CSIRO PUBLISHING

Historical Records of Australian Science, 2018, **29**, 51–55
https://doi.org/10.1071/HR17024

Lawrence Walter Nichol 1935–2015

Peter D. Jeffrey[A], *Donald J. Winzor*[B] *and Philip W. Kuchel*[C,D]

[A]John Curtin School of Medical Research, Australian National University, Canberra, ACT 2601, Australia.
[B]School of Chemistry and Molecular Biosciences, University of Queensland, St Lucia, Qld 4072, Australia.
[C]School of Life and Environmental Sciences, University of Sydney, NSW 2006, Australia.
[D]Corresponding author. Email: philip.kuchel@sydney.edu.au

Lawrence (Laurie) Walter Nichol FAA was Vice Chancellor of the Australian National University (ANU) from 1988 to 1993, and before that, of the University of New England (UNE) from 1985 to 1988. His independent academic career began in 1963 at the ANU as a Research Fellow in the Department of Physical Biochemistry in the John Curtin School of Medical Research (JCSMR). The department was headed by Professor Alexander (Sandy) G. Ogston FRS. Thus, Laurie's career finally circled back, after overseas sabbaticals and other appointments at Australian universities, to the ANU.

Published online 19 January 2018

Early Years

Lawrence (Laurie) Walter Nichol was born in Adelaide on 7 April 1935 to Mavis and Lawrence Nichol, the only son in a family of six children. He attended Norwood High School where in the final examinations of Year 12 (Leaving Honours) he topped the state in chemistry. He was the first in his family to attend university. Financial considerations dominated his decision to enter Adelaide Teachers College for his tertiary education; and the completion of a BSc in three years (1953–5) enabled him to study for an honours degree in physical and inorganic chemistry during his fourth year. The possibility of majoring in physical chemistry had become a realistic option at the University of Adelaide midway through Laurie's undergraduate study with the arrival from Nottingham University College (then still part of the University of London) of a new head of department, Professor D. O. (Doj) Jordan[1] at the beginning of 1954, as well as his former graduate student, Dr J. M. (Mike) Creeth a year later.[2]

Doj Jordan was an expert in the emerging chemistry of the DNA molecule, and his interest in life sciences had given the department an exciting biological twist, which was also reflected in new staff appointments. Laurie and his close friend and fellow BSc student, Donald (Don) Winzor,[3] were enthused by the potential application of chemical reasoning to biology. The location within the department of a Beckman Spinco model E analytical ultracentrifuge (transferred from Nottingham), and a newly acquired Spinco model H electrophoresis and diffusion apparatus, set the technical/analytical scene for Nichol's and Winzor's postgraduate entry into the biophysical chemistry arena.

Because of his commitment to the South Australian Department of Education, with its additional requirements for education coursework, Laurie was teamed up with Don Winzor, for a joint honours project under the supervision of Mike Creeth. This entailed modification of the model H optical system to attain the level of precision in diffusion measurements required for an envisaged goal of using deviations from Gaussian spreading behaviour as the ultimate criterion of protein homogeneity with respect to size and shape. Those studies on isoelectric ovalbumin plunged both honours candidates unwittingly into the field of interacting systems by virtue of the need to consider the flux of solvent components as the result of solute diffusional flow, even under conditions of constant solvent chemical potential.

In overview, their work used sophisticated mathematical theory of physical chemistry to begin to characterize large biological molecules.

Secondary School Teaching and PhD Candidature

In 1957, after gaining first class honours in physical and inorganic chemistry, and despite not completing his diploma of education,

Laurie began secondary-teaching duties at Woodville High School, in suburban Adelaide. However, he returned to the Physical and Inorganic Chemistry Department in 1958 as a senior demonstrator with a commitment to begin PhD study with Mike Creeth. The emphasis of Laurie's research switched from what he did in his honours project to the physicochemical characterization of jack bean urease. This emphasis prevailed after a nominal change of supervisor to the head of department (Doj Jordan) necessitated by Creeth's departure in early 1959 to take up a readership at the Lister Institute of Preventive Medicine in London. Of the four publications that emerged from Laurie's PhD thesis, two were on the ovalbumin work carried out in conjunction with Don Winzor during his honours project and the other two were on urease. The latter two papers provided the first detailed physicochemical characterization of urease by establishing that its pronounced heterogeneity with respect to molecular weight reflected the oxidation of sulphydryl groups that was slow on the timescale of its ultracentrifugal migration.

Upon submission of his thesis at the end of 1960 (PhD awarded in 1961),[4] Laurie travelled to the USA on a Fulbright Scholarship to work with Professor Gerson Kegeles at Clark University in Worcester, MA.[5] Trans-Pacific travel on the maiden voyage of the P&O liner *Oriana* introduced him to his future wife Rosemary (daughter of Madeline and John White). They married in early 1963 on his return to Australia and remained happily married, raising three sons, for more than 50 years.

Field of Work and Influence

The two years as a postdoctoral associate with Kegeles were pivotal in defining Laurie's professional life, in that most of his time had been spent writing a landmark review article on the migration behaviour of interacting protein systems. It was the first review of the field to incorporate the ground-breaking contributions made by G. A. Gilbert and R. C. L. Jenkins (University of Birmingham) on the migration of systems consisting of proteins in rapid association-dissociation equilibrium. The writing of this review article formed the foundation of his future scientific interests, namely the quantitative characterization of rapidly reversible protein interactions between similar or dissimilar macromolecules (including proteins and nucleic acids) and how low molecular weight ligands perturb such equilibria.

Early Academic Career

Laurie returned to Australia in late 1962 to take up a post-doctoral fellowship in Canberra with Professor Sandy Ogston,[6] the recently appointed inaugural head of the Department of Physical Biochemistry in the John Curtin School of Medical Research (JCSMR). Laurie had chosen to pursue research in the general area of the physical-chemical descriptions of biological phenomena and was very impressed by what Ogston had to offer in this respect.[7]

With this clear sense of direction, by the middle of 1963 he had re-commenced collaboration with Don Winzor, who had also recently returned to the CSIRO Wheat Research Unit in Sydney after a twelve-month postdoctoral associateship at Cornell University with Professor Harold Scheraga. It was during this time that Don had also entered the field of interacting-systems with his remarkable invention, frontal size-exclusion chromatography.[8] This was a new method for the quantitative characterization of reversible protein self-associations. The initial extension of the technique developed at Cornell to corresponding studies of reversible association between dissimilar proteins revealed that the Gilbert–Jenkins treatment of the migration of interacting systems could be regarded as a manifestation of the Johnston–Ogston effect, with the protein interactions now governed by the law of mass action rather than by physical factors.[9] This revelation had the beneficial effect of challenging Ogston into a concerted resumption of his investigations into the characterization of interacting protein systems.

In 1966, Laurie moved to the University of Melbourne to take up a Senior Lectureship in the Russell Grimwade School of Biochemistry, where his brilliant lecturing abilities came to the fore. Successful supervision of his first graduate student, Warwick Jackson, as well as assisted supervision of Kerin O'Dea and Geoffrey Smith, facilitated promotion to a readership at the University of Melbourne. This paved the way for his return to the Australian National University in 1971 as the successor to Sandy Ogston as Professor of Physical Biochemistry in the JCSMR. PhD students at ANU included Geoffrey Howlett (who transferred with him from the University of Melbourne), Peter Baghurst, Philip Kuchel, Bruce Milthorpe and Alan Mark (see Table 1).

PhD Supervisions

Of the work carried out with his PhD students, five papers spring to mind as epitomizing what most engaged Laurie's scientific interests. His most highly cited paper is based on an idea that occurred to him during an undergraduate lecture, delivered at the University of Melbourne in 1966. It is the idea that a monomeric enzyme might polymerize to yield a more active form; and that the extent of polymerization and hence catalytic activity is under the control of a low molecular weight ligand that acts like a molecular switch: an idea developed with PhD student Warwick Jackson.[10]

Laurie's emerging interest in quantitative frontal chromatography was based on the fact that it provided an alternative and much simpler tool than the analytical ultracentrifuge to study protein–protein interactions; or to study conformation changes that altered the hydrodynamic properties of proteins in various physicochemical environments. A fine example of this is a short note in *Nature* with PhD student Peter Baghurst.[11] The paper contains an elegant demonstration of the decreased elution volume of bovine serum albumin reflecting its expanded state in a low pH medium ('acid expansion').

The theme of protein polymerization and how this is perturbed during sedimentation in a centrifugal field linked Laurie's expertise in ultracentrifuge theory and his discovery of the modulatory effects of polymerization on enzyme activity. A quintessential paper in this regard is one with PhD student Geoff Howlett.[12]

Laurie's interest in the enzyme urease never left him; it had served him well as a model protein to explore general effectors of protein–protein interactions, but its kinetics had not been of direct interest since others had already extensively explored this. After all, it had been the first enzyme to have been crystallized, by J. B. Sumner in 1926, earning him the 1946 Nobel Prize in Chemistry. After examining a PhD thesis on the kinetics of coupled enzyme-catalyzed reactions and how interactions between enzymes might modulate the overall flux through the reactions Laurie decided, with Peter Jeffrey, to begin supervising a study of the coupled kinetics of arginase (from calf liver) and urease (from jack bean). This was admittedly

Table 1. MSc and PhD Students of Laurie Nichol

Student	Degree	Conferring University	Year of Graduation	Later/Last Appointment
Warwick Jackson	PhD	Melbourne	1965	CSIRO scientist, Armidale
Kerin O'Dea	PhD	Melbourne	1967	Professor of Nutrition, Deakin University
Geoffrey Smith	PhD	Melbourne	1968	Associate Professor in Biochemistry, ANU
Geoffrey Howlett	PhD	Melbourne	1972	Associate Professor of Biochemistry, University of Melbourne
Peter Baghurst	PhD	ANU	1973	CSIRO Scientist in Nutrition, Adelaide
Philip Kuchel	PhD	ANU	1975	Professor of Biochemistry, University of Sydney
Bruce Milthorpe	PhD	ANU	1977	Dean of Science UTS, Sydney
Robert Teasdale	MSc	ANU	1977	Director of Nuplant, Queensland
Alan Mark	PhD	ANU	1987	Professorial Fellow of Structural Biology, University of Queensland

an unnatural system. Nevertheless, after the development of the requisite theory to describe the coupled reaction, the work evolved into one in which the operation of the whole metabolic system that generates urea in mammals could be simulated on a computer. This was the first model of this metabolic pathway and, what was perhaps most novel, was the ability to simulate the metabolic profiles (metabolite concentration patterns) seen in babies with inborn errors of this pathway, with PhD student Philip Kuchel.[13] Philip recalls the delight Laurie expressed in learning about the mechanistic basis of these rare inborn errors, with their 'complicated names'; and of course, here was physical chemistry informing medicine on the causes of diseases.

The exploration of ultracentrifuge methodology to study protein polymerization continued to occupy Laurie's mind. A particularly elegant theoretical development with PhD student Bruce Milthorpe, which became known as 'Omega function theory', contains a combination of mathematical-physical reasoning and analysis, with his emerging interest in computer modelling and simulation of experimental outcomes.[14]

Departmental Headship

Laurie's move into pure research at the Institute of Advanced Studies at ANU had been a great loss to undergraduate education. He had been resoundingly successful as a lecturer at the University of Melbourne. Others recall how he was applauded at the conclusion of some of his undergraduate lectures. He supervised a small number of very successful PhD students throughout the early stages of his career; and as noted above, his ex-students, and research fellow recruits, have occupied senior academic positions in biological science faculties through Australia and overseas (Table 1).

During this period in the Department of Physical Biochemistry Laurie's closest collaboration was with Dr Peter Jeffrey such that all his PhD supervisions were carried out jointly with Peter (Fig. 1).

Figure 1. Laurie Nichol as seen by his colleagues and sketched by Peter Jeffrey.

This was a productive arrangement for the students, as by this stage Laurie's personal emphasis had moved entirely to theory, while Peter retained interests and hence the ability to guide developments in both theory and practical experimentation.

Honours and Awards

Laurie's research into the quantitative characterization of protein interactions led to the award of a DSc (in 1974) from the University of Adelaide. Other honours included the David Syme Prize from the University of Melbourne in 1966, and the Lemberg Medal of the Australian Biochemical Society in 1977. He became a Fellow of the Royal Australian Chemical Institute in 1971, and a Fellow of the Australian Academy of Science in 1981. The research carried out with students, post-doctoral fellows and a select set of colleagues (physical biochemists that continued to include Don Winzor, and William H. Sawyer of the University of Melbourne) resulted in nearly 130 publications in international refereed journals, plus two books on interacting protein systems (see Bibliography available as Supplementary Material).

Move into University Administration

During his headship of the Department of Physical Biochemistry at the JCSMR, Laurie also participated in the administration of the Institute for Advanced Studies rising to become chairman of the board from 1980 to 1985. Laurie's drive, self-organization, common sense, and ability to identify the essential elements of a complicated problem, were a great asset to the faculty board of the JCSMR, and the university as a whole. During his time, he developed a flair for, and a liking of, academic administration that led him to seek more senior roles.

His appointment as Vice Chancellor of the University of New England came in 1985. This move to Armidale also gave scope to Rosemary's interests in supporting social activities in the university, and in running what is one of the most idyllic university residences in the country. Of course, this move ended his active research career but it enhanced his administrative qualifications and led to a return to the ANU as Vice Chancellor in 1988. This position he held during times of radical change in the overall Australian universities sector and that weighed heavily on him, until his retirement in 1993.

JCSMR Publishing

Laurie's prodigious memory, algebraic ingenuity and persistence were a formidable combination in his theoretical approach to the analysis of macromolecular interactions in biological systems. His contributions to the understanding of such interactions received international recognition and played a large part in putting this area of research and the discipline of physical biochemistry on the scientific map in Australia. The application of mathematically based theory, notably algebra and calculus, allied with physical methods, to biological systems (which defines physical biochemistry) gained enormous impetus from the Nichol era in the JCSMR. Over 250 papers were published in scientific journals by members of the Department of Physical Biochemistry during this time.

The great majority of Laurie's publications were from the time when he was at the JCSMR: 16 were from when he was a Research Fellow from 1962 to 1966, and 81 were from when he was head of department from 1970 to1985, giving a total of 97. He gave generously of his fluent and persuasive lectures that publicised the subject to scientific groups in Australia and overseas, and to undergraduates at the ANU and beyond. Laurie wore his academic distinction lightly and was an unpretentious and entertaining companion. He enjoyed relaxing late on Friday afternoons with colleagues at the bar in University House for fertile exchanges of research ideas.

Academic Administration Overview

Laurie remarked at the unveiling of his portrait, as Vice Chancellor of the ANU, by Brian Seidel that he saw his position as part of a succession, and that his aim had been 'To help keep the ANU one of the world's great universities'. The university has consistently been listed amongst the top fifty universities in the world since around that time.

In farewelling Laurie on his retirement in 1993, the Chancellor, Sir Geoffrey Yeend,[15] noted that Laurie's six years in the post had been momentous, with many challenges arising from government green and white papers that introduced radical changes to the administration of the tertiary-education sector in this country. Nevertheless, ANU had made significant advances on many fronts. The University Council thanked Professor Nichol for his valuable guidance, wise counsel, and unfailing optimism and good humour during this difficult period.

Retirement

In 1993, Laurie and Rosemary moved to an apartment in North Sydney where they enjoyed the cultural life of the city, and also indulged their passion for travel. Laurie had a lifetime interest in cinema, especially MGM musicals, and was an enthusiastic re-teller of their plots and the careers of the major players. Other long-term interests were stamp collecting, fine art, and Spanish. He would often fill the long hours of international travel by learning Spanish, which he used on frequent trips to Spain with Rosemary.

Successors

Laurie passed away on 29 June 2015 in Sydney, after a short illness. He is survived by Rosemary and their three sons, Scott, Stuart and David, and two daughters-in-law, with grandchildren Jack, Hannah, Angus and Lucinda.

Conflicts of Interest

The authors declare no conflicts of interest.

Endnotes

1. J. H. Coates 'Denis Oswald Jordan 1914–1982', *Historical Records of Australian Science*, 6 (1985), 237–253.
2. The Creeth–Jordan team is best known for the discovery that calf thymus DNA is a double-stranded macromolecule with the two strands linked non-covalently by hydrogen bonds between bases on the two polynucleotide chains (J. M. Creeth, J. M. Gulland and D. O. Jordan, 'Deoxypentose Nucleic Acids: Viscosity and Streaming Birefringence of Solutions of the Sodium Salt of the Deoxypentose Nucleic Acid of Calf Thymus', *Journal of the Chemical Society* (1947), 1141–1145). After those graduate studies with Doj Jordan at Nottingham, Mike Creeth switched his research interests to the physicochemical characterization of proteins, first at the Courtauld Institute of Biochemistry

in London and then in the Department of Chemistry at the University of Wisconsin before his appointment as Senior Lecturer at the University of Adelaide and Reader at the Lister Institute of Preventive Medicine. The demise of the Lister in 1975 led to his transfer to the Departments of Biochemistry and Medicine at the University of Bristol, where he remained until his retirement a decade later. (S. E. Harding and D. J. Winzor, 'James Michael Creeth, 1924–2010', *Macromolecular Bioscience*, 10 (2010), 696–699).

3. D. Hall and S. E. Harding 'Foreword to 'Quantitative and analytical relations in biochemistry'—a special issue in honour of Donald J. Winzor's 80th birthday', *Biophysical Reviews*, 8 (2016), 269–277. On completion of PhD studies at Adelaide Don Winzor moved to Sydney at the beginning of 1960 to join the CSIRO Wheat Research Unit, where he remained (apart from a twelve-month period as a postdoctoral associate of H. A. Scheraga at Cornell University) until the beginning of 1968. At that stage, he accepted a Senior Lectureship in the Department of Biochemistry at the University of Queensland, from which he retired as Emeritus Professor in 2000 (D. J. Winzor, 'Six Decades of Research as a Physical Biochemist', *Biophysical Reviews*, 8 (2016), 279–281).
4. Laurie was awarded a PhD in 1961 on the basis of a thesis that led to four publications: two with Winzor and Creeth as co-authors on the diffusion characteristics of ovalbumin; and two with Creeth on the effect of sulphydryl oxidation on the macromolecular state of jack bean urease. J. M. Creeth, L. W. Nichol and D. J. Winzor, 'Physicochemical Studies on Ovalbumin. 1. Electrophoretic Fractionation and Characterization by Diffusion', *Journal of Physical Chemistry*, 62 (1958), 1546–1553; L. W. Nichol, D. J. Winzor and J. M. Creeth, 'Physicochemical Studies on Ovalbumin. 2. The Effect of Charge on Diffusion' *Journal of Physical Chemistry*, 64 (1960), 1080–1082; J. M. Creeth and L. W. Nichol, 'Evidence for the Chemical Interaction of Urease in Solution'. *Biochemical Journal*, 77 (1960), 230–239; L. W. Nichol and J. M. Creeth, 'Some Physicochemical Properties of Sulphite-Modified Urease', *Biochimica et Biophysica Acta*, 71 (1963), 509–516.
5. Gerson Kegeles rose to international prominence in the 1950s for investigations (originating in the Department of Chemistry at the University of Wisconsin) aimed at improving the optics and hence maximizing the potential of the newly developed Beckman Spinco model E ultracentrifuge for the physicochemical characterization of proteins. Of particular note was his ingenuity in taking advantage of the fact that the conditions for sedimentation equilibrium (no net flow of solute) always applied at the two extremes of the liquid column being subjected to ultracentrifugation. He thus pioneered the use of this Archibald approach-to-equilibrium method for the characterization of reversible protein self-association (M. S. N. Rao and G. Kegeles, 'An Ultracentrifuge Study of the Polymerization of α-Chymotrypsin', *Journal of the American Chemical Society*, 80 (1958), 5724–5729). The reign of this procedure was short-lived because of the realization in 1958 that the attainment of sedimentation equilibrium across the entire liquid column subjected to ultracentrifugation could be achieved in about 24 hours by decreasing the column length from 10 to 3 mm.
6. A. G. Ogston was Reader in Biochemistry at the University of Oxford until his move to Canberra in 1960 to become the inaugural Head of the Department of Physical Biochemistry in the JCSMR. In 1942, he assumed the responsibility for operation of the Svedberg oil turbine ultracentrifuge (A. G. Ogston, 'Life with a Svedberg Ultracentrifuge', *Trends in Biochemical Sciences*, (1977), N208–210 and N219–220): indeed, his introduction to the model E ultracentrifuge was in Canberra. Instrumental in his becoming a Fellow of the Royal Society was a short note to *Nature* that rationalized the observation of enantiomer specificity in enzyme kinetics in terms of the three-point attachment concept for formation of the enzyme–substrate complex intermediate (A. G. Ogston, 'Interpretation of Experiments on Metabolic processes, using Isotopic Tracer Elements', *Nature*, 162 (1948), 963)). This Letter has been cited 432 times in the scientific literature (Google Scholar) and is Ogston's fourth most highly cited work. It is amusing to note that it contains 347 words and symbols and therefore rates 1.24 citations for each of these, which must be something of a record in scientific publishing! It heralded the concept of pro-chirality that was taken up by John Cornforth and Vladimir Prelog, earning them the 1975 Chemistry Nobel Prize.
7. While Laurie had excelled in general chemistry, both at high school (see above) and University (first place in 3rd year Organic Chemistry), his true passion was for physical-chemical theory as applied to biological systems. On surveying the literature for the review with Kegeles and colleagues (see below and Bibl. Ref. 7) Laurie identified those areas of protein-protein interaction that were ripe for study. And, Sandy Ogston had recently published penetrating insights into crowding effects by random arrays of rod-like molecules on the restriction to permeation by spherical macro-molecules (A. G. Ogston, 'The Spaces in a Uniform Random Suspension of Fibres', *Transactions of the Faraday Society*, 54 (1958), 1754–1757); this appealed to Laurie.
8. D. J. Winzor and H. A. Scheraga, 'Studies of Chemically Reacting Systems on Sephadex. 1. Chromatographic Demonstration of the Gilbert Theory', *Biochemistry*, 2 (1963), 1263–1267.
9. L. W. Nichol and D. J. Winzor, 'The Determination of Equilibrium Constants from Transport Data on Rapidly Reacting Systems of the Type A ⇄ B ⇄ C', *Journal of Physical Chemistry*, 68 (1964), 2455–2463.
10. L. W. Nichol, W. J. H. Jackson and D. J. Winzor, 'A Theoretical Study of the Binding of Small Molecules to a Polymerizing Protein System', *Biochemistry*, 6 (1967), 2449–2456.
11. P. A. Baghurst, L. W. Nichol, R. J. Richards and D. J. Winzor, 'A Differential Chromatography Study of Macromolecular Changes Governed by Environmental Factors', *Nature*, 234 (1971), 299–301.
12. G. J. Howlett, P. D. Jeffrey and L. W. Nichol, 'The Effects of Pressure and Thermodynamic Nonideality on the Sedimentation Equilibrium of Chemically Reacting Systems. Results with Lysozyme at pH 6.7 and 8.0', *Journal of Physical Chemistry*, 76 (1972), 777–783.
13. P. W. Kuchel, D. V. Roberts and L. W. Nichol, 'The Simulation of the Urea Cycle: Correlation of Effects Due to Inborn Errors in the Catalytic Properties of Enzymes with Chemical-Biochemical Observations', *Australian Journal of Experimental Biology and Medical Science*, 55 (1977), 309–326.
14. B. K. Milthorpe, P. D. Jeffrey and L. W. Nichol, 'Direct Analysis of Sedimentation Equilibrium Results Obtained with Polymerizing Systems', *Biophysical Chemistry*, 3 (1975), 169–176.
15. J. Farquharson, 'Yeend, Sir Geoffrey John (Geoff) (1927–1994)', Australian National University, *Archived from the Canberra Times* on 2 May 2013.