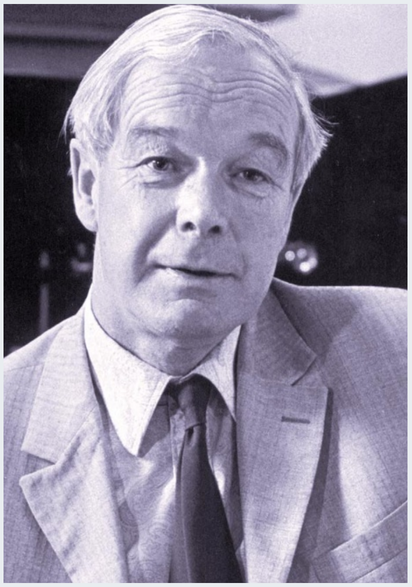
Obituary

Alan Hodgkin (1914–98)

Neurophysiologist



Alan Hodgkin, who died on 20 December 1998, was one of the greatest physiologists of the century. He set the foundations for much of modern neuroscience by explaining the origin of the nerve impulse, in an enormously productive collaboration with Andrew Huxley. Their work not only accounted for the explosive 'firing' of a nerve impulse, and for conduction of that impulse along the axon (nerve fibre), but it also opened up an entire new science of 'ion channels' — the sub-microscopic pores, embedded in the surface membrane of every cell, that regulate the passage of ions and control a multitude of cellular processes.

In July 1939, Hodgkin and Huxley, aged 25 and 21, succeeded in measuring the voltage on the inside of a nerve cell, all previous measurements of nerve activity having been extracellular. Working on squid at Plymouth, Devon, they dissected out the 'giant axon' (about 0.5 mm in diameter) and steered a fine glass capillary electrode along its interior. Their remarkable discovery (*Nature* 144, 710–711; 1939) was that during a nerve impulse the intracellular voltage reversed, from its resting level of −60 mV, to reach a peak of about +40 mV. This finding destroyed the dogma that had held sway since the turn of the century — that the impulse was produced by a loss of the membrane's resting ion selectivity — because a collapse of that kind would at most have taken the internal voltage to zero. But within three weeks of the discovery, their research was interrupted by the outbreak of the Second World War.

Most unusually for a physiologist, Hodgkin had taught himself mathematics as an undergraduate, and his adeptness at differential equations was enormously important not only to his later research but also to his wartime work on the development of airborne radar. Microwave communication was an infant technology, yet the spiral-scan and helical-scan centimetre radar sets that he helped develop for fighter aircraft were highly successful in detecting enemy bombers. The ordeals that he underwent, strapped into the tail of fighter aircraft fitted with prototype radar sets, were both thrilling and testing — not least because the 15 kV supply was prone to arc over in the rarefied atmosphere at 15,000 feet, occasionally setting fire to the equipment.

Far from being purely mathematical, Hodgkin's work was based on cutting-edge technology. When, from 1946, he was able to return to research on nerve, he built state-of-the-art electronic equipment — although modern-day electrophysiologists might be amazed that home-made cathode followers and vacuum-tube feedback amplifiers could have been exploited so successfully. One breakthrough was measurement of the current through the nerve membrane when its voltage was 'clamped' to different levels (thereby disrupting the positive feedback loop that generated the explosive rise in voltage).

But perhaps his greatest contribution was to invent a way of accounting for the measurements, through a set of differential equations representing separate sodium- and potassium-selective pathways. The results and analysis of those experiments were published in a series of five remarkable papers by Hodgkin, Huxley and Bernard Katz in 1952. The culmination, a quantitative description of the events underlying nerve activation (*J. Physiol.* 117, 500–544; 1952), remains a masterpiece. Hodgkin's personal account of the research, and of his wartime exploits, is told in *Chance and Design* (Cambridge Univ. Press, 1992).

That 'classical' description of the voltage-sensitive opening and closing of sodium- and potassium-selective conductances opened the way for modern molecular approaches. It predicted the existence of discrete ion channels for Na^+ and K^+, and it accurately specified their kinetic properties; it forecast their tetrameric structure, with four separate voltage-sensors; and it predicted the occurrence of 'gating currents' needed to open the channels. For more than 40 years, that work has been the standard against which subsequent 'patch clamp' and molecular cloning approaches have been evaluated.

Hodgkin's research was remarkable not only for its mathematical elegance, but also for the sheer beauty of his experimental results. He totally immersed himself in his experiments and their analysis, and to this end he always kept his research group very small, with just one or two collaborators. For these most fortunate colleagues the experience was richly rewarding, but demanding. He always took great delight in unexpected experimental findings, and in the intellectual exercise of accounting for the reality of nature.

In 1963 Alan Hodgkin was awarded the Nobel Prize for Physiology or Medicine, with Andrew Huxley and Jack Eccles; he was knighted in 1972, and the following year was appointed to the Order of Merit (a British honour restricted to just 24 people at any one time). From 1970 to 1975 he served as President of the Royal Society, and from 1978 to 1984 as Master of Trinity College, Cambridge, where (since 1932) he had been first an undergraduate and subsequently a fellow. Under his leadership the Royal Society became more open in its formulation of science policy, and made preparations to meet the major changes in science funding that were looming.

In 1970, Hodgkin turned his attention to the visual system, when the exciting new technique of intracellular recording from retinal neurons was brought to his laboratory by Denis Baylor. Hodgkin transformed the study of rod and cone photoreceptors, bringing to the subject the incisiveness and quantitative rigour that were the hallmark of his research on nerve and muscle. Our understanding of transduction in retinal photoreceptors is based on this work, carried out between 1970 and 1988.

For more than half a century Alan's career was supported by his wife Marni — herself the daughter of a Nobel laureate, Peyton Rous. She well understood the demands of scientific research, and revelled in the entertaining associated with his prestigious posts; together they shared a wide-ranging love of the arts.

Alan Hodgkin's wonderful approach to biology stimulated generations of neuroscientists to the study of nerve, muscle and photoreceptors. His death marks the end of a classic era in neurophysiology.

Trevor Lamb

Trevor Lamb is in the Department of Physiology, University of Cambridge, Downing Street, Cambridge CB2 3EG, UK.
e-mail: TDL1@cam.ac.uk