The pursuit of science in the mid-20th century

Chance & Design: Reminiscnces of Science in War and Peace, Alan Hodgkin, Cambridge University Press, 1992, 412 pages

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Alan Hodgkin discovered the ionic basis of nerve conduction. In this book, his autobiography, he discloses revealing childhood and family scenes and describes with ardor his undergraduate years at Cambridge, his first trip to America in 1937, and his early experiments with Andrew Huxley in Plymouth. Interrupted by the war, Hodgkin worked on airborne radar, and his recollections of this work will interest physicists and military historians. Hodgkin chronicles postwar Britain, and he outlines in brilliant detail the experiments that led to his discoveries. Finally, he recounts his ascendance to the highest ranks of British society and world science.

Hodgkin's 1937 trip to America divulges the theme of the book: the element of chance in life's choices and in scientific discovery. Before coming to America, he had corresponded with Joseph Erlanger, of Washington University, about work Hodgkin had done as an undergraduate. These experiments, which earned him a Trinity Fellowship, conflicted with Erlanger's views of nerve conduction. To investigate further the local currents and graded potentials in nerve, Herbert Gasser invited Hodgkin to work at the Rockefeller Institute. For two years Hodgkin lived in New York, where he met his future wife, Marni Rous, and by his own analysis changed from an amateur into a professional scientist. Before he returned to Britain, he visited Mexico and wrote this: "The sea here is so soft and warm that it feels like a new element and I was quite surprised to find that it tasted salt." The young romantic had seen the New World and begun his life's work. Questions formed in his mind. Do ions flow through the nerve membrane; do local currents then stream in the external salt solutions; does membrane conductance increase during action potentials; do subthreshold potentials really exist?

No mere catalog of queries, the book in fact reads like a great novel. The opening scene, for example, is strikingly reminiscent of Somerset Maugham's *Of Human Bondage:* the darkened bedroom, a child being told of a parent's death, the acquisitive disruption to the four-year old's life. Hodgkin's childhood foreshadows future events, like his discomfort with his mother's second marriage, his complicity in pre-war demonstrations, and his choice of science as a career. Prominent relatives have an impact on his life: "Uncle Doctor," for whom Hodgkin's disease was named; Grandfather Thomas, the distinguished historian; Edward, the banker, his deceased father's brother who had once given a popular lecture on "Light as a Repulsive Force," and who left Hodgkin an endowment without which he could not have chosen physiology over medicine. Outlandish relatives receive more attention, and Hodgkin describes them in picturesque language: Uncle Alderson, "a tubby, benevolent bachelor with a gleaming bald head, an appalling stammer and an absolutely uncontrollable laugh;" Aunt Katie, the eccentric, "intensely hospitable —to animals and birds as well as the friends and relatives who shared her many hobbies. When old and rheumaticky she shared her breakfast in bed with red squirrels from the garden . . ." Under her tutelage, Hodgkin recorded his first experiments on the location of bird's nests. "And after the bright days in the Easter wind, there were the evenings in the lamplit room when she talked of every part of the world and strange birds and butterflies. . ." Thoroughly scientific, she endowed science, and birds in particular, with a special appeal, as Feynman's father had done on similar outings.

The Society of Friends, to which Hodgkin's family belonged since the seventeenth century, had a lasting influence on his life. After a violent confrontation with prowar demonstrators in 1917, his mother pondered the reformer's dilemma; what to feel and do when the poor turn against their redeemers, questions that Bertrand Russell raised in the same era. In college, Hodgkin experienced similar emotions: first idealism for Quaker allotments in the poor village of Wigan, and then revulsion at the lives of the unemployed miners among whom he lived. Though sympathetic to the anti-war movement, he was deeply disturbed by a visit to pre-war Germany and had no conscience about fighting her.

Hodgkin loathed prepatory school. His descriptions of the wicked master and the suicide of a fellow schoolboy are reminiscent of Dickens, and his only charitable memory is that he learned to read widely and to work on his own. In college he read the collected works of famous and lesser known scientists, including his deceased father's friend, Keith Lucas, whose equipment Hodgkin used for his first nerve experiments. What mattered most was to have enough equipment "to do something new." A gadgeteer, he liked to build his own instruments and deemed amplifier noise a moral penalty for bad workmanship. Hodgkin never had a supervisor and never received a Ph.D. degree. Years later, as an esteemed scientist, he attended the Tercentenary of the Royal Society and wore his plain silver M.A. hood among a magnificent display of doctoral gowns and delighted that his un-

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usual silks were assumed to represent immense distinction.

Hodgkin had strong scientific and personal predilections. He found Lorente de No', "too dashing for my taste," and Harry Grundfest, "the best physiologist" in Gasser's group. He pokes fun at Lorente de No's one-thousand page monograph and "flimsy arguments" that frog nerves conduct impulses after removal of Na, and disdains his reluctance to rethink his arguments, in contrast to Eccles, who eventually embraced the theory of chemical transmission between nerve and muscle. "The crazy members" of the scientific community annoy Hodgkin, and he suggests that meetings include sessions on the "Wider Implications of Physiology" as a "dump for the loonies." When Gasser said he did not believe in graded responses, Hodgkin rejoined that he should work on single fibers. When Erlanger argued that the responses were unique to crabs, Hodgkin went to St. Louis and did experiments on frogs. Derisively, Hodgkin relates that when he saw the disputed event and asked "What's that?" Blair, Erlanger's colleague, replied: "I don't know, but it won't happen again."

Erlanger said he would believe Hodgkin's theory if altering the resistance of the external solution affected the velocity of propagation. "I thought about this on the long journey back from Mexico City and realized there was a simple way of doing this test . . ." He replaced salts with oil, the velocity decreased, and Grundfest shook his hand "like a character out of a C.P. Snow novel." He repeated the experiment in Woods Hole with Cole and Curtis on the squid axon. They, in turn, demonstrated that membrane conductance increased during an action potential, data that would become a logo for the Biophysical Society. Hodgkin says he learned a great deal from Cole, and he describes this initial interaction with appreciation as "the first time I have collaborated with anyone."

Hodgkin and Huxley left their Plymouth laboratory temporarily in 1939, "in the optimistic hope that the war might soon be over . . ." but they were not to return until 1947. Hodgkin's first war project was to design oxygen masks for aviators, who compared themselves with mountain climbers and were too cavalier to use them. He began work on radar at a time when communications experts knew more about carrier pigeons than Maxwell's equations or the oscilloscope, which had early ties to neurophysiology and was just coming into wider use. Designing airborne radar to keep pilots from flying into hills or to help gunners shoot down enemy planes required a mixture of physics and physiology: the range of bullets, how fast planes fly, the speed of light, the conduction velocity of human nerves, and human nerve itself. Hodgkin muses on the conflict between engineers (who focus on differences between theory and practice) and physicists (who maintain any snag can be overcome if the theory is sound), similar to his earlier comparison of zoologists (who thrive on animal differences) and physiologists (who concentrate on what is similar). Invited to become part of the Manhattan Project, he refused because he "disliked working on such a destructive weapon." When he heard the Americans had dropped an atomic bomb on Japan, Hodgkin responded enigmatically with, "Good Heavens, they've got it to work after all." Crossing the Atlantic in wartime, he had one of his most elegant ideas (unpublished until 1954): a dimensional analysis of nerve propagation that led to a formula for velocity and, eventually, to an optimal density for Na channels.

Hodgkin regrets he had not mentioned earlier that the reversal during an action potential might reflect transient selectivity to Na (once referred to as the Hodgkin hallucination). In explanation he cited a paper that Cole and Curtis published in 1942, according to which action potentials reversed by 118 mV and external sucrose had no influence. In *Membranes, Ions and Impulses,* Cole minimized these data and gave a different emphasis to the same details. Hodgkin overcame objections to his Na theory with the help of Bernard Katz, whose results reinforced the importance of external ions.

After the war, the experiments moved quickly: the shift away from carrier models in 1946, the separation of Na and K currents in 1947, and, in the same year, a clear statement of the Na hypothesis: "the active membrane, instead of being freely permeable . . . becomes much more permeable to Na than to K." Finally, the explanation: passive cable theory combined with active membrane phenomena in a formula that stands as a masterpiece of intellect and resolution. The Hodgkin-Huxley equations, published in 1952, summarized all that went before and have influenced all that has happened since. With molecular interpretation, these macroscopic equations pre-announced gating currents, noise, and ion channels.

Hodgkin and Huxley never worked together again. With Keynes, who made the isotopes they needed on a neutron pile, Hodgkin studied the flux of ions and the Na/K pump. With Adrian, he helped create one of the first Biophysics Departments. With Nastuk, he measured action potentials with microelectrodes and confirmed the Na hypothesis in muscle. Graham and colleagues used them to record resting potentials, and Ling had taught Hodgkin how to make them: they filled their electrodes with 120 mM KCl, which made them slow. Arbitrarily, Hodgkin suggested 3 M KCl, never intending that value to become a standard. The story evinces the occasionally mindless side of science, also described in *The Periodic Table* by Primo Levi after visiting a laboratory he had worked in, in which chemists followed slavishly his formulas.

Hodgkin is self-effacing. His first home, near the preparatory school he so disliked, was "a stage set for a malignant comedy;" his first award was inscribed to the wrong person, and his first lecture as a Nobel laureate, in which "even his critical children bathed in reflected glory," was given under undignified circumstances. The prize money, £6000, went toward central heating in improved quarters for his young family, and his most difficult task was to answer letters from people with neurological diseases, who hoped that his work might immediately help them.

The beginning of people's lives, Hodgkin asserts, is generally more interesting than the end. But he does not conclude with the protagonist, returned from war, victorious in his interrupted work. He registers instead in the last beautiful pages his tired ascendance to the presidency of the Royal Society, an office once held by Newton and that Hodgkin openly enjoyed for its social value. He worked on vision, became Master of Trinity, visited China, and retired to a home that suited him and his wife "down to the ground."

As the book closes, the sense is that Hodgkin could have solved any problem—he just happened to turn his mind to nervous conduction. Could he have existed, as Bertrand Russell could not have, in any other culture? If it is true, as Hodgkin and Russell both believe, that directness and planning do not coincide with scientific progress, and that breakthroughs occur "for perfectly dotty reasons," design would seem to have little consequence. Or perhaps chance is the engine of design. In 1978, in the hills near Erice, probably not unlike those near The Downs where he sought birds as a boy, Hodgkin looked for the prized wild orchids that a few conferees had chanced upon and brought back to the meeting room. When Hodgkin went out, he found the most, though he rarely picked any, and the prettiest ones, too. He knew exactly where to look.