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Australian Academy of Science - Science education
Interview with Professor David Curtis

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Professor David Curtis, neurophysiologist and former president of the Australian Academy of Science, was interviewed for the Australian Academy of Science's *Video Histories of Australian Scientists* program in 1993. The interview was conducted by Dr Max Blythe of the Medical Sciences Video-archive of the Royal College of Physicians and Oxford Brookes University in the United Kingdom. Here is an edited transcript.

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List of edited transcripts.

Family background: no biology

David, you were born in Melbourne in 1927 – a child of the '30s, really. Tell me about your parents and your early years.

I was a child of the Depression. We lived comfortably but we weren't very well off. My father was a communication engineer for the PMG's Department, and of course Public Service salaries took a crash during the Depression. Both my grandfathers were building contractors, and I grew up with a family

workshop both at home and with grandparents. I guess the decision to do medicine was somewhat strange, because I didn't do any biology at all until I went to university.

Were you close to your family?

I was very close to my mother and father. It was quite a wrench to leave home to go to university and then to be completely separate during the three resident years at hospital. My younger brother did agricultural science and now lives in Sydney. Both parents came from very large families, and we had so many cousins and second cousins that we never met a lot of them. But the contacts we did have were great. It was a very nice family to be born into.

School: mathematics and science but still no biology

And you went to school at Melbourne High School in its classical days?

Yes, when that and University High were the only selective high schools in Melbourne. We did one year at the main school building until the war broke out, when the school was turned into naval headquarters for Victoria. What an ideal place: the school was next to the major railway lines, so if anything had ever happened the naval headquarters and the railway lines would have gone!

Did any particular people on the staff turn your mind towards your future career?

I had a leaning towards mathematics, I think largely because of primary school and central school teaching, and I was fortunate to have masters at Melbourne High in mathematics, applied maths, physics and chemistry who were very distinguished teachers. The school had a reputation in those science subjects, and also in geology, for getting Exhibitions at the examinations. The idea was that if you didn't get the Exhibition at the end of the year, the school was in disgrace.

The mathematics master, Black, later had a very distinguished career in the Air Force Academy, which belonged to Melbourne University. Ferris, the physics master, eventually became the senior physics teacher at Scotch College. And Richards was an outstanding chemist who had a PhD but decided to remain teaching. Fortunately, in fifth and sixth years at high school we had the same masters going through. There were good labs and good assistance – excellent support all round.

Medical school: biology at last, plus billiards and snooker

You took those mathematical and scientific foundations with you to medical school at Melbourne University.

Yes. In those days at the end of the war, to get into the major schools at the university you had to matriculate in particular subjects. Having the right kind of subjects, I could do either engineering or medicine, and I couldn't make up my mind between them. I was offered a scholarship for engineering, but just the day before that I was offered one for medicine, and I had already signed the letter.

I still had a yearning, in first year, to attend – illegally – some of the mathematics lectures, but there really wasn't time. And I was having to catch up on biology. Biology wasn't taught in boys schools then, being something that girls did. So zoology and botany in first-year medicine were really the first introduction to a biological career.

First year was relatively simple, because this was a transition period from the old Leaving Honours years to Matriculation, and our high school teaching had been at a much higher level than first-year medical physics and chemistry. The year was largely spent catching up on biology and learning to play billiards and snooker – which was a wonderful thing later, during off hours at hospital.

Did you enjoy the biological sciences?

I did enjoy the biology, even though it was fairly pedestrian in those days. Anatomy was superb, biochemistry was superb, physiology wasn't the most brilliant department and I survived that. My chief fame in two years of physiology, I guess, was to have written an essay that was so bad that one of the demonstrators thought she should show it to the professor, Panzy Wright. Later on he was a very great friend of mine, but I never reminded him about that.

Syd Sunderland, who was an outstanding neuroanatomist, was the major influence on me. He gave brilliant lectures in neuroanatomy, which was just beginning to get together the wiring of the system. Nothing was known about how it worked. I think my interest in the nervous system developed from that kind of beginning, because the physiology was very primitive at that stage.

Linking theoretical and clinical medicine

You went on to the clinical courses. Was Melbourne University a good place to be in?

It was an excellent place. On the results of your preclinical years you could select the hospital you wanted, and I was chosen for the Royal Melbourne, just across the road from the university. So you could still keep university life while you were at the hospital, whereas in the outerlying hospitals – particularly the Alfred Hospital, at the other end of town – that wasn't so easy. There was only one medical school in Melbourne at that time, so we had a year of 160. I think 120 graduated. It was a very good period. Because of the war

the six-year course had been condensed down to five years: the course wasn't changed but we lost a lot of vacations. That was five years' hard work, but it was fascinating and it gave the opportunity in the last couple of years to spend more and more time at the hospital.

What kind of people made impact on you in the clinical field at that stage?

During my two years at the Royal Melbourne – the first year as a junior resident, the second as a senior resident – there were a few general surgeons and general physicians that put me off surgery and medicine as a career for ever. I did a couple of locums in general practice at odd times, I enjoyed working with patients and I was fascinated by clinical medicine, but I decided that sick people weren't going to be my problem forever.

The interest in the nervous system was reinforced by good contacts such as with Graham Robertson, the hospital neurologist. He'd spent a period at Queen Square and was a colleague of Denny-Brown's. The neurosurgeon was Reg Hooper, another Australian, who trained with Cairns and then came back to Melbourne. They were very supportive. They had to put up, for the first time ever, with having a junior resident in there running their 30-bed ward, whereas they'd always had registrars or much more senior people. They invited me back for the next year – a good sign, I thought. The hospital was very friendly, with a very good atmosphere and good people to work with.

'You watched that technique'

Largely, if you were going to go on in clinical medicine or clinical surgery, you had to sit for either the College of Surgeons or the College of Physicians, doing first-part examinations and second-parts. Most of us during our second-year residency were attending lectures at odd times for the first part, and the university had a lecture series to which it invited people to come.

In about 1952, during my second year, Jack Eccles was invited down to Melbourne to give a lecture. I'd never heard the likes of that before: it was on the latest kind of work being done on the nervous system – work still in press and being published. I don't think many people understood it, but I'd been doing a lot of reading from Sherrington and Eccles and all of those books, on stuff which seemed to have been building up naturally to this development. I think I was the only one who asked any questions at Eccles's lecture and then stayed to talk to him.

We got chatting, and I inquired simply what were the chances of doing this kind of research – and particularly of coming up to Canberra, because he was then just setting up with the ANU. He asked me who I was working with at the hospital and how I was enjoying it, but his answer to my simple question was, 'When can you start?' Well, I could have started the following day, but I had an obligation to finish that year at the hospital. Then delays in building the

laboratories here in Canberra caused me to spend another year in Melbourne. I landed a job at the Alfred Hospital – again as neurological and neurosurgical registrar – in a very distinguished group.

The neurologist was Leonard Cox, a self-trained neurologist; his assistant was John Game, who had spent some time at Queen Square; and the neurosurgeon was Hugh Trumble, who had been a general surgeon. When orthopaedics became a discipline, he became the orthopaedic surgeon, and then when neurosurgery became necessary he became the neurosurgeon. He was incredible – an outstanding person, a genius as a surgeon. He didn't like buying instruments but he liked making them and he made all his own. He called them 'jiggers', and a lot of them didn't have other names.

And you watched that technique.

You watched that technique, and you had to know which jigger he wanted when he wanted a jigger! His theatre sister was fine; she knew it all. But if you were operating with him at the weekend when there was a lass that wasn't used to it, it was, 'Not that jigger, girl. That other bloody jigger!'

So it wasn't wasted time, but very exciting?

That's so. It was full-time work, none of this 40-hour or 60-hour week.

I am impressed that the Alfred and the Royal Melbourne had such good neurology and neurosurgery teams.

Neurosurgery and neurology has been very well established in Australia. Sydney had the first Chairs in neurology, but the standards in Melbourne have been very high too. For many years the neurosurgeons and neurologists used to have their annual general meetings in Canberra, and I've kept in touch with people there. Douglas Miller, for example, is a very old friend. I'm a member or an honorary member of both the societies, as well.

Playing around with tetanus toxin

You came then to Eccles two years later.

We came here on February 16, 1954. The labs were still building. They were prefabricated huts that were only going to be there for a couple of years, but they're still there. They were ideal for the kind of work we could do, because we could take walls down, cut holes in the floor and so on. We worked in those huts till '57, when the new building was opened.

Who had Jack Eccles got with him at that time?

Jack had very few people. It was a problem of not knowing exactly when the

labs were going to be finished. Eventually, Paul Fatt went back to Bernard Katz at University College, and Sven Landgren, a Swede from the Karoline Institute, went back to Sweden and then had the Chair at Umeå, a very northern university there. Vernon Brooks joined us a bit later on from Canada, and went back to London, Ontario. In the workshop, the electronics engineer was Jack Coombs, an outstanding person who had been senior lecturer in physics in Dunedin when Eccles was there. It was a stage after the war when a lot of surplus equipment was becoming available from the Services, so it was really the beginnings of using cathode ray oscilloscopes and electronic devices, and Jack designed all of the early equipment for Eccles. A lot of the things that we did in those days were impossible anywhere else because they just didn't have the equipment. We had a very good engineering shop, we were able to design our own frames for animals and manipulators, and with my engineering interest I was able to join in with that. I learnt a lot there.

Perhaps you'd tell me a little bit about your PhD studies.

I started on a PhD in February, and I put in my thesis in just under two years, I think. The work was a combination. The main technique that Eccles and Coombs really pushed into neurophysiology was the use of glass microelectrodes to record from single cells, so I was able to get that technique fairly quickly. Then we looked at some of the simple kinds of things that were needing to be done.

With Brooks and Eccles we became interested in tetanus toxin. Eccles's work in New Zealand in 1949 and the '50s had established fundamental differences between synaptic excitation and inhibition, and we had known for some time that strychnine, which is a convulsant, had a very specific effect in blocking inhibition. Before that it was not clear what it did, because it could have enhanced excitation, but we had a nice pharmacological tool to dissect inhibition. Because tetanus is a similar convulsant to strychnine, although much more subtle, we then played round with tetanus toxin for a while. We showed that it did much the same as strychnine, but we weren't quite aware in those early days precisely what it was doing. (We developed other techniques later on.)

Then we had a minor incursion into trying to isolate transmitters from brain. We used to go out in the early hours of the morning to the abattoirs at Queanbeyan, collect fresh brain, freeze it and bring it back here, and try and find transmitters. The idea was to fractionate these and then to find out what these fractions did to the nervous system. It was a waste of time, really, although it taught us a lot of how not to do things. We didn't understand much about biochemistry and the biochemists didn't understand much about the nervous system. With all of the departments being new and developing, everybody wanted to go and do their own thing rather than get into multidisciplinary research.

The aspirations were right?

No, I think a lot of it was just basic pigheadedness and ignorance. We wanted to look at the brain, but it was the wrong way to do it. A lot of these transmitters are destroyed within milliseconds, and there's no way you can collect it like this.

Pharmacological tunes

What did you do after your PhD?

I was working closely with Jack. By about 1958 I had developed a technique for administering very small amounts of drugs near particular cells. That was really a development from some of the work that Katz had been doing in London, but also Bill Nastuck had started it up in America. It's a matter of having a compound in aqueous solution in a glass pipette, of knowing something about its nature and fixing the pH so that the bit you are interested in is either an anion or a cation, controlling it by means of electrical currents to stop it leaking out, and passing it out when you want it.

I was fortunate that double-barrel electrodes (just two tubes fused together) had been developed by Paul Fatt, who was working with Eccles. They were using these electrodes to record from cells – one barrel to record and the other to pass current through. They were pretty crude electrodes but later we persuaded the glassblower to take a round tube and put a partition in it, and then pull it down so we had a theta glass. By the time we were wanting to look at the pharmacology of single cells we were getting greedy, so eventually an English glassblower made for us five-barrel electrodes: a centre one with four around it. By the mid-'60s we were even more greedy, and it was easy to put six around a single one and have sevens. We developed the idea of cementing another electrode on the outside of this so that we could have a single or a double barrel inside a cell and the six or seven outside to play pharmacological tunes on it and get lots of information.

Exploiting acetylcholine

It was a good period. Other people were investigating the mechanism of synaptic excitation and inhibition, and electron microscopy was developing, so that you could appreciate what was going on at synapses with the morphological machinery; but also neurochemistry was developing. Neurochemistry, to me, is two disciplines. One is the design of organic compounds to affect the nervous system. The other is really neuro-biochemistry, understanding what is going on in the living brain. We didn't make major contributions to that aspect but it was being done elsewhere. It was a matter of refining analytical techniques, of being able to look at the concentrations of particular compounds, like some of the amino acids in a certain area, and then to do this after lesions had been made to particular

pathways and see if the amount of a particular substance fell.

We were able to exploit acetylcholine because of experiments which Eccles, Fatt and Koketsu – a Japanese who was visiting the department – had done here in the early '50s. There was a little system in the spinal cord that could have involved acetylcholine. The motor neurone sends its messages to muscle in the periphery with acetylcholine, and just before the motor axons leave the spinal cord a little collateral goes back and tickles up some cells. Paul Fatt had the brilliant idea, 'Well, if acetylcholine is released at the far end, it is likely to be released at this little terminal,' so they went looking for these cells. They were able to show that, if they administered drugs intravenously or intra-arterially, the pharmacology of that synapse was similar to the neuromuscular junction. But unfortunately acetylcholine itself, which is the transmitter, didn't get through the blood-brain barrier, so there was a gap.

Rose Eccles – Jack Eccles's daughter – had come back from doing a PhD in Cambridge and had become interested in this, so we looked at that system first. In retrospect we were very lucky, because it was a ten million to one chance that the system was acetylcholine, but we could play pharmacological cadenzas on that cell, developing our technique.

Fitting excitants into the amino acid collection

David, I know you got very interested in amino acid transmitters, and they have been a major part of your work.

The amino acids came into it when Geoff Watkins joined us. We built on biochemical knowledge obtained in the States, by Gene Roberts and his people, of the possibility that gamma-aminobutyric acid might be a transmitter. It was shown very simply to be an important inhibitory transmitter in Crustacea, and in Crustacea strychnine is not a convulsant but picrotoxin is. (That is another drug that was used clinically for convulsive therapy.) With the Roberts story of this GABA perhaps being a transmitter in the crayfish, and with a lot of GABA in the human brain, we had a beginning, because we knew picrotoxin convulsed cats and people.

But we had great problems there, because we could show that GABA had an inhibitory effect on cells when we squirted it out of our electrodes but we could never get picrotoxin to block it. We were well aware of the problem: because it is not ionised, it doesn't come out of the electrodes. That story had to wait to be developed till the early '70s: after Geoff Watkins had left us and Graham Johnson had arrived, we stumbled upon bicuculline as another convulsant, which was a very effective GABA antagonist. But before that, with Geoff Watkins, we had become interested in all of the amino acids we could lay our hands on. I should think I've got the largest collection of useless amino acids in the world, still in my cupboards.

We were able to show that GABA and glycine and related neutral amino acids – where the acidic group was carboxylic or sulphonic or sulphinic – inhibited cells, and that the dicarboxylic acids related to aspartate and glutamate were excitants. And that was something. The excitatory effect was new. We weren't aware of it, but a Japanese called Hayashi had thrown a massive amount of glutamic acid into the cerebral cortex of dogs some years before and they convulsed. We could have used tap water or potassium chloride or anything, but it was interesting that this was a compound which was known to be in brain and excited cells. We didn't know about this for some time, but we went on looking and collecting amino acids. They were fascinating but we just didn't think they were very important – we were a bit naive, a bit stupid.

I'd thought that cholinergic and adrenergic transmitters were the be-all and end-all.

The work with acetylcholine showed us that that was wrong, in the spinal cord anyway: only this Renshaw cell synapse was cholinergic – using acetylcholine – whereas acetylcholine didn't affect anything else. A major turning point was in '65-'66, when an American group reported that the amount of glycine in the spinal cord fell remarkably if they destroyed a lot of the inhibitory interneurones. This immediately linked glycine up as a possible inhibitory transmitter. They also showed that glycine affected neurones the same way as the inhibitory transmitter. We rapidly confirmed that, but in addition we had strychnine up our sleeve, knowing it should be doing something in that system. It very clearly blocked the effect of glycine.

Using antagonists to investigate transmitters

That put us back into business on gamma-aminobutyric acid, because that led, in another five or six years, to bicuculline and a lot of alkaloids that were not glycine antagonists but were antagonists of GABA. This was useful for our chemical colleagues, because we were able to analyse the glycine receptors and GABA receptors not only by playing tunes on them with a number of glycine and GABA analogues but also through the effects of strychnine-like and bicuculline-like compounds. Some very fascinating chemistry came out of that.

Penicillin, for example, is a GABA antagonist, and it was known a long time ago that in patients where penicillin had been used for, say, a cerebral abscess and had leaked out into the cerebrospinal fluid, this was a convulsant. Fortunately, penicillin doesn't get through the blood-brain barrier, so it doesn't normally have this action.

It is exciting to find critical areas like the brain massively regulated by amino acid transmissions.

Well, the story with the excitant amino acids was also confused. We didn't

think they could be transmitters because there's so much of them around. The brain contains a massive amount of glutamate – it's about 10 millimole if you just boil a bit of brain – and it seemed to be evenly distributed. Aspartate is distributed unevenly, and that gave us a clue. But with Watkins and then with Johnson we were able to use a vast number of other glutamate and aspartate analogues, some of which were naturally-occurring compounds, whereas others had been synthesised to be conformationally restricted, because glutamate and aspartate are very flexible. It dawned on us when we were finding different sensitivities for different neurones to a group of amino acids where we knew the structure, and we tried to relate this to the idea that glutamate might be the excitory transmitter for primary afferent fibres coming into the spinal cord and aspartate could be the transmitter for cells that belong inside the brain.

Geoff Watkins went back to England in '65, taking it up as his life work to develop antagonists for glutamate and aspartate. We kept on working with Johnson and also with the group in Denmark led by Krogsgaard-Larsen, but the Watkins group was far ahead. Eventually they and other groups have developed very specific antagonists, so that glutamate and aspartate now are recognised as the most important transmitters.

For years I used to call acetylcholine and noradrenaline and dopamine, 5-hydroxytryptamine, minor transmitters, and of course this upsets anybody who's working on them. But most cholinergic synapses in the brain are muscarinic and atropine is an antagonist. Although animals are as psychologically disturbed as we are by atropine, they can still walk around and do things, whereas if you give an animal either bicuculline or strychnine they're convulsing and they're different citizens altogether. And the amino acid antagonists, if they get through the blood-brain barrier, are very powerful depressants.

So there are major and minor systems, and really these other transmitters play background themes. They are very important, of course. For example, dopamine is a transmitter in parkinsonism and needs to be replaced with L-dopa. But they are a background regulatory mechanism.

Practices and limitations in animal use

You mentioned parkinsonism. Have you kept a strong interest in neurology and in drugs that might be used as inhibitors in important clinical contexts?

Yes. I keep aware of the neurological literature and attend neurological meetings and international meetings. We kept well away from parkinsonism because our animal facilities in those days did not enable us to have monkeys or higher primates, and it is impossible in cats and most other laboratory animals to produce anything like parkinsonism. The way L-dopa works is still a very confusing story, not by any means clear-cut. But it works, particularly

with the decarboxylase inhibitors. The fashion now is neuronal transplantation, which seems to be a complete waste of time.

I know there is a big lobby against the use of animals, but a lot of this very sophisticated research would never have come anywhere without the use of animals.

You really can't investigate and understand the brain unless you have got the brain in a reasonably intact animal. We have always been careful of our animals, and in 1969 the NHMRC published the first code of practice for the use of animals for experimental purposes. That was prepared by a committee led by Archie McIntyre, who was then chairman of the Department of Physiology in Monash. I have been on several committees that have since revised it and brought it more up to date, and the CSIRO and the state agricultural departments have been brought into the system. So there is now a booklet accepted all over Australia about the care and use of animals in experiments and in teaching, even including the breeding of animals and the training of technicians. Until recently we really haven't had major problems in Australia with animal liberation, even though Singer at Monash has created quite a stir with it. I think Australia has been much more aware of the problems than, say, the UK or the United States.

Transmitter release mechanisms: the odd effect of baclofen

By the '80s I think you had begun to work with some drugs that reduced inhibition.

We became interested in transmitter release mechanisms. Once you have got the transmitter, the way to do something about, say, a deficiency or an excess is to understand the release mechanism. We had earlier looked at baclofen, a drug which Ciba-Geigy developed in the early 1960s and patented, thinking it was a GABA analogue that would get through the blood-brain barrier. A lot of these amino acids, including glutamate, don't get through the barrier – which is just as well. Having developed this drug they found it had fairly specific effects on spinal reflexes, and in clinical trials it was found to be effective in patients with spasticity from spinal cord problems. It is used clinically now in multiple sclerosis and when there is spinal cord injury after trauma. It is no use at all in cerebral spastics, because the mechanism is entirely different.

We became interested in this because it was a GABA analogue but it didn't seem to do what GABA did. We showed that it wasn't activating the bicuculline-sensitive GABA receptors. And then in the late 1970s we were able to get hold of the optical isomers. We had realised with the amino acids that sometimes there were vast differences between the two optical isomers. It is not so apparent with glutamate and aspartate, but with some of the N-methyl derivatives and some of the other more complicated ones there is a marked difference. We, and others, found that it was the minus-baclofen which was

important. At that stage, we and some other groups found that it was specifically reducing the amount of certain transmitters, particularly the transmitters released from the terminals of sensory fibres. That has now led us into a major investigation of the properties of synaptic terminals within the spinal cord, and we feel that baclofen is having an effect of reducing the amount of calcium passing into those terminals, that then leads to reduced transmitter release.

That opens up an important range of prospects for clinical care.

Yes. This drug is useful, but I think this observation can be built upon to design drugs which will have similar effects but at other synapses. The nervous system, or the spinal cord, has got two major kinds of synapses apart from their being excitatory and inhibitory. It's got the terminals of cells that grew out of the neural crest. These cells are essentially outside the spinal cord and fibres grow in, so the cells are used to an extracellular environment very different from what is in the brain. And the other cells that develop from the neural tube stay in the nervous system and talk to each other. There seems to be a difference in the transmitter release processes of these two types of cells. There is no doubt that both involve calcium, because we can block them with fairly non-specific calcium antagonists like cadmium and some of the heavy metals. But baclofen has an odd effect on these cells.

I'm still working on that, although I don't think I'll ever solve it. The Ciba-Geigy people are fascinated by it too. We've just finished a study of a vast number of antagonists of baclofen, which are quite remarkable compounds that usually don't have any effect on normal animals.

An appreciation of Jack Eccles

Perhaps you could tell us about some people from those research years, beginning with Eccles.

I worked with Eccles from early '54 through to about '57-'58, until our interests diverged: he stayed in straight neurophysiology and processes there – after the spinal cord he became interested in the thalamus, the cerebellum and cortex – and we moved more into the chemical direction. He was not easy to work with but incredibly kind to me. He held my hand at the beginning, and after that there were no real restrictions placed on what I wanted to do. It was a stage when the department was expanding, when there was an adequate amount of money for equipment and for people. Each of the departments in the John Curtin medical school had a structure of about 11 people, but it would go up and down. He was able to attract a remarkable number of people from abroad to do PhDs or post-docs with him, and even after we diverged he was very supportive of my plans to develop neuropharmacology, to get chemical colleagues to come into the then department of physiology. He is an incredible, outstanding person.

What kind of a personality did he wield at the bench and in his administrative work?

Administration was always done very quietly; we didn't see much of it. It was remarkable that he was developing this department virtually at the same time he was developing the Academy as one of the Founding Fellows. Mark Oliphant was President. They were meeting very regularly to plan this building and were interacting with the government to get the Academy accepted as a source of advice. Also, Jack was on the governing body of University House.

It was an incredibly active period for him but he had his finger on the pulse in the lab and was always there for experiments. But in those days, although we started experimenting at, say, 8 o'clock in the morning, the animal wasn't into the recording room till after dinner at night, so there was all day to get it ready. Now if I can't get it in by lunchtime I don't think it's worth working on any further! Once a cat is anaesthetised, it is not quite the same animal as you started with, and this affects the brain and transmission processes.

We used to work all night then. We lived about three or four miles away but we didn't have a car till we'd been here three or four years, and many a time I'd ride home in the frosty morning, about 6 o'clock, having worked from the previous 8, and then have a shower and breakfast, go back and again work all day. We'd do that two or three times a week, and Jack would be doing that as well. It was an incredible learning experience. But having lived in a hospital environment, when I only had every third Wednesday afternoon off and one weekend in four, from noon on Saturday till 9 o'clock on Sunday night, this was easy, I thought! And you were doing what you liked to do, at your own rate. You weren't at the beck and call of everybody else.

You have stayed friends with Eccles over the years.

Yes. He went to the States – Chicago and later Buffalo, where I visited him – and then he settled in Switzerland. Until recently we have kept in touch and he has been interested in what we are doing. I went to his 90th birthday celebrations this May, in Frankfurt, but he wasn't very well. I think his health is not as good as it might be.

Collaborations and contributions

Another memorable person you have worked with is Katz.

Yes. Bernard was interesting. He was passing through Colombo when war was declared, and was nearly incarcerated there. He worked with Eccles in Sydney at the Kanematsu Institute, and was then in the Australian Air Force as a radar officer out in one of the forward islands. Bernard came out from England on a quick trip around Australia, to visit some colleagues and see some old friends,

when Rose Eccles and I were doing our first experiments on Renshaw cells. Bernard doesn't like animal experimentation and all of his work has been done on isolated tissue, particularly frogs, so whenever we would start working on a cat he would go for a walk and come back when we had it all set up and covered up, and he was happy. We learnt some nice little technical tricks from him, and we've kept in touch ever since. He's made some magnificent contributions to the biophysics of synaptic transmission.

I know you feel he has been a mentor in some ways.

Yes, especially through his papers and the fact that I could always write to him.

Any other people we should mention in particular?

Well, clearly Watkins and Johnson from the chemical point of view. The area has been so interesting and so diverse and wide that I don't think one person could do the whole thing. We do the animal work and the equipment – we design a lot of our own equipment and make it, in fact – and they've looked after the chemical side.

These collaborations are difficult and can't last forever. Everybody wants to do his own thing. Geoff Watkins went back to England because he wanted to live there again – first to Carshalton and then to Bristol, where he's retired but still working (he still has an MRC grant). And Graham Johnson got the Chair of Pharmacology in Sydney in 1982. We've kept in touch and I've collaborated with other chemists, but never on site because with changes in the department and in the structure of the school there hasn't been such an opportunity to get new people in.

Disturbing times at the John Curtin School

David, the whole of your research career has been lived at the John Curtin School. You got a personal Chair there in 1966, I think, just a year after being elected a Fellow of this Academy.

That's right. It was a personal Chair in pharmacology. Shortly afterwards Peter Bishop took over as head of the Department of Physiology, and the personal Chair was separated from physiology and turned into neuropharmacology in about '68. In 1973 I was appointed head of the Department of Pharmacology, which had been on the books virtually from the beginning of the school but had been delayed. Then, in '88, the school created divisions instead of departments, and I became temporarily head of the Division of Neuroscience until I took up the directorship in 1989.

A directorship in the Institute is not an easy job. I took it on largely because the school and the university had been so good to me. It was to be until the end

of 1992 (when I would be retiring) on the understanding that there was no time then to do anything dramatic about the school because the Institute of Advanced Studies was to be reviewed. There was really no way they could advertise for an external director to come in on a five- to seven-year appointment, not knowing if that might continue after the review.

A committee chaired by Sir Ninian Stephen was set up to review what the Institute had done and its place in Australian tertiary education, and to make recommendations about the future. It was thought that the review report would be in fairly general terms, but unfortunately for the medical school the report suggested very specifically that we were not playing our proper place within medical research in Australia and that the school should be separated from the university as an independent body – still on the university campus but funded for research by the National Health and Medical Research Council. That would have meant that instead of our having a block grant, the various groups and individuals would have to apply to be funded for research projects or even programs. This wasn't accepted at all by the school and the university council was very unhappy: it would lose its autonomy in running an Australian national university, because the funding would come from a different source. There were disturbances, and concern even among people outside the university.

Through Senator Tierney, the future of the school was eventually referred to the Senate Standing Committee on Education, Employment and Training (one of the major Senate standing committees). After lots of submissions and a number of days' sittings and inquiries, the Senate said fairly firmly that the review was not carried out properly. But on a 4:3 vote, the chairman voting with the government, it was decided to leave the funding where it was, because the minister had already transferred our $16 million from his education portfolio to the Department of Health – though not directly to the National Health and Medical Research Council, which at that stage was within the Department of Health. So the money now comes in via the Department of Health. There is to be another review of the Institute in 1995, and people are gearing up to prepare submissions. I just hope that everything will go back to the Department of Education. But perhaps in the next review another research school will be ripped out of the university.

I suppose it would be an understatement to say that in that period of preparing documents for the Senate and of the report coming out you were busily engaged.

It was a terribly busy time. There was a lot of concern among people within the school – particularly our young people but also tenured people – for their future. Although we had kept the ratio of tenured staff to non-tenured down to about 45 per cent, the proposed grants and program grants threatened to be quite a change. There was also the question of how the support staff, who had tenure within the university, were going to cope with being on three-year

grants. It was a very disturbing period. You really needed to be a Mother Superior, a confessor and everything, because there was a lot of general unhappiness in the school.

New directions at the Academy of Science

I'll turn now to a happier period: your Presidency of the Academy of Science from 1986 to '90. That must have been an interesting and fruitful time.

It was an interesting time. I can't really judge how fruitful it was – you can't do that yourself. You need to look back at it from the future and see what it looks like.

A lot of things happened. We were fortunate that the negotiations for acquiring Ian Potter House had been put in motion, particularly by Bede Morris and Arthur Birch, but there were lots of things to be done with that. There were major changes in the secretariat, reorganising so that the Academy could interact a lot with government departments and with ministers – not the kind of operation I enjoy very much but we just had to do it.

There were also the beginnings of the Australian Foundation for Science, an important venture. We thought at great length about taking on responsibility for collecting $10 million for this fund, but we had to get onto it and it enabled us to expand the textbook production, particularly back into primary schools.

We were having major financial problems with the *Web of Life*, the biology textbook that really put the Academy on the map. It was a wonderful thing. At one stage, 85 per cent of secondary school children were using it. Then there was a revision, and we had a Disease in Society project too. But book producing is a very expensive business and it is very hard to predict the outcome. The *Web of Life* just fell into a hole at the beginning because it was wanted and it was inexpensive to buy. It took off, selling like hot cakes. It was and still is a superb book, which set the curriculum for biology teaching in the '70s. But the curriculum changed and the book became less popular. The *Web of Life* led us into a chemistry book, a mathematics book, one for geology. *Biology: The Common Threads* is the new one.

I wrote a book in the '70s called Web of Life *and didn't realise that you'd got something with the same title going over here. Everybody was saying, 'Oh, you've been involved with* Web of Life*' – no-one ever remembered anything of my book; it was always the Australian saga that got the reference. To sum up, though: the Academy was a very different place in 1990 from 1986.*

Well, I think it would have been anyway. I had superb officers and a wonderful secretariat – and being just three minutes away I was able to continue doing research, which was the other interesting thing. But we used to have early morning meetings, we had telephone hook-ups and things. I enjoyed that

period.

You have had an impressive life. I've enjoyed talking with you and look forward to doing so again when you come to England.

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