Some Enduring Memories of Physiology

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My first real contact with Physiology came in 1962 when I had to make a choice between Physiology and Microbiology as second year subjects following on from Biology at the University of Adelaide. I initially chose Microbiology but after the orientation practical class at which the Professor made it perfectly clear that he was only interested in those students who had top distinctions from first year, I switched to Physiology, especially, as I had greatly enjoyed the anatomical and physiological aspects of the Botany and Zoology that made up first year Biology.

Although I didn't exactly star in the Histology part of the subject at second year, I passed it and was all set to proceed to third year Physiology. Unfortunately, one of its two lecture times per week clashed with an Organic Chemistry lecture which I was also taking. When I approached the subject co-ordinator, Dr. David Kerr, Reader in Physiology in the Department of Physiology and Pharmacology, with my dilemma, he was amazingly sympathetic and arranged for another Physiology lecturer, John McNally, and himself to repeat each missed lecture at lunchtimes for my benefit and that of one other student whose lecture timetable was also compromised. Third year Physiology included a significant amount of Pharmacology and practical classes where I had my initial introduction to glass micropipette electrodes (prepared for us by McNally). We used these to measure membrane potentials in toad muscle fibres. At this time, I developed some enthusiasm and pride in what I was doing, having success with the micromanipulation of the electrodes while other students kept on breaking theirs. This was the beginning of a career-long interest in how these devices originally came to be developed and how they have since been used.[1]

With my BSc completed, the South Australian Government Teaching Scholarship that I held demanded that I spend three years teaching high school, but here my interest in Physiology paid off as Kerr asked if I would like to do Honours. Some negotiation with the South Australian Education Department enabled me to defer the teaching and a small University Research Grant, as a scholarship, kept the wolf from the door. Before going off for summer holidays and returning for the Honours year, Kerr loaned me the American Physiological Society's *Handbook of Physiology, Section 1: Neurophysiology, Vol. 1* and suggested that I read Chapter 1, "The historical development of neurophysiology", by Mary A. Brazier. This had a powerful influence on me, not least Brazier's account of how Alexander von Humboldt studied and repeated the experiments of Volta and Galvani, who were in serious disagreement about nerves, muscles and electrical stimulation. Galvani was attempting to explain all aspects of his results in terms of intrinsic animal electricity and Volta, everything in terms of dissimilar materials in contact with each other. As well as repeating their experiments, von Humboldt also designed new experiments to test their interpretations and determined that

both were correct in certain of their conclusions and incorrect in others. Galvani's work led into the science of electrophysiology and Volta's to the inspiration for the electric battery.

For my Honours year, I was confronted with the task of determining sarcolemmal capacitance and resistance in the presence and absence of chloride. Otto Hutter and S.M. Padsha, his first PhD student, at the Physiology Department, University College London, UK, had not long before published results of the effects of nitrate substitution for chloride in the Ringer solution bathing frog muscle. In similar anion substitution experiments, Gertrude Falk and her colleague Jorge F. Landa from the Pharmacology Department at the University of Washington, Seattle, USA, used intracellular glass micropipette electrodes to show repetitive action potential activity when ferrocyanide replaced chloride. My project was to duplicate the simpler external electrode equipment of Hutter and Padsha and to test the effects of both permeant and impermeant anions on toad muscle. In the process, I learnt how to write letters to international experts, such as Hutter, for advice and comment, and then made modifications and improvements to his experimental method.

At the end of first term it was suggested that I attend the Monash Meeting of the Australian Physiological Society, to be held on the 20-22 May, 1964. I travelled overnight second-class return (sitting up) from Adelaide to Melbourne by train with Michael (Mick) Roberts. This was the same Michael Roberts after whom the AuPS Excellence in Physiology Education Award is named (he became the more formal "Michael" from about 1980 after returning to The University of Adelaide from extended periods in Melbourne and Leeds, UK). In 1964, Roberts was just finishing up his BDSci Hons year working with Antanas (Tony) Stepanas similarly completing his BMedSci Hons. These dental and medical science Honours years ran mid-year to mid-year, and so, Roberts and Stepanas actually had results of their Honours project to present at the Monash APS meeting. With no significant results for me to report after just three months, I went along as an observer. I learnt a lot, however, from the talks I attended that were presented by some extraordinary researchers including, Liam Burke, David Curtis, Mollie Holman, Paul Korner, Victor Macfarlane, Archie McIntyre and Michael Taylor.

During the meeting, most out-of-town visitors stayed in the Monash University College student accommodation on campus. One evening, John McNally suggested that we join the New Zealanders, John Hubbard and Peter Gage, in one of the rooms where they were holding something of a large and noisy party. Gage at the time was doing his PhD supervised by Hubbard at ANU. I guess that other "young gun" physiologists may also have been present, possibly Max Bennett, Brian Johnstone, Bob Rodieck, Mark Rowe, Ann Jervie Sefton, Jonathan Stone and John Young, but I really only remember these others from later APS and APPS meetings.

Sticking in my mind, particularly, from the meeting were the presentations by Hubbard and Gage on aspects of neuromuscular transmission, by Ian Pugsley on measurement of tip diameter in so-called "Ling-Gerard type micro-electrodes" and by Victor Macfarlane on sodium and potassium levels in body fluids of the Chimbu of the New Guinea Highlands. The last seemed especially interesting given the almost complete lack of salt (NaCl) in the diet of

the Chimbu but the high concentration of potassium in their mainly vegetarian diet. Equally impressive to me was the report by Mollie Holman, Archie McIntyre and John Veale that one impulse in a single afferent nerve fibre was sufficient to evoke a cortical response even in a deeply anaesthetised animal – a story that I recounted to my neurophysiology students throughout my teaching career.

Another profound memory from that meeting was being driven by John McNally (who must have come to Melbourne by car) and Peter Dellow with Mick Roberts (Dellow was his Honours supervisor) to the practically new Southern Cross Hotel for a pre-dinner drink followed by dinner at a, then famous, Chinese restaurant in Little Bourke Street, the Mei Wah. Dellow, and perhaps also McNally, had eaten there before and immediately ordered the restaurant's signature dish, Steamed Duck with Lemon Sauce and Bean Sprouts along with a giant serve of special fried rice. Only once since have I tasted any Chinese dish as good as that delicately lemon-gravied, succulent duck, decorated with rainbow strands of pickled ginger, and that was a few short years later, eating the identical meal at the same restaurant. Unfortunately, it closed soon afterwards.

Back in Adelaide's Physiology Department, I completed my Honours year, learning how to give Departmental seminars. On one occasion, being something of a show-off, I gave my seminar on firefly bioluminescence. I was able to source taped copies of the songs, "Glow Little Glow Worm" and "You Are My Firefly", using these on my reel-to-reel tape recorder to open and close my presentation. In between, I outlined as much as was known of the luciferin-luciferase reaction and its neural control in the firefly abdominal lantern. A flask containing a luminol solution, a sterile lancet, a finger prick of my blood and presto – cold light magically produced in the darkened seminar room – my chemiluminescent imitation of a firefly. Apparently, my seminars were well received, my small Honours thesis deemed satisfactory and I passed the end-of-year examinations, all well enough to earn a First Class.

With a bond of some £2,500, owed to the South Australian Education Department as a result of my Teaching Scholarship, I now had to pay it back or work it off by teaching for three years. With no hope of paying the debt, I went High School teaching through 1965 and did what I was told. With my Honours degree in Physiology, I taught Maths and English to year eight boys, Chemistry to year nine girls and, with unexpected success, Physiology to a mixed class of year eleven Science dropouts. At the end of that year, David Kerr offered me a Tutor/Demonstrator position back in the Physiology Department and the possibility of undertaking a PhD. With one year of my bond worked off, the Education Department allowed me to defer full payment of the remainder provided I repaid a nominal amount per month.

My PhD project proposed and supervised by Kerr was to discover the importance of chloride to the electrical characteristics of muscle using glass micropipette electrodes in the isolated rat diaphragm. From this point, my personal battle with the preparation and filling of glass micropipette electrodes began. In those days, glass capillary stock was inconsistent, varying in diameter and wall thickness. Since no one else in the Department was doing research with microelectrodes, I had to discover this for myself and learn to pick through and measure each piece to get consistent pipette shapes and resistances. Also, the supply voltage to the Medical

School varied, as I found, so that I needed to use a Variac (variable transformer) and voltmeter to set a constant voltage for my home-made electrode puller each time I prepared electrodes. I became paranoid about all this, monitoring the room temperature, the atmospheric pressure and holding my breath (to avoid draughts) while each pipette was pulled. Finally, adequate filtration of filling solutions was a problem so that I could often be seen muttering like one of the witches in Macbeth over low pressure boiling of electrodes in methanol and then in cold 3M KCl.

Notwithstanding the many unusable batches of electrodes and the variation from usable to unusable within a single batch, I began to get results. I recorded resting potentials and electrotonic potentials as well as action potentials in the isolated rat diaphragm at various temperatures. Initially, I was using Krebs solution, but soon noticed differences between my results and those of others and began to suspect that some of the dissimilarities might be due to variations in the compositions of the solutions they used to bathe their isolated mammalian muscle. This led me to question the whole foundation of Krebs's, Tyrode's, van Harreveld's and Ringer's solutions, all based on empirical concoctions or erroneous, obsolete interpretations of what kind of solution bathed living tissues *in situ*. With encouragement, especially from Sandford (Sandy) Skinner and Lawrie Mashford, I made my own measurements of the plasma concentrations of sodium and potassium in rat blood and gathered the best available evidence of the free concentrations of other ions and of plasma glucose and protein levels. Then using trans-capillary Donnan equilibrium values, I was able to make a best estimate of the composition of mammalian interstitial fluid and to prepare a synthetic version for use as a tissue bathing solution for my experiments. This was published in *Life Sciences* (after being rejected by *Nature* as being of insufficiently broad interest) in 1969.[2] It has since been widely and continuously used to bathe isolated mammalian (including human) muscle, skin containing sensory nerve fibres and other tissues. I had been encouraged to send my manuscript to *Nature* by Michael (Mike) Tyler, then a technician in the Department. He was an avid amateur naturalist without a formal qualification but who already had a number of publications, at least one of which was in *Nature*. Tyler subsequently became one of the best-known herpetologists in Australia, New Guinea and the South Pacific for his extensive research on frogs in the region.

One of the features of APS meetings were afternoon demonstrations showing off experimental techniques, new and innovative equipment, and practical class teaching methodologies. At the 1967 Adelaide meeting, organised by Mashford, I demonstrated the measurement of calcium ion activity in solutions using an Orion Specific Ion Meter and calcium specific, liquid ion exchange, electrode, the first of its kind in Australia. This was to prove invaluable in my synthetic interstitial fluid validations. Two of these fluids, one containing chloride as control and the other with chloride replaced by 3,5-diacetamido-2,4,6-triiodobenzoate (at constant calcium ion activity), were then able to be used to determine the importance of chloride to muscle. Sulphate that had been used as an impermeant anion in earlier research greatly suppressed calcium activity in physiological bathing solutions, low plasma calcium levels being well known to cause the spontaneous neuromuscular contractions know as "tetany". Chloride absence, itself (at the same calcium ion activity as in

the control chloride solution), initiated a different state in muscle, equivalent to that in the naturally occurring disease of humans, goats and other animals, known as myotonia in which action potentials and, consequently, contraction continued in muscle long after nerve or electrical stimulation ceased. Not only was I able to model myotonia in the isolated rat diaphragm (presented at the Monash APS meeting in May 1969) but I could also explain it in terms of a drastically increased membrane resistance due to virtual elimination of chloride conductance. Furthermore, mathematical modelling of the squid axon action potential after Hodgkin and Huxley and that of the muscle fibre after Adrian and Hodgkin, showed that a modelled muscle would produce repetitive action potentials (myotonic activity) if the membrane leakage conductance (ascribed to chloride) was greatly reduced. The same did not occur in the modelled squid axon although repetitive action potential activity (equivalent to veratrinic action) could be produced if the sodium conductance parameters were modified. At this time, most membrane physiologists/biophysicists were obsessed with sodium, potassium and calcium ions, and their involvement in cellular electrical phenomena, in excitation-contraction coupling, in excitation-secretion coupling and in synaptic transmission. My "lone-voice" research on chloride was considered somewhat eccentric at APS meetings.

During the mid to late 1960s the Adelaide Physiology Department tea-room was always a site of philosophical-physiological discussion with topics ranging from the possibility of man-powered flight to whether the Americans would, actually, get their astronauts into space on their apparently unreliable rockets. Of course, in mid-July 1969 we were all glued to the television in the tea-room to watch Neil Armstrong set foot on the moon. We also argued about what might be our chances of establishing a marine biological laboratory on the coast and whether a cannibal could consume and utilise the experiences and memories of the cannibalised. Already in 1968 we were fishing for squid, *Sepioteuthis australis*, off Hallett Cove in Gulf St Vincent, and, back in the lab, I was recording action potentials from the giant axon in artificial seawater with chloride and with chloride replaced by methylsuphate using glass micropipette electrodes. Also, I had a colony of planaria ready to go, to try to duplicate experiments in which minced, trained planaria had been fed to naïve planaria where it was claimed that memory was thereby transferred from the trained to the naïve animals. Within a very short time, this wild claim was rapidly extinguished, just as a trained response is, after strong negative conditioning.

We had brief visits from internationally renowned Physiologists, including the egotistical Ralph Gerard from Chicago, of "reverberant circuit memory and more permanent engram" fame, who, notoriously, did not invent the "Ling-Gerard" glass micropipette electrode although he claimed that he had and indicated that he had subsequently been nominated for the Nobel prize for doing so.[1] Justifiably famous Physiologists visited for extended periods including Robert (Bob) Elsner (the "diving response" in diving mammals) and Per Scholander (the Scholander apparatus for determination of blood gases) from Scripps Institution of Oceanography in La Jolla, San Diego, USA. These two were attracted to Adelaide by that grand old researcher, Lt Col. David Hugh (Lemmy) Le Messurier who ran the Physiology Department's aeromedical lab and who, among other things, had been responsible for developing the diving tables used by SCUBA divers of the Australian Navy to

determine their rate of return to the surface after diving to given depths – these to avoid developing "the bends". For us, Le Messurier had different claims to fame. He owned an abandoned stone windmill (flour mill) tower near Goolwa that he had converted to multi-story holiday accommodation and another holiday house at Blinman in the Flinders Ranges. To these, for memorable dinners, overnights or weekends, he invited friends and groups of graduate students. Kerr and Dellow, too, were generous hosts. Kerr and his wife Nancy treated us, his graduate students, to fine formal dinners while Dellow, the bachelor, was consummate in teaching us how to feed ourselves from his informal table of excellent cheeses, meats, breads, fruits and salad vegetables. While Kerr was a stimulating supervisor and knowledgeable on almost every topic from aeronautics, computing and electronics, through neuro-anatomy and neuro-physiology to music, Dellow was a provocateur, continually inciting me to read more widely and to broaden my mind by leaving pointed, intellectual quotations in my mailbox.

The Adelaide Department of Physiology and Pharmacology in 1968. Mentioned in the text are: In the front row, John McNally, 1st on left; Hugh Le Messurier, 3rd from left; Robert Elsner, 6th from left and David Kerr, 7th from left. In the 3rd row: Michael Roberts, 4th from left; Michael Tyler, extreme right. In the 4th row: Leon Le Leu, first on left; Allan Bretag, 3rd from left; Robert Morrison, 6th from left. Others of note in regard to APS/APPS/AuPS include, in the front row, Robert Whelan (Head of Department), 5th from left, and Derek Frewin, 9th from left; in the 2nd row, Eugenie Lumbers, 2nd from left and Barbara Dennis, 8th from left; in the 3rd row, Richard Head, 9th from left. Of these, Barbara Dennis, David Kerr and Hugh Le Messurier attended the Inaugural APS Meeting in Sydney in 1960. Inset top right is a photograph of Peter Dellow.

Throughout this period, I was also influenced by fellow graduate and Honours students. Among these were Robert (Rob) Morrison[3] who introduced me to the University Footlights Club where I worked backstage and built sets. Leon Le Leu[4] helped me build a primitive hang glider (see image below) hanging from which I was the first ever to fly horizontally for any distance (rather than plummeting vertically straight down in superman suits and cardboard biplane replicas) at any Adelaide University students' annual Bird Dropping

contest up to that time, leaping from the University footbridge into the Torrens River. Doug Freckelton[5] , with his Mirror dinghy, hooked me on a permanent addiction to sailing.

Allan Bretag piloting his bamboo and polythene "paper plane design" hang glider from the Adelaide University footbridge into the River Torrens during the 1968 "Bird Dropping" contest.

The APS/APPS meetings we attended were memorable for many reasons, not only their scientific aspects but also for their social occasions and for the many interesting characters whom I met. Lawrie Mashford's organisation of the 1967 Adelaide meeting was outstanding in the latter regard. For example, an incomparable spread of meats, cheeses, salad vegetables, breads, condiments, fruits and nuts, accompanied by a selection of South Australia's finest wines, was provided for the Welcome Reception. Later versions in other cities have paled into insignificance. On the other hand, some Society members in other cities were notable for their generosity, and that of their wives, in hosting extravagant dinners for out-of-town visitors at their houses during meetings.

As at the first APS meeting that I attended, there were also many lesser, but nevertheless unforgettable gatherings well oiled by cheap flagons of red wine. One of these was at the ANU meeting in May 1968. I had driven over in my Morris Mini Minor with Rob Morrison and Doug Freckelton and we were staying at the Canberra Lakes Carotel. Armed with three-quarters of a flagon of red, we had driven off somewhere one evening for the usual party but, perhaps because there was plenty of alcohol present, we left our flagon in the car, where it must have come close to freezing in the typical Canberra winter's night. On returning to our accommodation, we retrieved the flagon and took it into our nicely heated room. In the

middle of the night a loud clink and the sound as of gushing water woke us to an exploded flagon and our precious wine all over the floor. The next year, I drove to the Monash meeting. Again, there was a party, and at its end there were nine people who were stranded without transport back to our University College accommodation. With Ivan de la Lande (Adelaide's Reader in Pharmacology) lying flat, crammed up against the Mini's roof and held above the heads of the eight others of us who were sitting on seats and laps, I proceeded to drive steadily, dangerously and illegally back to the College.

Knowingly leaving out dozens of others, some of the stand-out persons, not earlier mentioned, whom I've met at these conferences have included, Helena Parkington and Harry Coleman, who rode motorcycles from Melbourne to interstate meetings, Annick Anselin, who turned out to play that most unusual musical instrument, the carillon, David Megirian, who lived half way up Mt Wellington in Tasmania and at whose house I first heard that animals other than humans also suffered hiccups *in utero*, Uwe Proske, who worked on the electro-sensory mechanisms of the bill of the platypus, Angela Dulhunty, who I saw as something of a later competitor after she also began studying the electrical characteristics of muscle and the effects of chloride on them, Dirk van Helden, who surprised me by showing that tiny lymphatic vessels were not passive sewers, Owen Hamill, who later became famous for accidentally discovering the "inside-out patch" in patch clamping, Peter Bishop, whose demonstrations of single cortical neuronal activity associated with directional movement of a light bar across the retina, and of inhibitory surrounds, fascinated me, and Lauren Marotte, who was stunningly beautiful and whom I could easily have fallen for at the 1967 Adelaide APS meeting except that Richard Mark seemed to have first dibs. I think that I came across Sir John (Jack) Eccles only once and that would have been at the 1964 Monash meeting, where, if I'm not wrong, he was made the first Honorary Member of the Society. Although some people hardly deigned to acknowledge my existence, many others, not already remarked on, were always friendly and prepared to chat, among these were Bob Porter, Steve Redman, David Curtis and Derek Laver from ANU, Stella O'Donnell and Jan Wanstall from UQ, Wilf Simmonds and Malcolm Sparrow from UWA, Mollie Holman and Rod Westerman from Monash, Dave Davey and Chris dos Remedios from Sydney, "Darty" Glover (who introduced me to Old Bushmills Irish Whiskey), Peter Gage and Mark Rowe from UNSW and, later, Graham Lamb from LaTrobe.

At these APS/APPS meetings of the 60s and 70s, a question time of five minutes typically succeeded oral presentations, when the "elders" in the congregation would pose difficult questions causing younger presenters to answer softly to cover their uncertainty. Whenever this happened, Melbourne's Physiology Professor, R.D. (Pansy) Wright, in his deep, gravelly voice, would shout out from the audience something that sounded like "Konntyeer!" (Can't Hear!). Wright gave the after-dinner address at the 1982 APPS Conference Dinner which I wish had been recorded as it was the most pertinent, entertaining and amusing that I've ever heard. As noted in his biography, Wright "was more brilliant than other academics……and more passionate. Above all, he was funnier."[6]

In 1970, I married Lesley Byers (who had been one of the Adelaide University Footlights Chorus Girls) an Arts/Psychology graduate and High School teacher. Although I had not

completed writing up my thesis, “Muscle Cell Membranes and Chloride Ions”, I was offered a lectureship teaching Histology and Physiology at the School of Pharmacy in the South Australian Institute of Technology (SAIT).[7] I took this job in the knowledge that it offered stability but with trepidation, fearing that my research career would have to be abandoned for teaching. At the end of my first year of lecturing and finally submitting my thesis, I felt an urgent need to do something practical and built my own Mirror sailing dinghy, much to the annoyance of Lesley who felt that I was neglecting her in favour of another woman (I was naming the dinghy Galadriel after the Lady of the Woods of Lothlórien in the Lord of the Rings). While on shaky ground with Lesley (and not the smoothest of seas) we managed to ride out 1971, waiting for my thesis to be examined and my premonition about not being able to do research at SAIT being realised. All was not lost, however, when I was encouraged by Kerr to apply for a Postdoctoral Fellowship from the Alexander von Humboldt Foundation which I was awarded and was allowed 15 months of leave without pay to take it up in Homburg/Saar, Germany.

Meanwhile, my mathematical modelling of myotonic action potentials in muscle was noticed by Byron Kakulas at the University of Western Australia who was organising the Second International Congress on Muscle Diseases to be held in Perth in November, 1971. He invited me to present my work at the Congress and suggested that I seek funding to attend from the Muscular Dystrophy Association of South Australia. This I did and afterwards, feeling indebted, worked for them in various voluntary capacities as Board Member, Vice President, President (from 1975 to 1985) and Director of Research to the end of 2018.

Lesley and I travelled to Homburg/Saar at the end of December 1971 where I worked on nodes of Ranvier with Robert Stämpfli who had, himself, earlier worked with Andrew Huxley to elucidate the mechanism of saltatory conduction in myelinated nerve fibres. We spent three weeks before and over Christmas 1972 in Edinburg and Cambridge, UK, where we met up with Richard Adrian and Shirley Bryant. Bryant had brought several myotonic goats with him from Cincinnati, USA, and was waiting to get them through quarantine. Later they recorded repetitive action potentials from the intercostal muscles of these goats and Adrian produced a mathematical model, similar to the one I had developed for my PhD, showing, not only how the repetitive firing of action potentials arose but also how it would spontaneously die away.

Our first daughter was born soon after our return from Germany in 1973 and this was followed by a period of homemaking. As well, although I had obtained a set of Nonner/Stämpfli voltage clamp equipment, my ability to undertake research at SAIT was severely restricted by my teaching load and the fact that SAIT did not award higher degrees, so I could not take on any Honours, Masters or PhD students. For a long time, I could only manage intermittent use of my equipment and was rather confined to theoretical calculations that I could easily lay aside and get back to when I found time. This is where I made mathematical models to describe the delay in onset of potassium conductance (known as the Cole-Moore effect) in response to a voltage step. At the time, there was a considerable interest in “subunits” that appeared in the electron microscope to make up cell membranes. My modelling of co-operative interacting subunits extended that of John Tille, who suggested

that particles at adjacent ion conducting sites might have to interact causing the Cole-Moore effect. I gave a presentation on this at the 1975 APPS meeting at ANU.

Over the next several years, Lesley and I added two more daughters to our family, we personally built half of each of two different houses which included hands-on bricklaying, carpentry, digging a cellar, laying a 50 square metre jarrah floor and tiling a roof. In between, we had the year from mid-1977 on sabbatical, revisiting Stämpfli in Homburg/Saar, learning how to voltage-clamp isolated single muscle fibres with Oger Rougier in Lyon, France, how to use the three-microelectrode, end-of-fibre voltage clamp with Adrian[8] in Cambridge and how to work with intercostal muscle biopsies from myotonic humans and goats with Bryant in Cincinnati, USA (experience gained in Bryant's lab later stood me in good stead regarding research I undertook and published on muscular dystrophy in sheep and rippling muscle disease, Torbergsen's Syndrome, in humans). Also, by taking on vacation scholars, working with them over long vacations, and co-supervising a few graduate students from The University of Adelaide, I managed some publications on muscle chloride and myotonia. This culminated in invitations from Physiological Reviews to referee a review of "Membrane Changes in Cells from Myotonia Patients" by Reinhardt Rüdel and Frank Lehmann-Horn and then to write a review on "Muscle Chloride Channels".[9] Eventually, in 1990, SAIT became the University of South Australia (UniSA) after which I had access to my own graduate students, post-doctoral fellows and ARC research grants. At this time, my title changed from Principal Lecturer to Associate Professor of Physiology (promotion to Professor occurred in 1997).

Long-distance collaboration with Thomas Jentsch and Michael Pusch in Hamburg, Jie Zheng in Davis, USA, and, closer to home, Michael Roberts and Christopher (Chris) Bagley at The University of Adelaide, along with Bernard (Bernie) Hughes at UniSA, and outstanding graduate students who included Trevor Lewis, David Astill, Deanne Hryciw (later Skelly), Edoardo Aromataris, Brett Bennetts, Michael Duffield, Jennie Cederholm, and Linlin Ma, as well as post-doctoral fellows, especially Grigori Rychkov, saw a dramatic change in my ability to undertake and supervise research. Jentsch was especially helpful in providing us, in 1992, with a clone of the rat skeletal muscle *ClCN1* gene so that we could express the channel protein and study it in Sf9 insect cells in tissue culture. My initial intention was to express it in large quantities, purify if and crystallise it for X-ray crystallography. This never eventuated due to extensive cytoplasmic fragmentation of the protein, none-the-less, we were able to determine structure-function relationships by patch clamping the channel in the surface membrane of the Sf9 cells after expressing site-directed mutants. Shirley Bryant, of myotonic goat fame, also visited for an extended period of pharmacological research on the expressed channel. On this occasion he did not need to bring any of his goats. Publications, almost all relating to ClC-1 and myotonia, flowed. During this time, I and my student and staff collaborators greatly enjoyed the Curtin Conferences, arranged by Gage in Canberra in the style of the Gordon Conferences in the United States. We presented our research at many national and international meetings and organised our own Annual Adelaide Ion Channel Conferences. Significant ion channel research was being undertaken in Adelaide in the 1990s,

in my group at UniSA, as well as, in Biology at Flinders and in Physiology and Botany at Adelaide Universities, and, also, at the Waite Research Institute.

Bryant chasing his myotonic goats in 1974 and with Carol Beck who sequenced the goat ClC-1 channel in 1996

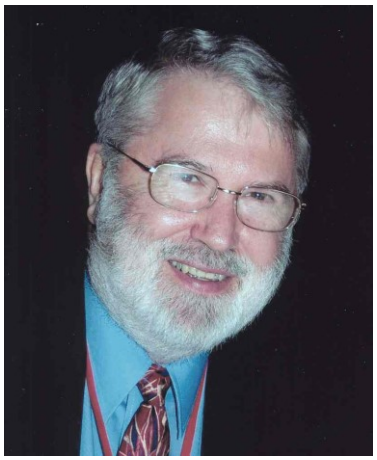
In 1997, I was the local organiser of the Annual Scientific Meeting of APPS held in Adelaide that year and in 1998, I organised the IXth International Congress on Neuromuscular Diseases also held in Adelaide and attended by ~850, mainly international, delegates. Among other roles, I have been President of the World Alliance of Neuromuscular Disorder Associations (WANDA, The Hague, 2007-2015) and a Member of the Executive Board of the Asian and Oceanian Myology Center (AOMC, Tokyo) since 2002.

My output of refereed research publications and their citations can be found on Web of Science, Google Scholar and ResearchGate. My most recent research has been in the area of the History of Science with several articles published as a result of presentations at Symposia of the Australian and New Zealand Associations of von Humboldt Fellows. One of these [10] published in 2015, has already been "read" more than 275 times on ResearchGate.

Over the years, my students and colleagues and I have collaborated on some 40 joint research presentations at meetings of APS/APPS/AuPS and ~100 at meetings of other Australian and International societies. In 2014, I was privileged to be awarded Honorary Membership of AuPS, having attended my first meeting of the Society 50 years earlier and joined as a financial member soon afterwards. In 2017, I received the Distinguished Fellow Award of the Australian Association of von Humboldt Fellows.

I am not only proud of these achievements but also acknowledge those of my wife, Lesley, who assumed the major responsibility in raising our daughters and simultaneously undertook graduate studies in Applied Psychology to become a highly respected Educational Psychologist, Clinical Psychologist in Private Practice and, finally, a Psychologist and Student Counsellor in the Health Service at Flinders University. Our daughters are also a source of considerable pride. Tess is an Educational Psychologist, Emmy, a General Practitioner, and Nina, a Pharmacist. Nina and her husband Arnie, a General Surgeon, have given us two beautiful grandchildren.

Overall, I can't emphasise strongly enough the support, encouragement, friendly provocation and camaraderie that I enjoyed as a student and young researcher from my fellow students, from my lecturers and supervisors and from Physiological Society members at meetings. It is all of this that I am so grateful for and hope that I have managed to reciprocate in some small part. No young researcher, now, has a permanent position offered to them in the way that I was, so appropriate mentoring is that much more important.



Allan Bretag

Notes:

1. Bretag, A.H. The glass micropipette electrode: a history of its inventors and users to 1950, J. Gen. Physiol. 149, 417-430 (2017) [published by invitation as a "Milestone in Physiology" and already "read" well over 400 times on ResearchGate]
2. Bretag, AH. Synthetic interstitial fluid for isolated mammalian tissue. Life Sc. 8, 319-329 (1969). [~250 SCI citations to March 2020]
3. McFee, P. Wright, Sir Roy Douglas (Pansy) (1907-1990). Australian Dictionary of Biography, vol. 18 (2012)
4. Professor Robert Morrison, OAM, after his on-stage performances in Adelaide University Footlights Club Reviews, later became famous for his role in the nationally and internationally renowned, "The Curiosity Show".
5. Dr Leon LeLeu, FAFOM, after helping me build that hang glider, is now, in complete contrast, an Occupational Health Specialist in Canberra.
6. Doug Freckelton, after teaching me the joys of sailing, is now, not surprisingly, President of Sailability Graceville, Queensland.
7. My first job at the South Australian Institute of Technology was to develop and teach a year-long course in Histology for Laboratory Medicine students and to lecture in Physiology to a mix of Allied Health students. Despite my poor grasp of the Histology component of Physiology when I was a student, I grew to greatly

enjoy teaching histology and loved helping my students learn how to set up their microscopes correctly.

8. Lord Richard Adrian had just been admitted to the House of Lords on the death of his father, Lord Edgar Adrian. Richard Adrian was very busy in London with his new appointment leaving Carlo Caputo and me to perform three-microelectrode-end-of-fibre-voltage-clamp experiments on frog muscle in his absence. After several months we had some very interesting results all recorded on film because only the voltage-clamp protocol was computerised. Unfortunately, we left the film development to the end and when, we processed it, we found that every record was contaminated with what appeared to be serious 50 cycle AC interference. This had been invisible on the oscilloscope screen and when finally shown to Adrian, he apologised saying that he had forgotten to tell us that the camera oscillated in resonance with a cooling fan in the equipment rack. He had made a special wooden prop that fitted between the rack and the camera to avoid the issue but had taken it out for some reason. Our work was, therefore, unpublishable, although I was able to give a presentation on it at the 1978 Flinders University APPS meeting.
9. Bretag, A.H. Muscle chloride channels. Physiol. Rev. 67, 618-724 (1987) [~240 SCI citations to March 2020]
10. Bretag, A.H. Myotonic diseases since Asmus Julius Thomas Thomsen (1815-1896) and Peter Emil Becker (1908-2000). Proceedings of the Royal Society of Victoria 127, 59-65 (2015)