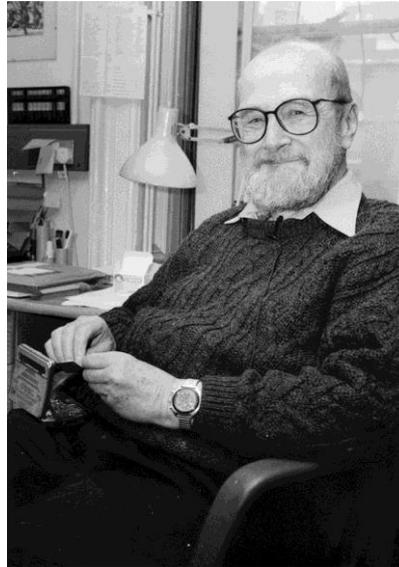


An interview with Patrick Wall (1925–2001)

Conducted by Martin Rosenberg and
Stephen McMahon in 1999

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Patrick Wall photographed by Martin Rosenberg
at St Thomas's hospital in 1999.

This interview with Patrick D. Wall (PW) was conducted by Martin Rosenberg (MR) and Stephen McMahon (SM) on 5 February 1999. This transcript has been corrected by the participants.

SM: So when were you born Pat? That's an easy one.

PW: In 1925 in Nottingham.

SM: When I was thinking about this, one of the many things that I realised that I never knew about you was anything about your family and whether there were any influences for medicine or science there, or whether you came out of the blue in that context.

PW: My family were very, very supportive. Nothing to do with science. My father did have a degree in geology, but had moved into education and then into educational organisations. So, while they were very supportive, there was no real science and certainly no medicine in the family.

MR: This was in Nottingham?

PW: Well, we moved to London when I wasn't in control of my motions, at the age of five. A key thing which tilted me towards medicine was at the age of eight I had an abdominal emergency and was admitted to hospital, and I was so impressed with this that I said 'right, that's what to do.' The family was very lively; I had a brother who was five years older than me, who was a pilot and aircraft engineer, and it was a good family.

SM: So you decided to get to start on medicine and you practised medicine at Oxford. Did you study there?

PW: Briefly. I went to St Paul's and for me had the advantage of the war breaking out and the school being evacuated into the countryside and a whole set of new teachers turning up, including one fabulous biology teacher, S. A. Barnett, who really influenced me and started me questioning. He was one of those teachers that anybody with any luck has at least once in their life. He was a Communist, and knew absolutely nothing about teaching. To help the discipline of the class, his brother was a classmate of mine. By the way smoking was compulsory in the class.

MR: Were there Marxist influences?

PW: The day started with reading the editorial from the *Daily Worker*, which was written by J. B. S. Haldane in those days. It was a very good start to biology. That really turned me on and I went from St Paul's to Oxford and in Oxford again had the luck of meeting a fabulous teacher, a friendly bloke, and that was [Paul Glees](#), and that really set me off on the idea of research, and while I went through medical school, I considered it as something of a joke, and coasted along with no intention of becoming a clinician but of getting my medical degree and going back to research as soon as possible.

MR: This was during the war years?

PW: Yes. That started me off on the first question and maybe we can talk in time about what the questions were. The first question was connectivity in the nervous system. I should say that in Oxford at that time [Sherrington](#) was still alive and the nervous system was really the only subject to work on and in fact the spinal cord was the only getatable bit. But the major issue of the time was connectivity and in terms of anatomy how did you find out if one place was connected to another. The [Cajal–Golgi method](#) really wasn't satisfactory. It wasn't experimental, you couldn't point at one place and ask where is it connected except by Cajal's method, which is very subjective. You pick out from the thousands of cells the one that shows the connection you want to see. Experimentally there were really only two methods available; one was the Marchi technique which was myelin degeneration, which of course everybody knew (a) you only found myelinated fibres and (b) even for those fibres you couldn't find the terminal arborisations of them because it only picked out degenerating myelin. At that time another technique was being invented, which was strychnine neuronography, putting little blobs of strychnine where you were interested and then looking electrophysiologically for where you could find a synchronous spike discharge. That had been invented by [Dusser de Barenne](#) and [McCulloch](#). A whole new anatomy was appearing at the time. Getting back to the anatomy of connectivity, Glees had invented a silver-staining method in which you could just about see degenerating terminal arborisations. You saw a series of dots in the area of terminal arborisation. That was what I did as an undergraduate with Glees and that was why I got my first job at Yale with [Fulton](#).

MR: Did you have much contact with Sherrington?

- PW: No. Sherrington had essentially packed up in about 1936 or 1937 when his wife died. He just ceased to take any interest at all, became a hermit and although he lived for another 10 years, he really did nothing in the lab.
- MR: His technician is still alive. [Tilli Tansey interviewed him](#). Do you remember anything about him?
- PW: No. But when Fulton moved from Oxford to Yale he took with him Francis Kerby from the Sherrington lab. Kerby dominated the working life of Fulton's lab for the next 20 years.
- SM: You told me a story once about a technician of Sherrington's who spotted the cats that were going to die. I wonder if that was the same one.
- PW: Fulton was American but had been in Oxford, first as a Rhodes Scholar and then with the Sherrington group in the 20s. Eccles had been his graduate student. So Fulton had really settled into Oxford. Yale had gone through a revolution in the late 20s, in which they decided to make themselves into a proper medical school and they had called in all sorts of people, including Fulton who was brought from Oxford to set up Physiology at Yale and he had brought whatever technicians he could and the full laboratory arrangement and he had one of Sherrington's technicians, called Kerby, who was there in the middle of Newhaven with this Oxfordshire accent and had seen 10,000 cats being decerebrated. It was quite impressive, because the medical school class started every morning with the decerebration of 10 cats, which was supervised by Kerby and done by people like me, and we set up all reflex studies on these cats.
- SM: At that very early time, though, the other big thing that must have been changing was the emergence of electrophysiology as an exciting new way of seeing what the nervous system actually did.
- PW: Absolutely. In 1934 Fulton and [Jacobsen](#) had removed the frontal lobes of two chimpanzees called Becky and Lucy and had seen changes of behaviour, including the delayed response failure and calmness. In 1936 Fulton had gone to an international neurosurgery conference and reported this change in chimp behaviour with frontal lobotomy. Present at that meeting was [Moniz](#) who asked if you could do that in people. So the [frontal lobotomy operation](#) had started from these two chimpanzees. Ten years later the war was over and Fulton decided to set up a project just to study frontal lobotomy in animals, since the whole epidemic in frontal lobotomy was based on two chimps. So he called in all sorts of people, me as the most junior, [Pribram](#), [Delgado](#), [MacLean](#), people who went on and did things. It was a very exciting group, very old-fashioned in their approach, it was all lesions, behaviour, and stimulation of cortex, and things of that sort. And curiously enough, essentially no electrophysiology; old-fashioned in that sense. With two exceptions. Lloyd, David Lloyd, had been there but had moved to the Rockefeller and left behind one fellow, a Chinese, [H. T. Chang](#), who was fortunately there for a short time, and Chang really knew electrophysiology, and so I learnt from him. He almost immediately afterwards, defected to China, which was a big deal in those days

and Chang is still alive and he became head of physiology in Shanghai and did all sorts of things. The other exception was an astonishing young electrical engineer called [Alex Mauro](#), who really understood electronics. So Chang taught me technique and I should say I used that technique to study the strychnine neurography, and the question was is it true that if you make explosions, neural explosions, in one place, and generate a synchronous volley, do they really not pass synapses, because the whole technique was based on that. So I promptly found places where they clearly did pass synapses and to that extent weakened the basis that it was on, which led to me meeting with McCullouch, which is really the second part of the story. But back to Alex Mauro. What Alex Mauro and I did, or he invented, [very small radio receivers for stimulation](#) and I made them into things that could be implanted. We implanted them subcutaneously in the monkey head and put the electrodes on monkey cortex and so we then had awake monkey and cortical stimulation. Mauro went to the Rockefeller, and cardiac pacemakers came out after that, and then as I will tell you 20 years later we hooked up again for the use of peripheral nerve stimulation in patients to test the gate control theory.

SM: You told me a story once about Peter Matthews and the monosynaptic reflex. And then at the beginning of the war he thought there was some artefact they had. That just kind of highlights the crudity in a way of some of the electrophysiologists.

PW: You don't mean Peter Matthews, you mean his father [Bryan Matthews](#), and that's quite true. Bryan Matthews was working on reflexes in the 30s, then went off and became the head of airforce physiology in the war. During that time Lloyd had defined the monosynaptic reflex and of course [Eccles](#) had used it. What Matthews had said was that before the war when he had been looking at the cat spinal cord, they had occasionally seen cord in an extremely excitable state, which they called explosive cords when they could see this reflex appearing, which they considered to be an artefact. He said that when he came back after the war, saw that the monosynaptic reflex had been labelled by Lloyd and was the sign of a cord working properly.

SM: So you finished medicine, with every intent on becoming a researcher and really you just abandoned any hopes of practising medicine, you had no interest there.

MR: But you did house jobs and things?

PW: Yes.

SM: So your first real foray into medicine is that you were recruited across the Atlantic and that was really at 25 or 26.

PW: Yes. Younger, because it was '48 when I was 23. And thanks to the war everything had been wonderfully speeded up so that one could get a label of a medical degree very quickly. Then because of my work with Gleebs, I was picked up by Fulton and went to Physiology at Yale onto this frontal lobe project. Very classical stimulation of cortex, looking to see changes and lesions in cortex, and

looking for anatomical changes. And what I did then on that project was to look for autonomic changes as a result of cortical stimulation and first found that in fact autonomic responses were very widespread, and that was because in monkeys the fifth nerve innervates the pia and you can get autonomic changes because you are stimulating the fifth nerve. But when you cut the fifth nerve, you can then see the true cortical systems. And so it was immediately apparent that motor cortex produced autonomic changes. These were blood pressure, heart rate, respiration changes, and then we rapidly found that there was a strip of cortex which starts in the cingulate cortex, goes forwards and over the supra-orbital cortex and then continues extending laterally to the insula. So we described for the first time this as an autonomic response area, although Papes had described it before. And then I set about finding out the anatomy. We published, showing orbital cortex projects directly to hypothalamus. The physiology of this area is still very much talked about. Psychosurgery began specifically to interfere with cingulate gyrus, insular and orbital cortex, which is really a strip. We'd really shown that it was a continuous strip, although people keep on picking up one or other part of this strip.

SM: Did you go there with a clear intention, was it a short term contract? You were going to travel and then do something.

PW: Oh sure. No I went there assuming that I would go for a year, maybe two, and then come back to Britain.

SM: So how long did you stay with Fulton at Yale?

PW: Two years, by which time because of my attack on strychnine neuronography I had been picked up by McCullouch, who lived nearby, had a farm. McCullouch at that time was in Chicago at the University of Illinois. McCullouch was cooperating with two absolute geniuses. One was [Walter Pitts](#), who was a mathematician and an all-round genius, and they had already started modelling, so the [Pitts–McCullouch neuron](#) is still the basis of many of the neuron models. And [Lettvin](#), who was actually a neuropsychiatrist, but had turned on to physiology. So McCullouch organised for me to get the job of assistant professor at the University of Chicago in anatomy and I was already labelled as an anatomist, although I had done precious little. Lettvin was a technical genius, and had really spotted the possibilities for electrophysiology. I went and joined these three people for three years in Chicago and we worked under extraordinary circumstances. Lettvin had set up his own lab in a lunatic asylum, called [Manteno State Hospital](#), a gigantic state hospital about 50 miles south of Chicago, and Lettvin used to work all night as a doctor and all day as a physiologist. And what was the problem? The problem was [Lloyd](#) and [Eccles](#), who we considered problems.

SM: The enemy.

PW: Exactly. They had defined circuitry within the cord, polysynaptic, monosynaptic reflexes and descending controls. So we set about first doing really very classical recordings. First mass recordings. Pitts who was very

strongly in with [Norbert Wiener](#) and had become fascinated with the nervous system. Wiener's *Cybernetics* was actually written largely by Pitts.

SM: Was Wiener in that same institution?

PW: No he was at MIT, which comes to the next stage of the story, which is why we four all then migrated after three years, in 1953, to MIT at the invitation really of Wiener and we were going to explain the nervous system in the ways that Wiener knew it worked.

SM: You were the young member of this team. I suppose these people had a phenomenal influence on you in terms of the way in which you thought and even the area in which you thought the most interesting questions were.

PW: Absolutely. There were some technical abilities which were appearing at that time, that is to say to do with the electronics. At Chicago at that time was [Gerard](#) and [Ling](#) and Gerard had made the first microelectrodes and in order to use the microelectrodes, you had to know about grid currents. All this became very, very simple as transistors appeared, in the late 50s.

MR: They made them by hand in those days didn't they?

PW: With electronic valves; they were already aware of grid current problems and impedance matching problems, because lots of other people were also concerned with recording small currents through very high resistances. So there was a sudden break in the technical possibilities. At the same time, and I was much less involved in this, was the whole idea of modelling of cybernetics. There were those who thought you really didn't need to look at the nervous system, you could model it with feedback and stability. So that was very much the hot issue of the time. Cybernetics came out I think about 1955 and evolved into artificial intelligence.

SM: Do you think that was a reflection of people's inability to be more empirical and make observations. Obviously when microelectrodes became more usable a whole series of new questions could be asked. You didn't have to sit in your armchair and model it, you could actually go and look and ask.

PW: Yes. But I think you have to see cybernetics coming out of the war-time control problems. How to have anti-aircraft guns linked to a radar set and with all the delays arranged properly.

MR: Did you have any connection with the people in Maddison, [Jerzy Rose](#) and [Joe Hind](#), the people who were putting electrodes also into the cochlear nucleus.

PW: Yes, just beginning at that stage. By the mid 50s people began not just to record mass potentials, which had obviously been done for a very long time, but now to record single unit potentials and to make various types of metal microelectrodes. Jerzy Rose had used a Woods Metal in glass with a big ball of platinum black on the end. So it was an exciting time because the technical possibilities had suddenly hugely exploded.

- SM: How many people took those up? Because you did very quickly. But I suppose everything is a case of lucky circumstances, but partly because you had people around you who were happy to help you with the electronics and the technical design.
- MR: Was it all a do-it-yourself environment?
- PW: Well, we then moved, as I said, in '53 to MIT. MIT was fantastic in terms of technical support, because they'd been the major developers of radar and we were in the research lab of Electronics, who had just fabulous technical support. There were computers of course, but they were very cumbersome things. MIT had a group of calculating women. It was an astonishing sight, a room of at least 40 women, calculating on hand-calculators, collision tracks, and a lot of cosmic ray data. It was possible for us to make multi-multiple recordings in the spinal cord of point variations and to give these ladies the numbers and they would hand calculate the interpolations and map field potentials and source–sink maps.
- SM: Just on the kind of flavour of how science would have been there: presumably there were no women scientists, or precious few? It was a male profession. It was funded. Did you ever worry about money? Or was it sloshing around.
- PW: No. It was an amazing time for the following reasons. The Cold War was going full blast and so the military, all of them, Navy, Army, Airforce, were fascinated with what they could get out of the next stage of studies of the nervous system. The National Science Foundation was only just started at that time and similarly the NIH had only just started. They were all competing with each other to give money away, plus a big supporter of us was the Bell Telephone Company, who were fascinated with communications and had started looking at all of the problems and defining very precisely their problems. For example in the 20s they knew that there was noise in radio transmissions and they went about looking for sources of noise. The whole of radio astronomy came out of that. Jaffe was the first one to see that the radio sources were in the stars. In another example, they knew that cables, transatlantic cables, had to have amplifier stations all the way down, they had the best of existing electronic technology with the amplifying valves in them, which they arranged to switch around when one failed and the other failed, but all the same every now and again at these amplifier stations they had to haul the cable up and replace the amplifying station, which is why they were saying find us an amplifier that doesn't break, and that's why transistors came in.
- SM: Transistors were just coming in the mid 50s weren't they?
- PW: Yes, but invented by Bell Telephone for this specific purpose and this was also very important for computers, because [Von Neumann](#) had pointed out that there was a finite size of computers; because of the reliability of the components, if you built a big enough computer it would never work because there would always be something broken. It was extremely exciting and I should add beyond the technical things there were the general problems. [Shannon](#) was there, having started at Bell Telephones, moved to MIT, simply

looking at information theory, which again was really an anti-noise strategy. These exceedingly practical engineers, physicists, electronic engineers were fascinated with the brain. Somehow the brain was doing what they would like to do. They had set up in this electronics laboratory, mainly militarily supported but no secrecy at all. There were secret projects going on, but they were completely divided and separated and funded separately.

SM: If you wanted to pursue an issue, essentially there was money already in place in the institution and you could just draw on it.

PW: And they were urging you to look at these wild things. ‘How does the brain work?’ Answer simple questions like that! In the same group at the same time, language was selected as a crucial target. [Chomsky](#), [Halle](#) and [Jakobsen](#) were supported by this same fund and working. None of us had regular faculty appointments. This was all soft money.

SM: And publication there? Was there a big deal or people published when they thought they should and when they had something to say.

PW: Yes. This mass publication business is fairly recent. If you look at [Adrian](#) or [Sherrington](#), they would publish serious papers. They didn’t publish more than one a year. They could easily have subdivided their papers into 10 papers, but no they published substantial bodies of work in single papers.

MR: It was a different attitude, wasn’t it, in those days?

PW: So we were regarded as going to lay golden eggs, but you could chivy the goose. There was a sense particularly by people like Wiener of huge confidence that he knew now the methodology by which you could understand complex circuits. It was then our job to prove him right, or that was his idea and he was convinced of this. Unfortunately as soon as we turned up at the MIT, essentially under the patronage of Norbert Wiener, but fortunately supported by the other people as well, Warren McCulloch and Norbert Wiener fell out over the virginity of Norbert Wiener’s daughter.

MR: What sort of character was he? Were these humourous people?

PW: No, no, no. Wiener certainly wasn’t. Wiener was a great massive, self-obsessed, manic genius. This was a difficult time but impressive people like [Jerry Wiesner](#), who was the boss of the whole thing, an electronic engineer who had been involved with radar and an absolutely brilliant organiser, he protected us from this crazy man.

SM: So on your own side, this must be at the time when you first started your own investigations on spinal cord.

PW: Exactly.

SM: Was it chaos and did you have a clear idea that you were going to define properties and hope to build a theory from that?

PW: Don’t forget what we did. And this really was a challenge ... this was Pitts’s idea, Lettvin’s idea; they were wonderfully disorganised people. I did the work

and they were extremely difficult to work with, because you'd do an experiment and would be delighted by the results. The next morning they would both have found various reasons why the experiment was not worth doing, etc. etc. I would just plod on doing the experimnts. The important thing we did was to do a source–sink analysis of the input to spinal cord, to try and follow a volley through spinal cord from dorsal root to ventral root. Then we manipulated it by inhibiting the reflex and remapping. And so that of course was very startling to show an inhibition precisely where it was happening and as far as we could see happening presynaptically. So here we came out with a new method which involved calculation, which involved understanding the second differentials, and you can imagine that that was enough for most physiologists and for most people. What are these people saying? And then we said that you could inhibit an impulse presynaptically, which everybody knew was absolute nonsense and impossible. However, [we published these maps and these conclusions in the *Journal of Neurophysiology*](#).

MR: Did you coin 'presynaptically', was that a term that was used?

PW: Yes. And this came out in 1955 and there was an astonishing episode as follows. There was the International Physiology Conference which was in Montreal and I went to this and gave these results. I was summoned to what consisted of a star chamber. It was [Penfield](#) who was the head of neurosurgery in Montreal, Adrian, Eccles and [Jasper](#). Jasper was the electrophysiologist with the Montreal Neurological Institute; he was on his home territory. So they called me in, just the four of them to Penfield's office and said would you explain to us what you have been saying. So I gave them a sort of five minute summary and they then said right out in the open, look here Wall you are obviously a smart guy, you have been to the right places, but you are in the wrong company. This is simply impossible, this is some sort of artefact you are wasting your time on. Goodbye! That really was something, as you can imagine.

MR: Was Penfield a strong man in that?

PW: Oh Eccles was the strong one.

SM: All of this presumably from a selfish ..., guarding their ports, their area, and they were putting the frighteners on you.

PW: Absolutely. Yes.

SM: So what was your response to that?

PW: I thought my God if those characters are going to tell you that this is nothing more than an artefact as a result of using electrical stimuli and so on. So in fact we backed off.

SM: But it was about that same time that you were then deliberately pursuing the whole ... one bit of you must have said I will go and prove this in another way that they can't refute it and it doesn't involve second differentials.

- PW: Exactly. So there was a question is there some other way in which you could follow the passage of nerve impulses, other than mass recording? There was also the problem at that time that nobody was successfully recording from small cells and certainly not from small axons. It was just on the edge of being possible. Lettvin went off looking at small axons and started on the optic nerve of the frog and out of that came Lettvin and [Maturana, What the frog's eye tells the frog's brain](#) [Lettvin JY, Maturana HR, McCulloch WS & Pitts WH (1959). What the frog's eye tells the frog's brain. *Proc Inst Radio Engr* 47, 1940–1951]. I thought of another method, because I was impressed by Katz and Schmidt who had shown that if you took one group of active nerve fibres, and looked very carefully at the threshold of the neighbours, you could see as the volley went by in the active fibres group there was this slight shift as a result of the field spread in the other fibres. I thought here's a way in which we could see whether impulses have passed in one group of nerve fibres, we'll test the threshold of another group of nerve fibres. So that's what I thought I was going to do, but what happened of course was that I then saw huge threshold changes as a result of presynaptic depolarisations.
- SM: So if the model in your mind was of a kind of passive swopping over, then presumably you had to mull a fair bit on what would be the source and the mechanism for these large threshold changes?
- PW: Well, don't forget that [Barron and Matthews had shown dorsal root potentials](#) twenty years before and [Lloyd had analysed the likely source of those](#), although Barron and Matthews thought that they were potassium leakage from one fibre to another.
- PW: So we were talking then about how I came to be measuring the threshold of groups of fibres or single fibres. I thought, as you said, I would just spot the passive reaction of that fibre. It turned out that there was some gigantic active effect. So that produced the whole business of primary afferent depolarisation.
- MR: Had you thought about pain before this? [No, no]. You hadn't got into pain at all?
- PW: No, I am just coming onto that.
- MR: You had not mentioned it before.
- PW: No, no, because at that time it was all to do with Sherrington, Eccles, Lloyd and reflex circuits, which were after all a physiological event which wasn't anything to do with behaviour or sensation or anything of that sort.
- SM: At that time you had this idea which you presumably started to talk about and write about of presynaptic inhibition and presumably the field was dominated by people like Eccles at the time, so did you need his blessing?
- PW: Eccles having said this was all an artefact then took up my technique and it suddenly became the popular accepted technique.
- SM: So he didn't believe you that it was an artefact, this was political.

- PW: Oh, at first he needed a technique that he could use which was microelectrode stimulation in order to find the threshold shift of terminal arborisations. So Eccles became extremely complimentary of me, never gave me any credit, but complimentary, and he proposed that I must come to Canberra, which I happily resisted. No. So then here in the spinal cord, I could work in the spinal cord and I could see these threshold shifts all being done with relatively large microelectrodes, metal microelectrodes, but the circuitry had improved and now I could use real microelectrodes and I shifted to glass potassium chloride filled microelectrodes. Then I could easily see single units. And so then I started recording single units in dorsal horn and first of all classified what the cells did, and it was at that stage that the question of pain arose because I went naturally onto a search for cells which would only respond to intense stimuli and I simply couldn't find them and I still haven't seen one really.
- MR: That's natural stimuli or electrical stimuli?
- PW: Both.
- SM: And at that time the dogma was, I mean people understood that they were bunches of primary efferents that would make relays in spinal cord.
- PW: Oh yes, but by that time Adrian, [Zotterman](#) and Bishop had decided that there were modality specific peripheral nerve fibres and therefore it was extremely natural to expect modality specific cells, relay cells, in the spinal cord.
- MR: Was Zotterman around in those days?
- PW: Oh yes.
- SM: So when you first started to essentially just collect data, gather and collate, that was published again with resistance? Or were people more passive, they took it as just more data?
- PW: No they thought I was somehow missing the point. I could find cells which only responded to low threshold afferents, that was clear, touch cells, but I simply couldn't find these nociceptive specific cells.
- SM: I know in some of those early papers and this must be the mid to late 50s really, you became very ingenious in trying to use inhibition or mixtures of stimuli and again that was just fortuitous was it, you were just trying to define precisely ...
- PW: No don't forget that was also very classical. That sort of thing had been set up certainly by Lloyd and Eccles and it was exactly what they were doing. As was Lundberg.
- MR: He was defining the flexor reflex.
- SM: Did that enable you to start defining inhibitory mechanisms on a single unit basis? And presumably was that the origins of your thoughts for the gate control, trying to make sense of how these inhibitions would operate.

- PW: Sure. And one inhibition I found actually came from an accidental personal observation. McCulloch had a farm where we used to spend weekends. All had to work like hell on this farm, and one of my jobs was mowing vast acres of lawn with a hand-pushed motor mower with a hellish vibration. I began to realise that after enough vibration, my hands were really remarkably numb, and I thought well let's try that on a cat. So [Cronly-Dillon and I published](#) on the fact that vibration outside the receptive field of a cell would inhibit it. That was the first trigger for the gate control.
- SM: And [Ron Melzack](#) at this time, how did you know Ron, how did you first meet Ron?
- PW: Ron happened to be at that time in psychology at MIT, and psychology at MIT at that time was a very low level. It was in fact in the business school. But Ron had worked with [Livingston](#) who was interested in pain and had raised puppies in isolation and said they took some time to develop pain. And he had done work in Oregon, so he was interested in the physiology of pain and we just started talking together and put together everything we knew at that time. This was all talk, but it was partly his experimental work and a lot was my experimental work.
- MR: So he did animal experiments himself?
- PW: Right, right. Mainly behavioural, but some electrophysiological.
- MR: Would he call himself a neurologist or a psychologist?
- PW: Oh he is a psychologist. So it's interesting that we wrote two major articles, [one published in Brain](#), describing our views on gate control. It had no effect at all.
- MR: When did you first say 'gate control.'
- PW: I think for [the Science article](#), the one that is always quoted. And we had in fact been swapping our names backwards and forwards, some were Wall and Melzack and some were Melzack and Wall, it happened to be his turn to be first.
- MR: So it was like Rolls Royce, in alphabetical order.
- PW: I drew that god damn diagram.
- MR: But when did you first think it as that term 'gate control'.
- PW: Because we were always using triode valves which had a gate. That was my meaning of the word gate. We'd been struggling with gate currents and used a gate control all the time for varying amplification. In that diagram which is an absolute minimum diagram, I'd introduced the smallest number of possible components, and some pure guesswork like the fact that the proposal that the substantia gelatinosa was the origin of the inhibitory control. We already knew, and this again goes way back, that there were descending controls. It really goes back to Sherrington, who knew that decerebrate animal had conspicuous proprioceptive reflexes. If you spinalise the decerebrate animal,

the cutaneous reflexes dominate. So we knew that cutting the spinal cord released the cutaneous reflexes so we could install in the gate control a descending control onto a local circuit which was being affected by the type of impulses that came in and the activity of the local cells.

MR: Had you thought of the periaquiductal grey at that point?

PW: No, but way back everybody looking at spasticity and such things had assumed that somewhere in the medulla brainstem there must be descending inhibitory circuits and a certain amount was known including [Magoun's](#) reticular spinal pathways.

SM: One of the reasons it must have appealed to so many people was that you were trying to define things at a cellular level, but also trying to explain real phenomena, and actually saying what this circuitry was for. I don't know what your preference was and apparently, as you say, you made a cartoon, a drawing, which I don't know if you think that was important, that it was going to be correct, or perfect, or did it just encapsulate the idea?

PW: The original paper explained that the diagram was a cartoon.

MR: Have you regretted that diagram then?

PW: In some ways yes. Particularly because people didn't look at the caveats. For example, that diagram is run entirely by presynaptic control and we knew at the time there were also postsynaptic inhibitions, it said so in the paper, but it was always a squabbling point.

SM: Why did the paper in *Science* come about? You just said that you had been publishing these ideas in longer and shorter forms.

PW: And you see the previous ones hadn't been related to pain, it was related to all sensory inputs, which I still think is the case, and we decided OK just let's talk about pain.

SM: So you really generated the idea that you ought to tell the world again and through the medium of *Science* and they were happy with it or ... I don't know what *Science* was publishing in those days, perhaps lots of ideas papers were acceptable.

PW: Yes.

MR: Was reviewing difficult? Was there more antagonism in reviewers?

PW: Not from the reviewers, but there was antagonism from the physiologists.

MR: Yes, but it got published though.

PW: Schmidt has a paper, which calls for the cessation of the use of this term 'gate'.

MR: Which Schmidt was this?

PW: [R. F. Schmidt](#).

- SM: Well that again must happen to all scientists, you find your work starting to be of great relevance to a particular field and that field presumably had its king pins at the time and they presumably were the Schmidts.
- PW: Oh absolutely. Adrian and Zotterman and [Perl](#). So the dictum of the physiologists was very, very strong in favour of specific transmission and here was a challenge to them, which made them very, very annoyed. Well, two things happened. One was that I could already see this powerful inhibition produced by low level inputs, so immediately started trying it on ourselves; we made up simple stimulating gadgets to stimulate peripheral nerves, and then I went to [Sweet](#), who was the head of neurosurgery at Mass General at Harvard, and we tried on ourselves and then we tried on patients and came up with [TENS](#) and a paper called '[Temporary abolition of pain in man](#)'. Now that of course was then a very difficult challenge for a physiologist to dismiss, since it worked, and furthermore it recruited the clinicians. So the clinicians immediately leapt on this as an explanation for the various hyperpathic states and so on.
- MR: Who were your allies in those days, apart from Melzack of course?
- PW: Well, as I said, the anaesthetists caught on very rapidly indeed. [Noordenbos](#) was an important ally from the clinical world and it spread, but surprisingly slowly. As a matter of fact in the citation index, it eventually became a citation classic, and they wrote an article on this, pointing out this was a highly unusual paper, that usually a paper comes out and is cited essentially immediately, the highest citation is within the first year and then it peters off. This one took something like five years before people were beginning to cite it and that was this whole recruitment, not of physiologists, but of the clinicians, pharmacologists, and so on.
- SM: I think in many cases there is a sort of politics of envy, some smart arse comes along with a great idea and it upsets everyone, it upsets people, why didn't they think of this, why hadn't they seen it in this way?
- MR: Did anybody say 'I thought of this, I am glad you have shown it now?'
- PW: Well, a little. You see Zotterman, for example, had wondered what scratching was about.
- MR: Of course, scratching and tickling.
- PW: Exactly and so he recognised why do you itch? It's because itch fibres are excited, that's according to Zotterman, but how/why does scratching then work? There must be somewhere an inhibitory process. Livingston had and Noordenbos as clinicians had said 'look here there must be central interactions to produce what we see in the patients.'
- SM: And at this time I guess that you were working more alone and that although Lettvin and the others were still there, they had got interested in slightly different things by then.

- PW: Right. Lettvin had gone off into vision and I then had some very good students, Mendell for example, and Mendell and I showed wind up, so then we got into facilitation as well as inhibition.
- SM: Around this time there were a couple of big events occurring politically in America. You had been through McCarthyism and the Vietnam War was brewing up nicely I guess.
- MR: Did your St Paul's background come up in the McCarthy affair?
- PW: Well, I maintained a very low profile, with respect to that, and fortunately although I had been a member of the Communist Party, I had resigned early on, and actually over Czechoslovakia, but it was a very peculiar situation. Because of this military connection, I was actually on the airforce 'Office of scientific research Lifesciences Committee', which was fairly odd. I'd never changed my passport, which meant that when I went to these meetings at places like [Wright Field](#) they had to assign an officer to escort me to the loo. I had a number of very interesting trips for them; I went to Japan and looked over the Japanese scientists, because they were anxious to start supporting foreign scientists, which they did extensively in Europe and were looking further. And I also went to Vietnam in '65 and that really brought me to a crisis of conscience. 'What the hell am I doing as a representative of the US Airforce in the first place and secondly being at MIT with all its prestige in terms of industry and the government.' I was a full professor by this time. I really became very, very embarrassed at my own situation. I didn't like the society I was living in, although I was living very high off the hog, and it was clear one could just zoom straight ahead. So I simply began looking around for a job back here and with good luck knew [J. Z. Young](#) and J.Z. had set up a research group at University College, which was in trouble, and so they appointed me director, which was great. I really made my decision in '65 as a result of going to Vietnam and then in '67 I could come back here.
- MR: I remember when you came here, you were regaling the assembly with your experiences in the room they used as the tea room.
- SM: So that was an active decision to leave because of Vietnam. I don't think you were ever told, but ... Olds told me that you had encouraged students to burn their call-up cards.
- PW: That added to the embarrassment because here I was beyond the age of being called up, but cooperating openly with the military, and every second knock on the door, two things would happen at that time at MIT, one is somebody would come in and ask me did I think the brain was like a computer, and the second person would come in and say how the hell could they get out of the draft.
- MR: Did you say that you had American citizenship.
- PW: No I didn't. I'd never changed my passport, because of continued discomfort with the society.

- MR: Did the McCarthyism affect the working of the laboratory. Did people vanish from the lab?
- PW: Sure, sure. And everybody was playing their cards very close to their chest and it was difficult. You didn't easily find people's political opinions, until you got to know them very well. It was interesting by the way, you know the one really free media at the time was science fiction and we were all mad science fiction buffs, because anything could be written in science fiction, usually completely critical of governments.
- SM: So you spent in total 10 years or so at MIT.
- PW: Fourteen.
- SM: And when you made the decision to return that was easy for you. Personally you were married at that time to your first wife.
- PW: In terms of returning. Having no children makes things more easy. My wife was English so returning here was not a problem.
- MR: You were married before you went to the States?
- PW: Well no actually while I was in the States and I married an old friend. There were the positive things in favour of returning like ageing parents. It was very nice to be with them. I had more sympathy with Britain and British society.
- MR: You felt very English in the States?
- PW: Oh absolutely. Yes.
- SM: So when you first came and set up shop maybe we can say a few things about J. Z. Young as I know you have written on J.Z. and were impressed by what he created at UC, but also the practical things. You came and I know you brought your lathe, your rig, with you from MIT.
- PW: Right, so here then came the generosity of the people at MIT and the grant-giving people. I arrived with a complete lab. Everything. Absolutely everything.
- MR: You mean you brought it over, or they paid for it here?
- PW: No, no, I just packed up my lab in Boston and unpacked it in University College and within literally two weeks was doing the first experiment.
- SM: At that time Professor J. Z. Young hadn't been there long.
- PW: Oh no, he had been there since '45, and he really was an astonishing character. In the first place he had revolutionised anatomy. The first ever non-medic to become the head of an anatomy department, deeply concerned with research, and promptly filled up the anatomy department at University College with an extraordinary collection of people. He was interested in everything that was being done, even if it was not specifically in his field, or to do with the nervous system. But psychology, electron microscopy in Britain was really invented there. He was fascinated with the octopus. Lettvin tried hard and I had tried somewhat to make the next step for the octopus which was to do the

electrophysiology of the octopus. Lettvin spent a year in [Naples](#) and I spent two summers completely failing because the octopus is such a big active animal that it has got a number of tricks that it has developed to prevent electrophysiology. Octopus, right on the edge of its oxygen supply, all the time needs a hugely rapid circulation and made two errors with its blood supply, never invented haemoglobin – got a lousy oxygen carrier – and never invented a clotting mechanism.

SM: So the experimenter's dream, or nightmare.

PW: But octopus substituted for the clotting mechanism vascular contraction, so as soon as you made the least bit of damage, all the blood vessels around closed down, so you could have an octopus climbing out of the tank, but the bit you were recording from was stone dead, because it had closed down. And of course what should have been done was then done with *Aplysia*, an exceedingly dull animal, but with small ganglia that could be handled in isolation.

SM: At UC at that time [John O'Keefe](#) joined you fairly soon, and you set up, I guess the MRC unit.

PW: Well, it already existed, I actually joined it.

MR: What cerebral functions unit? Was that J.Z.?

PW: Yes, he'd invented that, again with the idea of psychology coming in. So I then brought with me various people. Jean Merrill and John O'Keefe. I had developed a method of recording from awake animals and had looked in the spinal cord with animals walking around with a microelectrode rig on their backs. You could make recordings but I simply couldn't understand the results, because the spinal cord was moving from one state to another. So I said right let's move to something simple, and John O'Keefe then tried on dorsal column nuclei and that turned out to be quite difficult technically. His thesis had actually been on the amygdala and so he moved to hippocampus as something which was technically easier to use those rigs on and his whole career then started from those findings. Plate cells were his first discovery.

MR: Was Julian Millar there?

PW: Yes, Millar was a graduate student in London.

SM: One thing about your lab. I mean over the years you've deliberately avoided the temptation to have a big lab and presumably that was an active decision.

PW: Absolutely. And I was really always very selfish, I don't know about selfish, I think honest, I don't understand in detail anybody else's experiments, unless I have been there and seen the animal from the moment of first anaesthesia on through to the end, so I remain very much a hands-on chap. And I had no interest in developing an empire, because I knew an empire took you away from hands-on to organising.

- SM: And in the same way you steadfastly refused to take on administrative jobs as well?
- PW: Right, another selfish move.
- MR: Did you do much travelling, working abroad. I mean there was the Jerusalem work.
- PW: This was beginning in 1970. I had in general and particularly in Britain, asked experienced scientists to come and join me, rather than depending on graduate students. So I was always recruiting people, and one chap turned up, [Peter Hillman](#), who actually was a fantastic physicist who had decided that life sciences were more interesting than physics, and came to me really as an apprentice, having resigned as head of physics at the Weizmann Institute, and came into the lab. It was a very odd year in which you had this tall gangly chap saying to you 'why are you doing that?' in a very gentle polite way, and it made you say 'why am I doing it?' I don't know. So we had a very productive year. He then went off to the Rockefeller and turned to *Limulus* eyes, which was more up his line than the spinal cord.
- SM: Did he start your connection with Israel?
- PW: And then he invited me to Israel where there was an exciting group and very exciting woman who I married. So I then set off.
- MR: Where was that in Israel?
- PW: At the Hebrew University in Jerusalem. So I then set up a group there and we are still go strong. There is a fellow there called Bob Werman, who's an absolutely brilliant neurophysiologist who was busy setting up a neurophysiology lab and I joined in with them and recruited some people, first Mike Gutnick. He and I started looking at damaged nerve. We found that damaged nerve is not just sick normal nerve, there is something more to it than that. So that was then a real switch of behaviour, stimulated somewhat by the warfare going on and the number of peripheral nerve injuries that were rather obvious. And so after a few years, having been joined by Devor, and Devor then took up this problem and continues on the consequence of peripheral nerve injury. And we quickly saw that while there were fascinating things going on in the periphery and the dorsal root ganglia there were also changes going on centrally.
- SM: That's another topic that met a lot of resistance. When I first started reading your work, it was very confusing and literature was full of people who were essentially doing a lot of hard work simply to disprove what you were claiming, and I don't know if again you found that depressing to feel that there was a conspiracy out there of some people against you, or whether you liked the challenge of adversity.
- PW: Well, yes I liked the challenge, but I also took them seriously. You were dealing with a plastic reactive system, and perfectly honest competent research workers, like Brown in Edinburgh, or Peter Snow in Australia, could come up

with apparently contradictory perfectly good experiments in which I think the real challenge is that we both had to be right.

MR: Did you cross swords with Iggo?

PW: Oh God, of course Iggo was the leader of the specificity band and simply couldn't understand the possibility of any different scheme.

MR: But did you have useful discussions with him?

PW: No. There are central cells which respond to touch and pressure and temperature and so on. He just said that those are nonsense cells, 'I don't know what they are doing, there is something wrong with them, and I am not interested in them, they are not proper cells, proper cells would only respond to a unique input and hold it fixed.'

SM: Going back to Science, at that time you were involved in bringing together British neuroscientists. That was with who? With Steven Rose?

PW: I'll tell you the story of that. It began in Boston. Steve Kuffler was the most important neurophysiologist there with his Harvard set-up that was developing which included Hubel and Wiesel and Potter and all sorts of people, and Kuffler who was a very decent enormously kind man who spent his summers at Woods Hole where he said that everybody talks with each other and they have meetings every evening and they know what each other's doing, why doesn't this happen the rest of the year? So he set up the idea that we neuroscientists involved in Cambridge and in the whole of New England have some joint meetings. So he set this up and I happened to be the first speaker at the first meeting and in fact described the laminar organisation of the dorsal horn. The meetings went on simply to inform other neuroscientists. It was obviously a very good idea. So coming to London I realised that the isolation of workers would be present and probably even more so, so I actually got some money from a foundation, like £1000, maybe £5000, to set up an organisation like that in London. When I turned up in London, it turned out that Steve Rose and Cragg and Evans had already had that idea and had started it up. Chris Evens ... very interesting physicist at the NPL. We reckoned that there was a built-in inhibition in any university building, so we would not hold it there. So what was the alternative? And the answer was pubs. Pubs always have upstairs rooms that you can hire. So we started in a pub called the Black Horse and for a long time these were called the Black Horse meetings and we would have them monthly.

MR: Where was that again?

PW: The Black Horse is at the bottom of Charlotte Street; it's still there. And they worked very well. Two things happened. One is that sometime after I had started this up, Ed Perl happened to be visiting London and I said by the way come along to the Black Horse meeting.

MR: This was the beginning of the Brain Research Association.

PW: Yes I will come on to that in a moment. Ed Perl said what a great idea and went back and started the [American neuroscience society](#). Anyway we went along with this in a very, very informal way, and suddenly at one meeting a fellow called Richter stood up and said how do you people have the nerve at this time to run this elitist organisation with no elections, no structure, and so on – so we were a bit shocked. So we held elections and the three of us were appointed Chairman, Secretary and Treasurer, and what sort of insulting word could we call it? Because brain research association is BRA, right we'll call it the Brain Research Association!

MR: Before that it had no name?

PW: It was the Black Horse meeting. But actually that was imitated in many different places. People in Bristol and Cambridge and other places set up this type of informal meeting. That's the origin of both the American neuroscience society and the [British Neuroscience Association](#).

SM: Well, they bottled out of the name BRA. Ultimately they were embarrassed after 20 years, so they have changed it to the BNA now. So back to Science. At this stage I guess is kind of mid 70s. Scientifically you are starting to think about longer term changes, the stability in the nervous system, and partly that emerged from those experiments with Gutnik.

PW: Right. But don't forget – it slightly got lost. We had another experienced visitor, David Egger, and David Egger and I did two experiments in his year with us. One was very simple, which was to look in the thalamus at the incoming afferents, before and after we had removed the nucleus gracillus. What happens if you removed nucleus gracillus obviously is that the leg area of PPL just becomes silent, you can't get anything from the leg.

And this now goes back to H. T. Chang, the chap I mentioned as being the only electrophysiologist in Yale, and he had been involved in some very important experiments, as it turned out, which was the idea of thalamic cortical reverberating circuits, which was taken up later by Eccles and Lundberg. The idea was that if you send a volley in dorsal column nuclei to thalamus and cortex, and then looked in the thalamus and in the cortex, you could see there was a long after-discharge. They said at the time, ah look it's getting up to the cortex, firing back to the thalamus, re-exciting and coming back, and you are setting up a reverberating circuit. Chang had looked at that with [Clinton Woolsey](#) and had said let's wait a bit, let's give it a bit of time, and that was Chang's contribution, because if you give it a bit of time with the cortex out, the thalamus starts reverberating again, but it takes a few hours before it will reorganise, so it's not a thalamic cortical reverberating circuit but some inherent mechanism. So having seen this blank hole in the thalamus, thinking back to Chang, I said let's give it a bit of time, so we then mapped by the day and the answer is that after a day or two you begin to see the hand area expanding into what had been the foot area. No wonder that didn't catch on very much, because here was a complete denial of everything in the stability of classical connectivity since we had shown that foot cells could convert to hand cells.

- SM: We were talking about the challenge to the idea that the nervous system was hooked up in a somatotopic way that would then persist.
- PW: And the background was that the nervous system was believed to be hard wired and that soon after birth you would not see any modifications of connectivity. Now what could be the explanation? Previous foot cells became hand cells. One possibility was sprouting. And just about that time [Raisman](#) had shown sprouting to occur in hippocampus.
- MR: Geoff Raisman?
- PW: Yes. And so there was then the possibility that this was sprouting, but it was much too quick and we saw of course massive cortical reorganisation as well as thalamic reorganisation. So here was plasticity of connection, in which there were two possibilities. One was anatomical sprouting and the other was that there were silent synapses which had become activated for some reason in the presence of de-afferentation. I then went back to the spinal cord, which I was more familiar with, and reckoned you could manipulate the input more carefully. [Basbaum](#) came, another example of a post-doc, and we looked at the effect of cutting dorsal roots on the organisation of dorsal horn. We saw the same thing, i.e. the cells went through a period of silence and then took on bizarre receptive fields taking advantage of the nearest intact afferents. That of course was opposed, because the whole classical picture starting with the anatomy of the nervous system is that there is no regeneration in the eNS and therefore what you have at birth is what you are left with for the rest of your life and that's it, you can't see any changes.
- SM: Just to give you an example of you starting another industry, as you know I sort of started work at the beginning of that time, but I bet before then there was not a huge amount of people making chronic manipulations of animals, which now is very common, and in fact it is becoming hackneyed; we need better words because everyone is so interested and so acceptant of these processes. At the same time you were relating this to pain; was that because your interest was predominantly in understanding chronic pain, so you were seeing long-term changes in the context of chronic pain states, or was that just a convenient excuse to get money?
- PW: It was a bit of both. Because I was really interested in the basic fundamental properties, almost on a cellular level, but it turned out that it was relevant to pain processes. That's a different story, which now starts almost precisely 25 years back, but really in '73 or so, that I realised that the reverberations of this were going through the pain field, but one really needed to organise that a bit. And then I had a huge ally and that was [John Bonicar](#) in Seattle who was a great organiser, a great character, almost pure clinician, who invented the thought that pain was a special problem, clinical problem, that it needed lots of experts focusing in, even on an individual patient, set up the idea of a pain clinic, and he had the idea of starting an organisation, an international organisation. First he set up his own clinic in this cooperative way in Seattle and then wanted to expand it. And I was always affected by [C. Judson Herrick](#). C. Judson Herrick said if you want to succeed in science, you must do three

things, first find something nobody else is working on, and he found the brain of the tiger salamander; second write a book about it, so he wrote a book called *The Brain of the Tiger Salamander*, which is a very important book. It was the beginning of detailed comparative neuroanatomy. And third you have to start a journal and he started the *Journal of Comparative Neurology*. So I followed along this. Nobody was working on pain, because it was simply completely understood and there was no point in working on it. Now there was a question of starting a journal and Melzack and I had [written a Penguin](#), so the book was there.

MR: Did you have any trouble getting Penguin to take that up, because it's quite a different kind of book for them.

PW: Yes, somewhat, but I think they were more liberal in those days than they are now. But while you are on that topic, we then decided to write [The Textbook of Pain](#) and that was astonishing. We went to publishers and they said pain, that's not a subject. You know they had their boards of advisors, who said it's ridiculous, it's just not a subject. So one was really up against it. Eventually [Churchill Livingstone](#) published it and to their absolute astonishment it was a huge success and they were overwhelmed by that. Anyway, as a result of that while Bonica was setting up the [International Association for the Study of Pain](#), IASP, I said right here is a chance to start a journal, because I still thought that this is an orphan journal, nobody is going to buy a journal, we need a society whose members will automatically buy it. So Bonica and I were in agreement and this thing was set up, and this year is the 25th anniversary of that journal [Pain](#).

SM: As you approached retirement, the notational retirement age, you moved from UC here to St Thomas's. Do you want to say anything about that?

PW: Yes. I have always been very surprised at people who can't cope with retirement. I was influenced by my father who said you have to retire at the earliest possible moment, which he did, and lived for another 28 years, having a ball. But also as you know here I was head of a going lab, but not seeing it as my empire in any sense, just happy that there were other productive working people around there. So I very carefully started five years before I retired making other people associate directors and then full directors, particularly Steve McManon was there at that time and Cliff Woolf and Maria Fitzgerald. So they were all nursed into leadership positions and I saw myself in seamless retirement in which I would now just retreat into a lab. I think that the sight of the old lion padding around at the back of the den is never a very happy one and so I give my thanks to Steve who offered me a chance to come here while they continue fortunately in a friendly way at University College. So I remain extremely grateful to St Thomas's, Steve, that I was given a home here. We are almost at the end.

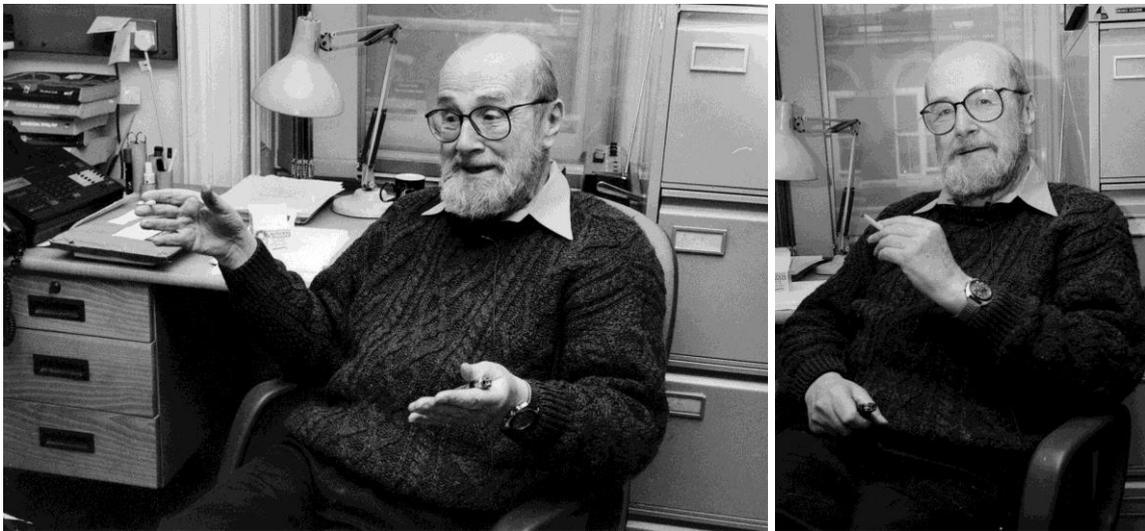
SM: One of the things that is unusual about you, one of the many things, though is that today you may be going to do an experiment, is that something that you would recommend for other people? I mean do you think it is necessary to be

involved? Do you think scientists actually lose it when they become administrators.

- PW: It clearly depends on the subject. [Sol Schneider](#) wrote an autobiography recently in which he proudly said that he had never done an experiment in his life, but he was very good at encouraging other people, which may be true. As I said, I find experiments of the variety that I have been involved in something that you have to be really deeply involved in. I am inspired by the data as it comes out of the animal, not by somebody's report later on down the line.
- MR: This is what I was going to ask. What gives you the kicks. Some people actually enjoy the physical thing of doing a dissection and preparing a nice preparation, others enjoy analysing the data, others are prepared for other people to do that. Where do you fit in?
- PW: Well, I think for me most of the ideas that I have had, I have had as the data was appearing, and I have seen obviously many, many of my friends who had backed off, relied on graduate students and so on, splendid as they are, and they back further and further away and get lovely manuscripts delivered or theses. Obviously as editor I read manuscripts and I would honestly say that deeply I don't understand anybody else's manuscript, because I don't know precisely the processes that have been gone through; I understand the conclusions and what might have gone on, but I don't feel it personally, and for that reason I think as soon as you start being an organiser and an administrator you are away from that. Now I do understand that there are certain types of biochemistry, for example where the actual experiment is so mechanical that assuming that people are technically competent, you don't need to see the process.
- SM: I have two more questions. One is following on from that and that is you have obviously worked in neuroscience at the leading edge of neuroscience over four or five decades now, do you like the way science is in Britain now? Do you think the thing is improving as a discipline.
- PW: Well one answer to that question is that of course throughout this time there has been a steady increase in the role of biochemistry first, pharmacology, molecular biology, and a sign of people going down to smaller and smaller units and all the dangers of reductionism that is clearly the spirit of the times. All this time I have been saying eventually the tide will turn, they will realise that going down to such small units, that if they try to refer the meaning of those small units to some higher level of organisation, they are going to be in trouble, and they will have to get back to looking at cellular biology, systems biology, and so on. I have to say that I don't think I am going to live to see that tide turn.
- SM: Just one last question and that's that one of the reasons I think you have been immensely successful scientifically is that you recognised when a question was right for exploiting, and you told us you had a little credo as to how to spot it, but if you were starting again now as a 25-year-old what topic would you pick on to satisfy someone for their working life?

- PW: I would be very tempted to look at imaging. What is happening now is a hilarious music hall stage of imaging when they use these wonderful 21st century gadgets to prove the 19th century was right. You know there is the microphrenology of the brain going on in which they are slapping labels on this spot and that spot. That I think is nonsense and you could see what nonsense it is. But at the same time I think these images and the way they are being produced – NMR imaging – you will be able to see the brain as an integrated structure.
- MR: Do you think electrical recording, single unit recording, will ever be superseded by ...?
- PW: Well, obviously it is exceedingly limited. As soon as you get away from the idea that any one fibre or any one cell is going to tell you the entire story, which was the reasonable assumption in the first place and it just ain't so. Even the labelling of cells as sensory or motor is now in strong doubt.
- MR: Every hospital now has a pain clinic I think. Do you think this derives from your work?
- PW: There's a practical reason for that and that is that the anaesthetists decided that people could not get their FRCA until they had done x months in a pain clinic, so no training hospital can be a training hospital unless it's got a pain clinic. Now it is true that that idea came certainly from Bonica, with me encouraging obviously. I think it remains in doubt whether this is the right approach and whether what actually happens in a pain clinic is what was supposed to happen. You know sixty per cent of the pain clinics have only a single consultant in one subject, well that's instantly against the ideal.
- MR: Now the TENS machine, now every ordinary patient has heard of a TENS machines and they will be offered them and so on and so forth.
- PW: True. No I think in that case there were very satisfying things that came out of the laboratory. TENS is one. The spinal action of opiates came straight from the research of Basbaum and Yaksh. I think especially where therapies emerge from the lab as for example in the work of McMahon on neurotrophins, hugely exciting real biology, but with the promise of some therapeutic advances.
- MR: More acceptance of acupuncture?
- PW: On the contrary.
- MR: OK. What are your views there?
- PW: Acupuncture is really drifting down in use, both in China and here, and brings up a topic, the role of the placebo, and I don't think until you understand the placebo, you are going to understand the pain mechanisms, because it's otherwise a completely nonsensical paraphenomenon; you've got pain on the one hand, and the whole mechanism producing pain, and then it turns out that giving a blank tablet does just as well or a blank needle.

- MR: What do you think was the most exciting, the thing that gave you most satisfaction scientifically?
- PW: The nice thing is I had large numbers of moments of excitement.
- MR: Is there any sort of regret, scientific regret, that you should have done that earlier? Or things fallen into place?
- PW: Oh yes, oh yes. You'd need another tape for that, on regrets.
- MR: Thank you very much.



Pat Wall photographed by Martin Rosenberg at St Thomas's Hospital in 1999.



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