Life in Sherrington's laboratory

His last decade at Oxford 1925–1935

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Teaching – the life of an undergraduate

I was privileged to be intimately associated with Sherrington in his laboratory for the whole of his last decade. I am the sole survivor of this whole phase of the Oxford School, as it came to be named. Granit, Gibson and many others were associated for several years of that period.

I arrived at Oxford in October 1925 as a Rhodes Scholar already with a medical degree of Melbourne University. However, Magdalen College required that I read the Final Honour School of Physiology and Biochemistry, so I had the experience of being an undergraduate in Sherrington's department for 2 years. Besides Sherrington, there were Carleton, the histologist, Douglas and Priestley, giving lectures and practical courses in Respiration and Clinical Physiology respectively, and Liddell, supervising the practical physiology together with Creed and Sybil Cooper. The senior technician, George Cox, had been Sir Charles' factotum for 30 years. He acted as business manager and controlled everything including four laboratory boys. There was also a good mechanical technician, O'Neill, who repaired equipment and constructed instruments in a fairly well-equipped workshop.

As an undergraduate I had experience of the lecturing and of the practical courses. Sherrington lectured on neurophysiology and on blood and circulation. My detailed notes and diagrams testify to the excellence of his lectures on neurophysiology at that time. It was in his later years that his student audience dwindled to zero, partly at least because of his inaudibility as he spoke to the drawings he was creating on the blackboard, and the acoustics of the lecture room were very bad. The other physiology lectures were by Douglas and Priestley. It was in the Oxford tradition that no attempt was made to cover the whole of physiology even though it was in the medical curriculum. There was no endocrinology, no peripheral nervous system, no special senses, no reproduction, and no alimentary canal. All that was supposed to be looked after by the college tutors and the independent reading by the students. R. A. Peters had just come as Professor of Biochemistry and had set up an excellent course. The new biochemistry building was being constructed at that time, but in my two student years physiology and biochemistry were crowded in the old building.

The famous feature was the mammalian laboratory class – the cat class – which was the creation of Sherrington during the latter part of the war years, the text of this unique course being published in 1919 in *Mammalian Physiology: A Course of Practical Exercises*. This laboratory manual was illustrated by drawings of dissections and by kymograph records of blood pressure, secretion and movements made by students in the formative stage of the course. For 2 years I was a student with Sherrington, Liddell, Creed and Sibyl Cooper as demonstrators, then for 10 subsequent years I was a demonstrator. The students could hardly realize the intensive preparation that preceded by 1 h the commencement of the class on each Thursday. Up to 20 decerebrate or decapitate cats were prepared. One of the demonstrators carried out the surgical procedures, and the whole technical staff under the stern eye of George Cox were mobilized in the anaesthetization and subsequent care of the preparations with attention to haemostasis, respiration and temperature control. It was rather like the feverish preparation before some dramatic performance. But when the curtain went up at 10 a.m. the prepared cats were awaiting the students. There were two students to a cat, so they had excellent technical training in the canulation of arteries and veins, in i.v. injections and in nerve dissection and stimulation. Throughout the 3-hour session several demonstrators checked the students' dissections and their relevant physiological knowledge. During the class the best experiments were displayed and at the end of the class the smoked kymograph tracings were preserved in varnish for illustration by the students in their practical notebooks. In 1952 Liddell wrote about Sherrington and these classes:

'His enthusiasm and zest in the conduct of that class were the key to its success. His urgent emphasis on correct procedure, his scorn of slovenly work (which could be surprisingly emphatic), and his excited interest in good results kept every member on his toes.'

In my 2 years as a student I did not see Sherrington carry out an experiment. In addition to my student classes I was fully

Sherrington during the 'Liverpool Period' (courtesy W. C. Gibson).

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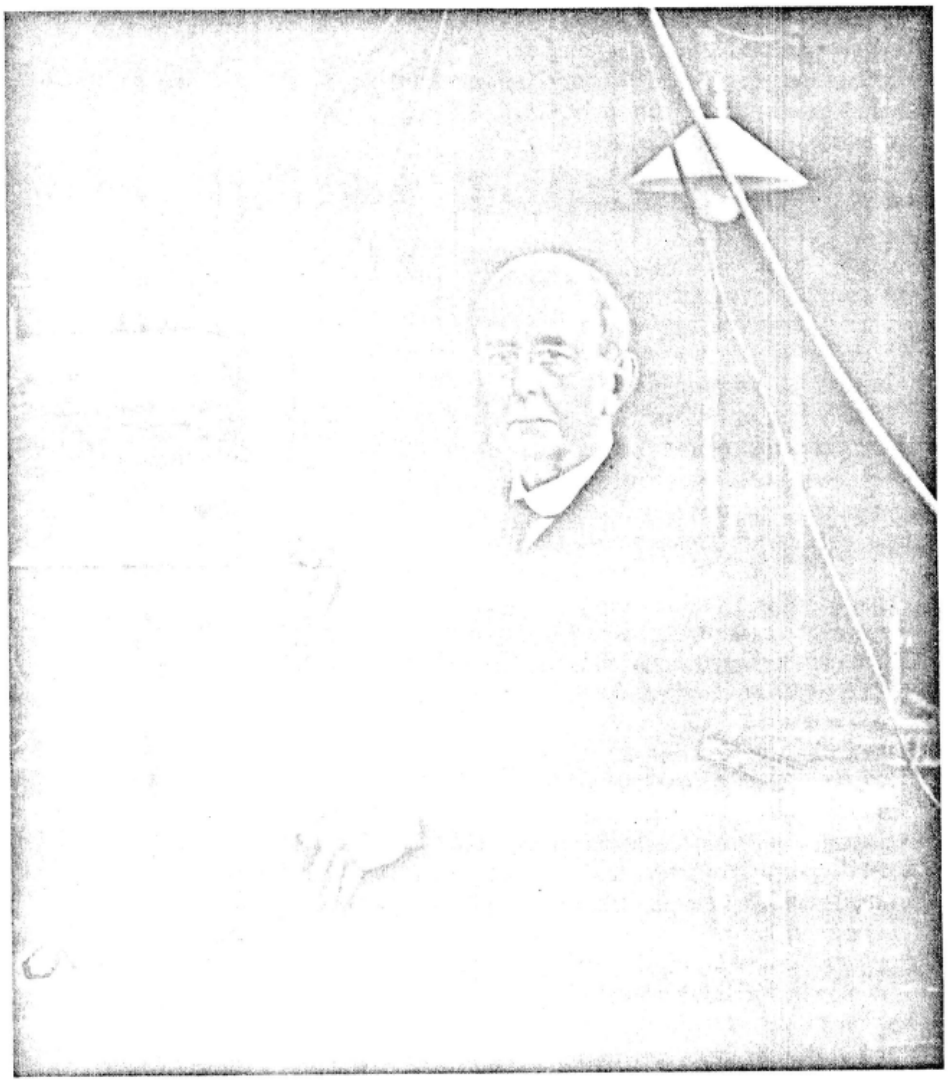
occupied in an intensive reading course in the excellent Radcliffe Library, and in writing an essay each week for my college tutor. However, I was often at the Sherrington house, 9 Chadlington Road, for afternoon teas. Lady Sherrington kept open house for students and friends every Sunday at 4 p.m. in term time. One was never invited, the door was open and one entered into the large living room and joined the company that had gathered. Then Sir Charles descended from his study and joined in the informality, regaling us with his memories, so rich and so varied. Also, there were cultural events to discuss – the books just published, particularly poetry and poetic criticism and art exhibitions. In these fields he had superb knowledge and judgement. In fact he had published a book of poems in 1925, and was still contributing verse to the Cornhill magazine. There were also topics of the university and of science, but almost nothing on politics!



Charles Scott Sherrington (courtesy W. C. Gibson).

Research – the life of an investigator

In the 1920s and into the 1930s Sherrington's laboratory would have been generally regarded as the leading laboratory of the world in the field of CNS physiology. This exalted status derived of course from the greatness of Sherrington. Yet it was amazingly modest, ill-organized and ill-equipped by present day standards. It will be surprising to know that in the whole Oxford period there was no secretarial assistance, not even a typewriter. Sir Charles did all of his enormous correspondence by hand, and did all of the filing of his records and letters. George Cox acted as business manager.

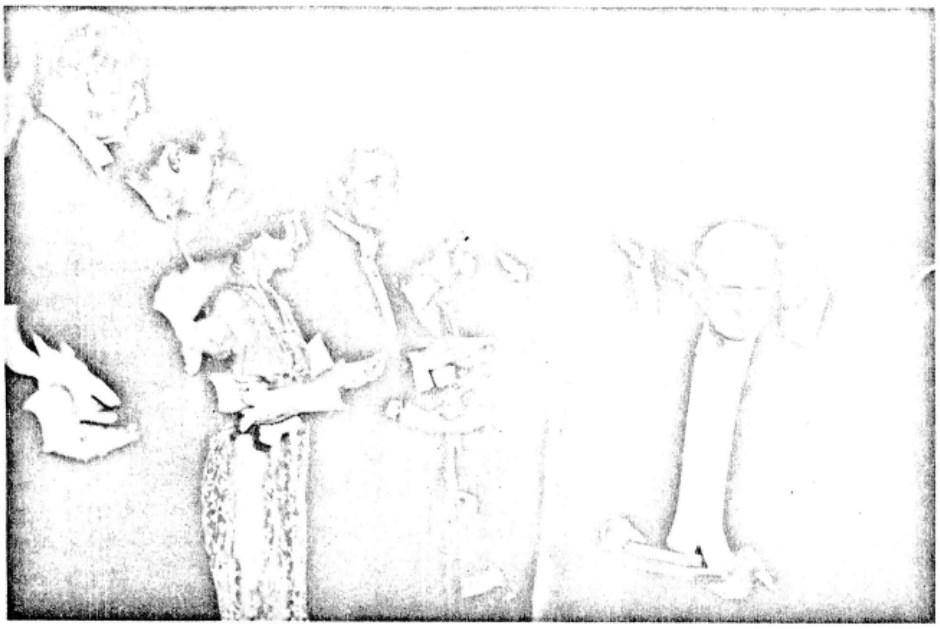
Even when biochemistry moved into its new laboratories in 1927 the physiology facilities were poor. Denny-Brown had inherited the sole well-equipped room from John Fulton in 1925. It had the only electrical recording system, a string galvanometer, and it had the other standard equipment of a falling plate camera, optical myographs and stimulating equipment built up of various key arrangements for single and repetitive stimulation using induction coils. In October 1927 I had been accepted as a D.Phil. student with Sir Charles as my supervisor. During 1928 five of us, who were all research associates, were quartered in the old mammalian laboratory with no office equipment other than a table, a chair and a partial privacy given by a folding screen; that was Granit, Denny-Brown, Olmsted, Marcu and myself.

An important scientific work in the department from 1925 to 1928 was by Denny-Brown who was studying the reflexes evoked by stretching extensor muscles, usually the pale fast gastrocnemius and the slow red soleus. With string galvanometer recording he was able to study single motoneurone firing. In a classical study he showed that inhibition slowed the frequency of firing of single motoneurones and he demonstrated that an increase in reflex response was due to the faster firing of individual motoneurones and the recruitment of additional motoneurones. He also introduced the antidromic impulse in the analysis of motoneurone responses. A kind invitation by him and Liddell gave me my first research experience late in 1927 on the effects of cerebellar stimulation on spinal reflexes.

Fortunately, late in 1927, Creed asked me to join him in a research problem on inhibition. When he moved into vision research I inherited his research room. That was most valuable for me because in January 1928 Ragnar Granit came from Helsingfors to work in Sherrington's laboratory, and Sherrington thought that we could work together, a choice for which we are eternally grateful. In those primitive days research problems were not easy to formulate or to implement when your total equipment was an optical myograph, a falling plate camera and sundry induction coils. Our chosen problem was to do for the crossed extensor reflex what Sherrington, Cooper and Denny-Brown had done for the ipsilateral flexor reflex. It was on the theme that dominated the research projects of the Oxford School at that time, namely the interaction of reflexes.

An overview of the Laboratory with personal remembrances

As I try to recover some general ideas on Sherrington's laboratory in the decade 1925–1935, foremost in my mind is the atmosphere of personal freedom with a minimum of collective effort. An outside observer would call it haphazard. There were no departmental colloquia. Nor were there any general directives from Sherrington or Liddell, who was next in charge of the neurophysiology. We were free to do what we wished, and to develop our research programmes, and to choose topics for our research associates. This was possible in an age where research grants for the whole laboratory were no more than a thousand pounds a year. Such manufac-



At the Nobel Ceremony, Stockholm, 1932 (courtesy W. C. Gibson).

tured equipment as was available, was relatively simple and cheap. It was at the very beginning of the electronic age. We built most of our equipment such as stimulators from inexpensive components or from remnants of discarded equipment. Stimuli were provided by induction coils by various key arrangements, some of very tricky performance. It was therefore quite an occasion when in 1929 A. V. Hill and his technician drove up from London with the present of a neon tube stimulator.

O'Neill constructed the precision optical myographs, which were the pride of the laboratory, allowing isometric recording of muscle contractions, which remained the most reliable measure of reflexes for the whole Sherrington era. Up to 1929 the isometric twitches had a distinctive time course, the contraction rising to a plateau that terminated in an 'angle' at the onset of relaxation. It was a feature much investigated by Fulton and was accepted as authentic by all in the laboratory and also elsewhere. In 1929 I planned to investigate the elasticity and viscosity changes responsible for the 'angle' by analysis of the damping of oscillations applied during the isometric twitch. To do this I had O'Neill change the support of the torsion rod from a V-shaped slot to an axial knife edge resting on a steel plate. To my initial chagrin, twitches recorded with this modified myograph had no 'angle'. My problem had evaporated! Twitches of the same muscle recorded with the old myograph had good 'angles'. It was immediately obvious that the 'angle' was entirely an artefact due to friction. I was greatly disturbed by my discovery and confided in Sir Charles that same afternoon. He recognized the error and we made a conjoint paper to the next meeting of the Physiological Society, where it aroused great interest. Meanwhile I had the unhappy task of telling John Fulton, who had built so much of his research career on the 'angle'. I was then only 26 and felt that I had inadvertently hurt my friend, but our friendship continued to flourish.

I tell this story to illuminate the deep commitment to scientific truth, that was basic to the philosophy of the Oxford Laboratory. It was a wonderful atmosphere to grow up in. There was no secrecy in projects or in discoveries. We all shared them in informal discussions. There were no lunch facilities at the laboratory. The important social occasion was the afternoon tea in an alcove of the library where members of both Physiology and Biochemistry departments met very informally from 4 to 5 p.m. It was a very enjoyable social occasion with opportunity to talk scientific gossip.

I had the wonderful privilege of working with Sir Charles from 1928 to 1931. It began with his invitation to help in determining the average tension developed by the motor unit in twitches and tetani. He had already prepared the animals with pure motor innervation of hind limb muscles by operative excision of the dorsal root ganglia some weeks previously, the ventral roots remaining intact. My task was to record the twitches and tetani of a series of muscles and then to count the motor nerve fibres in osmic acid stained sections. An unexpected collateral discovery was the dual size composition of the motor fibres, now recognized as the alpha and gamma fibres. However, inexplicably we missed the correct interpretation of this duality, the large fibres innervating the tension muscle fibres and the small the muscle spindles.

This collaboration extended to investigations on the basic synaptic mechanisms of excitation and inhibition that, as postulated by Sir Charles in a previous theoretical publication, were the central excitatory state, c.e.s., and the central inhibitory state, c.i.s. The experiments carried out in 1929–1931 brought to a close Sir Charles' life as an experimentalist. He was in his 74th year, and the experiments were very arduous. They fully corroborated his c.e.s., c.i.s. hypothesis as tested by experiments on flexor reflexes of the spinal cord recorded both mechanically and electrically by the string galvanometer. A special feature was the use of impulses fired antidromically into motoneurones as a powerful analytical tool.

Life in the Sherrington laboratory was enriched by many visitors who came to participate in research for months to years. Fulton returned for the years 1928, 1929 and there were a large group of American visitors: Olmsted, McCouch, Rioch, Ruch, Ingraham, Oldberg, H. E. Clark and E. C. Hoff. Even Alex Forbes came for some months and Gibson came from Penfield's laboratory. Most notably from Europe was Granit from Helsingfors who came for two long research visits, Karl Matthes came from Germany, Obrador from Madrid and Odoriz from Buenos Aires. In 1932 G. L. Brown spent six very enjoyable months with me. Thus, over the last years the Sherrington Laboratory had an international composition that was quite remarkable for that age. In 1932 there was published *The reflex activity of the spinal cord* that can be regarded as an authentic record of the Sherringtonian Oxford School.

The culmination of the Sherringtonian era came at the end of 1932 with the award to Sherrington of the Nobel Prize conjointly with Adrian. On an evening late in October 1932 the news of the award was heard by Granit on the BBC broadcast. By telephone, the whole laboratory staff and wives were mobilized to come that night to the Sherrington home for a never-to-be-forgotten celebration. Granit as a Swede was at the centre of that great occasion, with much drinking of sherry to Sir Charles and Lady Sherrie as we affectionately called them. The Sherringtonian Laboratory at Oxford had achieved the ultimate in world renown.

This article commemorates the 50th anniversary of this award. It came out later that Sherrington had been invited to nominate for the Nobel Prize that year and his nominee was Adrian. I am sure that if Adrian had had a similar invitation he would have reciprocated.

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