonise the action of synaptically released transmitters. David's background

[3] McPhee (1999). McPhee (2012).
[4] Curtis (2006).
[5] Curtis (1964).

interest and personal involvement in design and construction of mechanical and electronic equipment was important in determining the approaches that were used in these studies, all of which examined the physiology of nerve cell activity in the spinal cord of living anaesthetised cats. He personally created his unique recording room, walled by electronic devices and shielded from external interference. This set-up, in which he worked to conduct all of his experiments, was christened the 'Tardis' by his colleagues and visitors, reminding them of Dr Who's unique machine.

Throughout his career, David used living animal preparations. He became increasingly concerned with the trend to use isolated tissue, and he was very outspoken about it. He described such preparations as 'bits and pieces of the nervous system after they have been mechanically, chemically and enzymically assaulted. Such salami and soup neurophysiology and neuropharmacology may provide significant and detailed information about membrane and receptor-associated events, but there remains an essential need to continue investigating the mammalian central nervous system under *in vivo* conditions, especially to assess the relevance of *in vitro* findings'.[6]

Synaptic transmitters

David's own description of forty years of scientific work is so meticulously detailed and objectively reported that it deserves to stand as the definitive account of his accomplishments. Throughout the description, he is characteristically matter-of-fact and attributes credit to his many collaborators for their significant contributions, especially in chemistry (Jeff Watkins, Graham Johnston and Povl Krogsgaard-Larsen). Any attempt to summarise this account of his lifetime's work would fail to do justice to it, but a few highlights can be mentioned.

David first demonstrated the potential of the electrophoretic technique in the central nervous system (CNS) by providing strong evidence supporting the 'Dale principle' that a neurone releases the same neurotransmitter from all its multiple terminals. With Rose Eccles, he showed that acetylcholine (ACh) was the transmitter released at excitatory synapses on Renshaw cells in the spinal cord.[7] These synapses are formed on motoneurone axon collaterals. This was in fact the first direct demonstration that ACh does act as a transmitter in the CNS as well as peripherally. Indeed it was the first definitive demonstration of the synaptic action of any transmitter at any synapse in the CNS.

In subsequent decades, with chemist Graham Johnston and other colleagues, he made key findings in support of the concept that gamma-aminobutyric acid (GABA) and glycine were inhibitory transmitters at other specific synapses in the CNS.[8]

In between these two major discoveries, he laid the foundations for the much later acceptance of L-glutamate as a major excitatory transmitter in the CNS. Jeff Watkins' account of this investigation (given at David's memorial service) illuminates David's cautious and critical scientific approach.[9]

L-glutamate is now generally accepted as the most ubiquitous excitatory synaptic transmitter in the mammalian central nervous system. It took nearly twenty years to establish this role categorically, with the involvement of many laboratories, but it was David's key discovery, in early 1958, that L-glutamate excited neurones by a mechanism that involved a transmitter-like depolarization of their external cell membranes, that laid the foundation for this eventual conclusion.

Ironically, however, David originally downplayed the possibility that L-glutamate could actually be a transmitter. This was mainly because its action, in the way it was being demonstrated, did not perfectly accord with that of the natural transmitter, or transmitter*s* (plural), that were active during actual physiological neurotransmission in the CNS, and moreover, because L-glutamate was already well established as a key substance in a wealth of intermediary metabolic pathways. Established transmitters in the peripheral nervous system were highly specialised for synaptic transmission alone, and it was just assumed that central transmitters would be similarly specific in that role.

His scepticism grew out of his acutely critical approach to scientific research. All factors had to be rigorously taken into account before any major claim could be made, or even the possibility suggested, that L-glutamate could be a transmitter, and at that stage not enough features of its action supported that possibility, and a multitude of factors suggested otherwise.

Jeff Watkins paid tribute to David's scientific acumen at David's memorial service:

> David's general approach to scientific research was inspirational for me as the younger colleague, exhibiting the highest professional standards in experimentation, deriving exclusively only those conclusions warranted by the results therefrom, and impeccable scientific writing in publication of our findings. If it now seems he was perhaps over-critical and over-cautious at times, this can only be seen as a consequence of his exceptionally high standards.[10]

Working with a large number of colleagues and visiting scientists, all of whom are acknowledged fully in his autobiography, and including Jeff Watkins, David Kerr, Graham Johnston, Tim Biscoe, Arthur Duggan, David Lodge, Phil Beart, Hugh McLennan and many international collaborators, particularly Povl Krogsgaard-Larsen, he examined the effects of an exhaustive range of amino acid candidates, modified versions of these, chemically manufactured compounds and available substances that could be used to mimic or modify synaptic actions. Many PhD scholars, post-doctoral fellows and international visitors benefitted from participation in David's experimental work. These include John Phillis, Ron Ryall, Michael Crawford, Chet de Groat, Dominik Felix, Christopher Game, Max Headley, Joel Bornstein, Martin Peet, John Leah, Richard Malik, Bruce Gynther, David Beattie and Gary Lacey.

The John Curtin School of Medical Research

David spent his entire scientific life at the John Curtin School of Medical Research, apart from several periods abroad and a

[6] Curtis (1993).
[7] Curtis and Eccles (1958).
[8] Curtis and Watkins (1965). Curtis and others (1968*a*). Curtis and others (1968*b*). Curtis and Johnston (1974).
[9] J. C. Watkins, Canberra, pers. comm., April 2018.
[10] J. C. Watkins, Canberra, pers. comm., April 2018.

post-doctoral year (1959–60) at the Brooklyn Medical Centre in New York. He arrived in Canberra as a PhD student (to work with John Eccles) in February 1954. After he submitted his thesis in July 1956, he was appointed as a research fellow, followed by a promotion to Fellow (tenured) in December 1957. He was given his own laboratory within the Department of Physiology, where he began to direct his research towards pharmacological aspects of central excitatory and inhibitory synaptic transmission. This was to become the focus of his research for the rest of his career.

In 1966, he was appointed to a personal chair of pharmacology, within the Department of Physiology. When Peter Bishop was appointed to the chair of physiology, after Eccles resigned, David's Chair was renamed in 1968 as the Chair of Neuropharmacology.

The university council established a Department of Pharmacology within the JCSMR in January 1973. David was appointed foundation head and professor of this new department. Space became available following the retirement of Adrien Albert (medical chemistry) the previous year. Major laboratory refurbishments were needed to convert the chemistry laboratories to electrophysiological/pharmacology laboratories, each with an electrically shielded room for recordings. David occupied these laboratories until his retirement. The additional space allowed David to make tenured appointments. One was to Graham Johnston, an organic chemist who worked with David on the central pharmacology of amino acids. Others were Arthur Duggan (peptide transmitters, opioids and transmission in nociceptive pathways), Ian Hendry (nerve growth factors controlling the development of neurones) and Caryl Hill (autonomic neurotransmission).

Following a major ANU review of the school's research activities in 1988, the departmental organisation was replaced with four divisions. In January 1989, David was appointed as head of the Division of Neuroscience. This appointment was very brief, as in March 1989, Robert Porter, who had been director of the JCSMR since March 1980, resigned to take up the position of dean of the Faculty of Medicine at Monash University. David was invited by the university council to accept the directorship until his retirement in December 1992. In an interview for the Australian Academy of Science's archive, David said he took the position from a sense of duty 'largely because the JCSMR, and the ANU, had been so good to me'.[11] It was seen as an interim appointment, as the Institute of Advanced Studies, of which the school was a part, was to be reviewed in the near future. It would have been difficult to advertise for an external long-term appointment with the review pending.

The outcome of this review was largely favourable to the institute, except for the JCSMR. The review committee, chaired by Sir Ninian Stephen, recommended that the JCSMR be excised from the ANU, some of its research activities discontinued or transferred to other parts of the ANU, and for the remaining research to be funded by the NH&MRC. This was a difficult time for the school, and particularly for David. David spent considerable time and energy responding to this review and participating in numerous negotiations and discussions with NH&MRC representatives about future funding and administrative arrangements. He worked tirelessly to have the school's precarious position reversed.[12] The decision to separate the JCSMR from the ANU was not accepted by the ANU council. It was also referred to a Standing Committee of the Parliamentary Senate, which led to the government accepting that the JCSMR should remain part of the university. Its funding was formally restored as part of the ANU block grant in December 1996, following a change of government.

After all these distractions, David was anxious to return to hands-on-research. He resigned the directorship in March 1992 and returned to his laboratory. He retired at the end of that year, but stayed on as a university fellow for another three years with an ANU grant. His final experiment was in December 1995, in the laboratory he had designed and occupied for twenty years. A complete bibliography of David Curtis' published work is included in the Supplementary Material that accompanies this biographical memoir.

Australian Academy of Science

David was elected as a Fellow of the Australian Academy of Science in 1965. He served on council (1974–77) and was a vice-president (1975–7). He also served on several sectional, standing and national committees, and as the recipient of the Burnet Medal, delivered the Burnet Lecture in 1983.

In May 1986, he was elected president for a four-year term.

It was a period of considerable change for the academy. Growth in staff numbers meant the academy could no longer be accommodated in the Dome. Ian Potter House was next door, and it was acquired and refurbished for the academy. Rental income from part of this property enhanced the academy's financial position. A major expansion in textbook publishing took place. The *Web of Life* had been the sole textbook produced by the academy,[13] and while David was president, books in the same genre were produced for chemistry, mathematics, and geology. *Biology: the Common Threads*[14] replaced the *Web of Life*.

The Australian Foundation for Science was launched. The objective at that stage was to raise ten million dollars for this fund, with the main purpose to expand textbook production and to strengthen the academy's financial position.

His presidency was one of strengthening the academy in all its fundamental roles; while expanding its textbook publishing, and putting it in a stable financial position.

Australian Neuroscience Society

Together with Laurie Austin, David initiated the organisation of meetings that brought together active neuroscientists and clinicians to form the Australian Neuroscience Society. The first meeting was held at Monash University in November 1972. Further one-day meetings were held annually under an informal structure, until February 1980, when a formal structure was established. A council was established, consisting of a president, a secretary, a treasurer, an editor, and representatives from each state and from New Zealand. The society has flourished since those days. David was awarded the Distinguished Achievement Award of the Society in 2009.

[11] Blythe (1993).
[12] Full details of this saga may be found in Fenner and Curtis (2001).
[13] Morgan and Best (1967).
[14] Australian Academy of Science (1990).

Family Life

Having met playing tennis, David and Lauri were married in 1950 in Melbourne. Lauri was born in Melbourne in November, 1926. Her parents were bank manager Harold Sewell and his wife Ada. The family lived in East Malvern, and Lauri matriculated from the Presbyterian Ladies College. She trained as a midwife, and when she met David she was running an ancillary service for migrant women.

They had two children: Christopher, born September 1952 in Melbourne, and Belinda, born October 1954 in Canberra. Both children were educated in Canberra. Christopher became a sound engineer for movie productions while Belinda became a social worker. From their marriages, Christopher and Belinda gave David and Lauri four grandchildren and there are six great grandchildren.

Belinda recalls wonderful summer holidays at their cottage by the beach in Broulee. David loved the beach and was a keen body surfer. In Canberra, the family went on regular bush walks. Dinners at home with overseas visitors were common. Jeff Watkins recounts the many happy times he dined there eating 'spaghetti bolognaise, a Lauri speciality, washed down with copious quantities of good wine'.[15]

Lauri loved to paint, and David framed her paintings. Her other hobbies were tennis, music, gardening and cooking. David was an avid tennis player. He was also an accomplished pianist. He had a home workshop and loved tinkering. He called himself a Womble.[16] He became a skilled wood-turner and he had an impressive hoard of seasoned timber to work with. During retirement, wood-turning was an important hobby for him.

David relied on a wheelchair for safety after he turned 90. He died in December 2017, aged 91. Lauri died a few months later in May 2018. They were a devoted couple.

Conflicts of interest

The authors declare no conflicts of interest.

Acknowledgements

The authors wish to acknowledge the considerable assistance they received from Belinda Curtis and Jeff Watkins while writing this memoir. The authors received no funds for writing this memoir.

References

Australian Academy of Science (1990) *Biology: the Common Threads*, Canberra.

Blythe, M. (1993) 'Professor David Curtis, neurophysiologist', in 'Interviews with Australian scientists', https://science.org.au/learning/general-audience/history/interviews-australian-scientists/professor-david-curtis, viewed February 2020.

Curtis, D. R. (1964) 'Microelectrophoresis', in *Physical Techniques in Biological Research*, ed. W. L. Nastuk, New York, pp. 144–190.

Curtis, D. R. (1993) 'Early excitement about amino acids', plenary lecture, Australian Physiological and Pharmalogical Society.

Curtis, D. R. (2006) 'David R. Curtis', in *The History of Neuroscience in Autobiography,* vol. 5, ed. L. R. Squire, Burlington, Mass., pp. 171–225.

Curtis, D. R., and Eccles, R. M. (1958) The excitation of Renshaw cells by pharmacological agents applied electrophoretically, *The Journal of Physiology*, **141**(3), 435–445. doi:10.1113/JPHYSIOL.1958.SP005987

Curtis, D. R., and Johnston, G. A. R. (1974) Amino acid transmitters in the mammalian central nervous system, *Ergebnisse der Physiologie, Biologischen Chemie und Experimentellen Pharmakologie*, **69**, 97–188.

Curtis, D. R., and Watkins, J. C. (1965) The pharmacology of amino acids related to gamma-aminobutyric acid, *Pharmacological Reviews*, **17**, 347–392.

Curtis, D. R., Hosli, L., and Johnston, G. A. R. (1968*a*) The hyperpolarisation of spinal motoneurones by glycine and related amino acids, *Experimental Brain Research*, **5**(3), 238–258. doi:10.1007/BF00238666

Curtis, D. R., Hosli, L., and Johnston, G. A. R. (1968*b*) A pharmacological study of the depression of spinal neurones by glycine and related amino acids, *Experimental Brain Research*, **6**(1), 1–18. doi:10.1007/BF00235443

Fenner, F., and Curtis, D. R. (2001) *The John Curtin School of Medical Research*, Gundaroo, NSW.

McPhee, P. (1999) *Pansy: a Life of Roy Douglas Wright*, Melbourne.

McPhee, P. (2012) 'Wright, Sir Roy Douglas (Pansy) (1907–1990)', in 'Australian Dictionary of Biography', **18**. http://adb.anu.edu.au/biography/wright-sir-roy-douglas-pansy-1068/text26066, viewed February 2020.

Morgan, D. G., and Best, E. W. (eds) (1967) *Biological science: the web of life*, Canberra.

Valentine, E. (2005) *The War of the Soups and the Sparks*, New York.

[15] J. C. Watkins, Canberra, pers. comm., April 2018.

[16] Wombles are fictional burrowing animals who help the environment by collecting and recycling rubbish in creative ways.