

Sir Alan Hodgkin

Alan Hodgkin was one of the leading experimental biologists of the middle years of the 20th century. He achieved an almost complete understanding of excitation and conduction in nerve fibres at the level possible with the techniques available at that time. This paved the way for subsequent unravelling of the molecular mechanisms, which followed from improvements in electronic techniques and the growth of molecular genetics. He also made major contributions to other aspects of the physiology of nerves and muscles, and especially to the mechanism of vision. During World War II, he was a member of the team that developed short-wave airborne radar, a development that was crucial to many of the successes of the RAF. His career was completed by holding the two most distinguished positions open to an academic scientist in Britain, the Presidency of the Royal Society (1970–1975) and the Mastership of Trinity College, Cambridge (1978–1984).

It was his war work that led him to write his autobiography, *Chance and Design: Reminiscences of Science in Peace and War* (1992). The development of airborne radar had not been covered in any of the histories of the war and Hodgkin felt that he had a duty to the memory of his colleagues, several of whom had died in accidents during test flights, to record their achievement. When this was complete, he added a very full account of his boyhood, his time at Cambridge before the war, and his post-war scientific work, with an outline of his activities as President of the Royal Society and Master of Trinity. The result is a delight to read, enlivened by frequent quotations from his letters to his mother and his wife’s to her parents in the U.S.A. Inevitably, parts are too technical for some readers but the book is laid out so that these can easily be skipped.

He was born into a strictly Quaker family shortly before the outbreak of World War I. His father George was resolute that his principles did not allow him to undertake any work that would help the war effort, an attitude that generated a degree of hostility that is difficult to believe for those of us who lived through the second war when the attitude of genuine conscientious objectors was readily accepted. George Hodgkin took part in relief work in Armenia, and on his way to that country for a second visit in 1918 he died of dysentery in Bagdad. Alan’s mother made a second marriage in 1932, to Lionel Smith, Rector of the Edinburgh Academy and son of the redoubtable A. L. Smith, Master of Balliol College, Oxford. Alan’s main boyhood interest was natural history, which he was able to pursue during his many visits to Quaker relatives in various parts of the country and at his two schools, The Downs near Malvern and Gresham’s at Holt in Norfolk; he was not a mere bird-spotter but made several serious studies of bird behaviour.

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Alan won an open scholarship to Trinity College, Cambridge and went up in the autumn of 1932 to read for the Natural Sciences Tripos. His original intention was to specialise in zoology with the idea of a career in applied biology, probably overseas, but on the advice of his Director of Studies Carl Pantin (later Professor of Zoology at Cambridge) he took physiology together with zoology and chemistry in Part I; he became more interested in physiology and chose it for his Part II. It was also on Pantin’s advice that he taught himself much mathematics outside his university courses.

In Trinity, Hodgkin stepped into a tradition of interest in the mechanism of nerve action. This had been started by a friend of his father, Keith Lucas (killed in a flying accident in 1916), a Fellow of Trinity, who established that each nerve impulse is an “all-or-none” event, i.e., the size of the event that travels along a fibre is the same whatever the nature or the strength of the stimulus that set it off. Lucas’s pupil E. D. (later Lord) Adrian, also a Fellow and later Master of Trinity, carried this line of work further, recording the sequences of impulses set up by sense organs or sent from the brain or spinal cord to muscles, and inspired Hodgkin by his lectures; another link in the chain was William Rushton, a member of the teaching staff of Trinity.

Hodgkin completed an important piece of research on nerve during his first postgraduate year and was immediately elected to a junior Research Fellowship at Trinity, an unusual distinction. In this work, Hodgkin gave the first experimental evidence for the “local circuit theory” according to which the electrical event at each point along the nerve fibre causes current to flow and to activate the next point along the fibre. The experiment had actually been planned with a different objective, so the outcome was an example of the “chance” that forms part of the title of his autobiography.

Hodgkin’s next piece of research was another example of “chance.” He was recording from bundles of fibres from a nerve from a crab, and one bundle gave an exceptionally large response which obeyed the “all-or-none law”: evidently it consisted of a single fibre of unusually large size. This preparation enabled Hodgkin to detect an active “local response” even when the stimulus was not strong enough to set up an all-or-none propagated impulse.

In 1937, Hodgkin went to the U.S.A. to spend a year at the Rockefeller Institute in New York. He records that he found much resistance both to the local circuit theory and to the idea of a local response: the latter was regarded as a breach of the all-or-none “law.” Hodgkin met K. S. (Kacy) Cole, who was using as experimental material the recently-discovered giant nerve fibre of the squid. This fibre, about 0.5 mm in diameter, is large enough to make many experiments practicable that
would be impossible in other fibres. In an exceptionally elegant experiment, Cole had demonstrated a large fall in the electrical resistance of the surface membrane of the fibre during the passage of an impulse. Hodgkin collaborated with Cole in another experiment; this was his introduction to the squid giant fibre which was the material he used in the most important of his later experiments.

One of the famous members of the Rockefeller Institute was Peyton Rous, who later received a Nobel Prize for his discovery of a cancer (in chickens) caused by a virus. Through him Hodgkin met his daughter Marion (Marni), whom he later married, but their acquaintance was interrupted by the outbreak of war. In 1944 Hodgkin returned to the U.S.A. for a few weeks in connection with his war work; he renewed his acquaintance with Marni, they married and succeeded with some difficulty in getting permission for her to come to Britain.

On his return to Cambridge, Hodgkin was appointed to teaching posts in the university and in Trinity. During 1938–1939, he built a new set of electronic equipment based on expertise that he had learnt at the Rockefeller, and together with Rushton he showed that applied currents too small to excite a nerve fibre caused electric changes similar to those in a non-living cable.

I went up to Trinity as an undergraduate in 1935; Hodgkin and I both lived in college and we met occasionally in friends’ rooms. In 1938-1939 I did Part II Physiology and received some teaching from him. He invited me to join him at the laboratory of the Marine Biological Association at Plymouth during the summer of 1939 to do some experiments on the squid fibre. Our first experiment was abortive, but—another example of “chance”—Hodgkin saw that we had the fibre in a position where we could push a fine saline-filled glass tube down inside the fibre to act as an electrode with which we could measure directly the potential difference between the interior and the exterior of the fibre. At rest, the interior was about 50 millivolts negative relative to the external solution, but on stimulation the internal potential rose by about 100 mV, so that there was an “overshoot” of about 50 mV beyond the resting potential, a result that would be impossible on the then current theory. By the time that we had checked this result, war was imminent so we packed up and left Plymouth; two days later Hitler’s armies marched into Poland. We published our result in a short Letter to *Nature*, with no explanation for the overshoot. We met a few times during the war and published a full-length paper in 1945, containing no less than four possible explanations for the overshoot, all of which proved to be wrong. It was also in 1945 that Hodgkin and I began discussing the idea that turned out to be correct.

During the first six months of the 1939–1945 war, Hodgkin
worked at the Royal Aircraft Establishment on the physiological problems of high-altitude flying in unpressurised aircraft. He was involved in the design of an “economiser” that avoided the waste of oxygen, and in the investigation of “bends,” the painful consequence of nitrogen bubbles coming out of solution in the blood, which Hodgkin experienced himself as an experimental subject in a decompression chamber. From February 1940, Hodgkin was working on airborne radar, initially at a number of places but finally in Malvern College. He was already skilled in electronics but learnt much more that was valuable in his post-war research. Airborne radar was already in service for detecting ships; its wavelength was 1.5 metres, too long to achieve precise direction-finding with aerials small enough to be carried on an aircraft. In 1940, the cavity magnetron was invented, making high powers available at wavelengths of a few centimetres. Most of Hodgkin’s work for the rest of the war was the development of airborne equipment working at 9 cm and later 3 cm, including much flying to test the equipment. Initially, he was on equipment for night fighters but was transferred to work for bombers, first for target location and later on gun control. Like most of the scientists engaged on these projects, Hodgkin was strongly opposed to the bombing of open cities, which was the principal aim of Churchill and his adviser Lord Cherwell; persuasion from Patrick Blackett and others succeeded in getting a few of the radars designed for locating ground targets diverted to antisubmarine purposes, where they had a decisive effect in reducing our shipping losses.

Hodgkin returned to Cambridge and research on nerve in the autumn of 1945 and I joined him at the beginning of 1946. Our first question was the origin of the overshoot. The action potential was thought to be caused by a sudden increase of permeability of the membrane to all kinds of ions, making a short-circuit so that the internal potential would rise towards that of the external solution but no further. The increase of permeability had been confirmed by Cole’s experiment, but the overshoot remained a puzzle. With hindsight, Hodgkin and I later felt that we had been stupid not to have seen at once that it would be expected if the increase of permeability was specific for sodium ions: these would diffuse inwards because they are much more concentrated outside than inside the fibre and would carry their positive charge inwards. This was shown to be the correct explanation by Hodgkin, together with Bernard Katz, in the summer of 1947.

The experiments before the war in which Hodgkin had seen local responses had led him to believe that the increase of permeability of the membrane was graded with the amount of the change of internal potential. As the internal potential was raised the permeability increase would allow entry of sodium ions whose positive charge would raise
the internal potential still further, so that the situation would be unstable and the internal potential would rise explosively, causing the all-or-none character of the action potential.

The instability also makes it difficult for an experimenter to control the situation so as to investigate the causation of the permeability change. Hodgkin realised that the instability would be avoided if a wire were pushed down inside a giant nerve fibre and used to draw off the current carried inwards by sodium ions. This could be achieved with a feedback amplifier, an arrangement that came to be known as a voltage clamp. Cole had the same idea and was the first to have such an equipment running, in 1947, but he made only limited use of it, showing only that current through the membrane did indeed vary continuously with potential, with a region in which the relationship would be unstable if the feedback were not operating.

Hodgkin visited the U.S.A. again in the spring of 1948. He learnt from Cole about this experiment and in turn told Cole of the experiments with Katz on the effects of low sodium concentration. Hodgkin’s voltage clamp equipment was ready for the Plymouth season of 1948. He and Katz started work with it and I joined them later, obtaining results generally similar to Cole’s. We improved the apparatus before the 1949 season, when Hodgkin and I did our final series of experiments, in which we recorded the effect of altering the external sodium concentration. We separated the components of current carried by sodium and by potassium ions, and we fitted their time courses with equations that seemed plausible if the currents were carried by the ions diffusing through “gates” in the membrane which were opened or closed by changes of membrane potential. We obtained a satisfactory fit to our observations on the basis of these “Hodgkin-Huxley equations” and calculated from them the time course and the velocity of an action potential to be expected; these agreed satisfactorily with those recorded experimentally.

These results were published in five papers in 1952, and led to the award to us, jointly with Sir John Eccles, of the Nobel Prize in Physiology or Medicine in 1963. To my surprise, these “Hodgkin-Huxley equations” have survived with relatively little modification, though at the time I thought that they were very provisional and would soon be superseded.

Shortly after the war, Hodgkin was the Ph.D. supervisor of Richard Keynes, and encouraged him to develop radioactive tracer methods for measuring the movements of ions in and out of nerve fibres at rest and during the impulse. Later, they joined forces at Plymouth to investigate, with other collaborators, the working of the sodium pump that restores the internal concentrations of ions to their resting values. They also discovered the phenomenon of single-file diffusion of potassium
ions through nerve membranes, and proposed an explanatory model that has very recently been shown to agree well with the actual atomic structure of the potassium filter.

In the intervals between the summer seasons at Plymouth, Hodgkin did other important work at Cambridge. A major technical advance was the further development of a method of recording the internal potential of a cell by pushing the very fine (0.001 mm) tip of a saline-filled glass tube through the surface membrane, so that it could be used for recording short-lived action potentials as well as the steady resting potential. This method of recording immediately became a standard technique.

When we had completed the work on the squid fibre that we published in 1952, we could not see what could be done next to take the understanding of the excitation process to a deeper level. Huge advances have been made since, but all have depended on technical improvements or on advances in other branches of biology—notably molecular genetics—that were unforeseeable in 1952. Hodgkin therefore switched to other aspects of nerve physiology.

The final phase of Hodgkin’s scientific work, from 1970 onwards, was on the mechanism by which the rods and cones of the vertebrate retina respond to light. In this work he had several collaborators, most notably Denis Baylor from Stanford University. They played a major part in elucidating the unbelievably complex process, involving many steps of biochemical amplification and complicated interactions with calcium ions, by which the absorption of a single photon by one of the billion or so photosensitive molecules in a single rod or cone cell suppresses the entry of several million sodium ions.

As President of the Royal Society (1970–1975), Hodgkin reestablished scientific contacts with Japan and with China. There had been no formal contact with Japan since the war, and Hodgkin was a member of the first formal delegation to that country. The outcome was the establishment of an exchange agreement, on the lines of those already existing with many other countries. His visit to China did reestablish occasional contacts but no more: the Cultural Revolution was still in progress and made anything but the most directly applied science impossible. An event which was painful to Hodgkin in more ways than one was the publication in 1971 of Lord (Victor) Rothschild’s report proposing the “customer-contractor principle,” according to which much of the work of each Research Council should be decided by the related Government department acting as customer and paying for the work with funds transferred from the Research Council. Hodgkin, together with most working scientists, disagreed strongly with this idea which was likely to stifle initiative in basic research, and a unanimous report of the Royal Society Council opposed the extensive use of the principle.
This did not dissuade the Government from adopting the principle, although some of the proposed transfers of funds were reduced. The personal aspect of this disagreement was that it overshadowed the long-standing and deep friendship between Rothschild and his wife and the Hodgkins.

The Mastership is a less demanding post in Trinity than in most colleges, because the Master is appointed by the Crown, and the Fellows, remembering a tyrannical master in the eighteenth century, give him less power and fewer duties than in colleges where the head is elected by the Fellows. The Master’s Lodge gave him and Marni scope for their talent as hosts, both to junior members of the college and to many senior persons. They restored the custom of inviting the visiting High Court judge to occupy part of the Lodge during his occasional tour of duty in Cambridge. Under Hodgkin’s guidance, the courts known as Whewell’s Courts were renovated and much of the Fellows’ Garden was replanned. The decision to admit women undergraduates to Trinity had already been taken; it was a change of which Hodgkin wholeheartedly approved, and the admission of the first batch coincided with his becoming master.

Hodgkin had been freed from teaching duties in 1952 when he was appointed Foulerton Research Professor of the Royal Society. In 1969 he was elected John Humphrey Plummer Professor of Biophysics in Cambridge University. He remained active in his research on vision throughout the time when he was President of the Royal Society and Master of Trinity. His laboratory work was curtailed after his retirement as Master by a sequence of illnesses, though he continued with the help of his colleague Brian Nunn until the latter’s premature death in 1987. His medical problems culminated in an operation in 1989 to relieve pressure on the spinal cord from one of the intervertebral discs in his neck, which left him unable to walk without support and with progressive disablement.

Hodgkin received many honours, most notably membership of the Order of Merit (1973), which was preceded by the KBE (1972). At the Royal Society, he was elected FRS in 1948 at the unusually young age of thirty-four and received a Royal Medal in 1958 and the Copley Medal in 1965. He was awarded the Baly Medal of the Royal College of Physicians (1955). He was Chancellor of the University of Leicester (1971–1984) and President of the Marine Biological Association (1966–1976). He was a member of many foreign academies and received honorary degrees from many universities in Britain and overseas.

Hodgkin had a remarkable ability to recognise important problems in his area of interest and to see a way of tackling them. As a result, he was usually ahead of the field and could afford to carry on at his own
pace without worrying about being overtaken by other laboratories. Apart from three or four early pieces of research carried out alone, he did his experimental work with one, two or sometimes three collaborators. From shortly after the war, he had the help of a highly skilled instrument maker, R. H. Cook. Hodgkin had no wish to build up a large group as is often done nowadays. As well as his own collaborators, he usually had one or two visitors doing their own research and publishing independently; he was free with advice and help to them, as he was to me when I was not actually in collaboration with him. He was always ready to discuss current unpublished work with others. I have tried to model my style in science on his, and I regard myself as fortunate to have served my scientific apprenticeship with him.

He remained a very modest man, despite his achievements and his distinction. He had many interests outside science, notably literature, art and travel. His wife Marni shared these with him, except for fishing which he mentioned among his “recreations” in Who’s Who. She was for many years in charge of the children’s book section of Macmillan. Their marriage was ideally successful, and it is tragic that their last years together were overshadowed by his disabilities, throughout which she cared for him devotedly. She survives him, together with the three daughters and one son of the marriage; the son has followed his father into biological research, and his election to the Fellowship of the Royal Society in 1990 gave great pleasure to his father.

Elected 1967

Sir Andrew Huxley
Formerly Master of Trinity College, Cambridge

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