BIOGRAPHICAL MEMOIRS

David Keynes Hill. 23 July 1915 – 18 August 2002 Elected FRS 1972

Andrew Huxley


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David Hill followed his father, A.V. Hill FRS, into the study of muscular contraction. Using a wide range of experimental techniques, he made several important advances of which the most important was the discovery of the ‘short-range elastic component’, a phenomenon which implied that even in the resting state there was an interaction between the thick (myosin) and thin (actin) filaments. He also studied physical changes in nerve when stimulated.

FAMILY

David came from strongly academic families on both sides. His father, A.V. Hill (FRS 1918; SecRS 1935–45; ForSecRS 1945–46; Nobel Prize, 1923; always known simply as A.V.; see Katz (1978)) had held the chairs of physiology at Manchester (1919–23) and at University College London (1923–26) before becoming Foulerton Professor of the Royal Society (1926–51). A.V.’s sister married T.S. Hele, biochemist and Master of Emmanuel College, Cambridge. David’s mother, Margaret (née Keynes), was the sister of the economist Maynard Keynes and of the surgeon, bibliophile and author Geoffrey Keynes, who had married a grand-daughter of Charles Darwin and was the father of R.D. Keynes (FRS 1959), with whom David collaborated in his work on nerve. Margaret’s father, John Neville Keynes, was for many years Registrary (chief administrative officer) of Cambridge University, and his wife’s brother, the physician Sir Walter Langdon-Brown, was Regius Professor of Physic at Cambridge from 1932 to 1935.

In this memoir I shall refer to David Hill simply as ‘David’ and to A.V. Hill as ‘A.V.’.

David had one elder sister, Polly, a distinguished economist concerned mainly with West Africa; his younger brother, Maurice (FRS 1962, died 1966; see Bullard (1967)), was an oceanographer, and his younger sister, Janet, a doctor (died 2000), married the immunologist John Humphrey (FRS 1963, died 1987; see Askonas (1990)).
David married John Humphrey’s sister Stella in 1949. She already had one daughter by a former marriage to an American serviceman, and she had three more daughters by David, two of whom are married. David is survived by his sister Polly and by his wife, his step-daughter, his three daughters and four grandchildren.

Stella was very fond of animals and kept dogs, poultry, fancy pigeons and horses; their youngest daughter later became a top-level performer in eventing. After their marriage David’s work was at Hammersmith in west London but they lived outside London, first at Arkley near Barnet, then at Furneux Pelham, Hertfordshire, then in Gloucestershire and from 1986, after David’s retirement, near Ripon in North Yorkshire, close to the home of one of his daughters. A result of having animals to look after was that they did not travel as much as they would otherwise have done. David accompanied his father to three of the three-yearly International Congresses of Physiological Sciences before World War II: 1932, in Rome, where A.V. gave the inaugural address (the speech of welcome was given by Mussolini); 1935, in Leningrad and Moscow; and 1938, in Zürich, followed by a meeting on high-altitude physiology at the research station on the Jungfraujoch headed by Alex von Muralt. David attended only two of these Congresses after the war: 1947, in Oxford; and 1974, in New Delhi. He quite often attended meetings of the (British) Physiological Society.

EARLY YEARS

In the notes he left with The Royal Society, David wrote as follows:

We moved to London in 1923 when my father was appointed as Jodrell Professor of Physiology at University College, and I have many memories of his laboratory, where he delighted in instructing us in some of his skills and in employing his children as subjects for physiological experiments. We had a large house and a two acre garden in Highgate (the purchase of which had been assisted by the Nobel Prize my father received the year we moved). In 1926 we participated in the demonstrations at the Christmas lectures on ‘Living Machinery’ to a ‘juvenile auditory’ at the Royal Institution.

My father liked to have his children around when he was in his lab, as well as to have them take part in his recreations such as running and walking, or grinding-in the valves of his car. From 1929 the family owned a holiday cottage, ‘Three Corners’, near Ivybridge in South Devon, close to Dartmoor and 9 miles from Plymouth. The situation was chosen partly because it was near the Marine Biological Laboratory at Plymouth, where my father worked occasionally during the holidays. We enjoyed the aquarium, and the trips to sea trawling for fish. Much entertainment of scientists (some working at the Plymouth laboratory), of relatives or friends took place at ‘Three Corners’, where we spent at least two months of every year when we were young. We were greatly attached to the place and the surrounding country which we covered on foot and on bicycle.

From the age of ten onwards I occasionally helped my father, in some humble capacity, with his experimental work, writing down columns of figures, perhaps reading the galvanometer, or turning the handle of the calculating machine. He was a considerate, if somewhat exacting, taskmaster. It was probably good training for the eye and hand of a future scientist, helping to instil the habit of precise and careful observation.

EDUCATION

While A.V. was professor at Manchester, they lived in Altrincham and for two years from 1920 David went to Culcheth Hall, which he described as ‘a gentle children’s school’. In 1922 he entered Bowdon College, which turned out not to be satisfactory; he left after one term and
had a governess at home for the rest of the year. After the move to London in 1923 he was at Byron House School, ‘a delightful school’ and in 1925 went on to Highgate School, a well-known public (that is, fee-paying) school. At first he was in the junior school but in 1928 he won a scholarship to the senior school, ‘an excellent school’. David mentions the following masters ‘with particular respect and gratitude’: J.A.H. Johnston (Headmaster and mathematics), J.L. Thomas (mathematics), P. Bateman (physics), A.C. Kaye (chemistry), J.L. Stephen- son (English) and A.C. Wallwork (biology).

He was not good at ball games but was active in cross-country running until he broke a ligament in his knee when doing the long jump (the injury was not disabling). He enjoyed being a member of the Officers’ Training Corps and did well in both small-bore and full-bore rifle shooting, as his father had done. David was a member both of the school shooting eight, which competed for the Ashburton Shield at Bisley, and of the English Public Schools team, which competed in Canada for the Governor General’s Prize.

Despite never winning academic prizes at the school, he won a major entrance scholarship to Trinity College, Cambridge, in the examination at Christmas 1933. During this examination, he was interviewed by the Master of Trinity, J.J. Thomson FRS (PRS 1915–20), who had discovered the electron in 1897.

David therefore came up to Trinity in October 1934, to read Natural Sciences. At Cambridge, the degree examinations (‘triposes’) are divided into two parts; in the Natural Sciences Tripos two years are allocated to Part I and one year to Part II. For Part I it was necessary to take three sciences, and David took physiology, physics and biochemistry, obtaining first-class honours. He had registered as a medical student, because in those days a medical degree was a necessity for obtaining a teaching post in physiology, and he took some of the necessary preliminary examinations (1st MB) in 1935. He spent his third year doing anatomy for a purely medical examination (2nd MB Anatomy). At that time, many medical students took three years over Part I and a minimum requirement for the degree of BA was to be classed in Part I of the Natural Sciences Tripos with three years’ residence, so David was able to take his degree in 1937 on the strength of his First in Part I and a ‘certificate of diligent study’ in his third year. He then took Part II Physiology in 1937–38, again obtaining first-class honours.

His teachers in physiology included Sir Joseph Barcroft (head of the department), H.K.F. Blaschko, W.S. Feldberg, F.H.A. Marshall, B.H.C. (later Sir Bryan) Matthews, F.J.W. Roughton, W.A.H. Rushton and E.B. Verney, all of whom either already were or were later elected Fellows of The Royal Society. E.D. Adrian (PRS 1950–55) was in the department and succeeded Barcroft as its head in 1937, but until then he had no teaching duties because he was one of the Foulerton research professors of The Royal Society, the other being A.V. At Cambridge, a ‘tutor’ is responsible for the general welfare of his pupils and does not teach them in the ordinary sense. David’s tutor was the historian J.R.M. (later Sir James) Butler, son of a former Master of the College. I went up to Trinity in October 1935, one year after David, and my career in the College was almost identical to his, including my third year being spent in anatomy with the intention of becoming medically qualified. My tutor was also J.R.M. Butler, and through this circumstance it came about that David was one of the very first undergraduates in the college that I met. He was extremely good to me, inviting me to his rooms and introducing me to his friends. These included Alan Hodgkin (FRS 1948, PRS 1970–75, who became my mentor), John Humphrey (immunologist, FRS 1963, whose sister Stella he later married), Philip Gell (pathologist, FRS 1969), Martin Pollock (pathologist, FRS 1962), Erasmus Barlow (psychiatrist and later Head of the London Zoo), Mark Pryor
(zoologist, later Senior Tutor of Trinity), Glenn Millikan (University lecturer in physiology), and Martin Wright and Hugh Gordon, who both worked later at the National Institute for Medical Research. All of these were some years older than me and were living in the College as I was, and contact with them was one of the most important influences on me during my undergraduate years. David took part several times in the Trinity Lake Hunt, an annual event in which a group of Fellows and undergraduates of Trinity stay for a week at Seatoller in the English Lake District and play hare-and-hounds over an area containing Great Gable and several of the other Lakeland hills.

After completing his Part II, David began research as a Research Scholar of Trinity. He did not register for a PhD and therefore did not have a formal supervisor, but he would not have been short of advice because A.V., A.L. Hodgkin and Glenn Millikan were all at hand. His first work was recording the time course of oxygen consumption by a muscle when it was stimulated (1, 2). He used apparatus made in the laboratory, and obtained much higher precision and consistency than others had done. He found that the extra oxygen consumption took place entirely after the actual contraction, showing that it was related to recovery processes and not to the contraction process itself. His next work was recording the heat production by muscle in the same situation (3). Recording the heat production by muscle had been his father’s main work, and for this series of experiments David used his father’s equipment at University College London. He found that the time course of heat production was closely similar to that of the oxygen consumption that he had already measured.

David also recorded the much smaller production of heat by muscle when stimulated in the absence of oxygen (4). A slow phase of heat production was prevented by working at pH 6, at which no lactic acid is formed; there was then an initial phase of heat absorption followed by a phase of heat production that in some cases was so small that the net heat production was negative. David also recorded the production of hydrogen ions by muscle during contraction in the absence of oxygen (5).

This was a remarkable achievement in a first year of research. On the strength of it, David was elected to a junior Research Fellowship at Trinity in October 1940. On account of the war, he was not able to take up this Fellowship until the end of hostilities. He was also awarded the Gedge Prize in 1940. This prize is awarded in alternate years for an essay on a topic in physiology by a research student, normally based on a piece of research performed in the Cambridge Physiology Department.

**WAR WORK**

On the outbreak of war in September 1939, David began clinical studies with the section of University College Hospital Medical School that had been evacuated to Cardiff under Max Rosenheim (later Baron Rosenheim; FRS 1972). However, in March 1940 he decided that he wanted to do something more related to the needs of the war and moved to the Postgraduate Medical School at Hammersmith Hospital to work with the physician and physiologist J. McMichael (later Sir John; FRS 1957) on the changes in blood volume associated with crush injuries sustained in the air raids on London (6–9). In September 1940, however, David was transferred to war work of a different kind.

In World War I, David’s father, A.V., had been leader of the team that developed anti-aircraft gunnery at H.M.S. *Excellent*, the naval gunnery school at Portsmouth. In 1940, A.V. was
in touch with General Sir Frederick Pile, G.O.C.-in-C. Anti-Aircraft Command, and felt that Pile needed scientific advice. A.V. introduced the physicist Patrick Blackett FRS (later Baron Blackett; PRS 1965–70) to Pile and Pile appointed him as Scientific Adviser. Blackett naturally needed assistants but all the mathematicians and physicists were already busy on war work, so A.V. provided him with a team of three physiologists: L.E. Bayliss, lecturer in physiology at University College and son of the more famous physicist Sir William Bayliss FRS; A.V.’s son David; and, through David, myself. All of us had read Natural Sciences at Cambridge and the broad Part I course had provided us with the amount of mathematics and physics that we needed, and our training in biology prepared us better for dealing with the uncertainties of war than a training in the physical sciences would have done. We were part of the Army Operational Research Group and our task was to try to find what actually happened during operations; that is, when anti-aircraft guns were firing against enemy aircraft. We were concerned only with heavy anti-aircraft, namely guns of 3.7-inch and later 5.25-inch bore that were deployed on gunsites around cities. We were under the Ministry of Supply, and at first we worked in one or other of their buildings in London. After a few months, however, we settled in to what had been the Vicarage at Petersham, near Richmond Park.

Our main task was to find how best to make use of the very imprecise data given by the radar sets of that time. The predictors then in use were designed to accept data from optical telescopes by which the enemy aircraft was tracked after it had been caught in a searchlight beam. Gunfire controlled in this way soon drove the bombers to heights beyond the useful range of searchlights and often above cloud, so the only information about their position came from radars. These worked on a wavelength of 3 m and gave the bearing (azimuth) of an aircraft with errors of about 1°. As originally designed, the radars did not give the elevation of the aircraft (angle above the horizontal), but an addition designed by L.H. Bedford of Cossors Ltd gave a value. However, the range of the aircraft was given with much greater precision than by optical rangefinders. A value for the height of the aircraft could thus be calculated, and the procedure was to assume that the aircraft would fly straight and at constant height.

We spent much time on gunsites around London, both during practices when the radar tracked a target aircraft and during actual night raids. We would often watch the radar operators at work, trying to judge how much of the errors in the radar data was due to the operators and how much to the inherent deficiencies of the equipment. Most of the electronic and radio problems were dealt with by a related group also based in Petersham Vicarage under the physicist J.A. Ratcliffe (FRS 1951), mainly concerned with training radar operators. We did, however, have to assist in dealing with one radio problem. The measurement of elevation depended on reflection, at the ground surface, of the radio waves returning from the target aircraft; if the ground was irregular it was necessary to lay a flat surface of wire netting around the radar to act as a reflector. We took part in checking the effectiveness of this device.

In March 1941, Blackett moved to Coastal Command of the Royal Air Force and our group was taken over first by the physicist Professor N.F. (later Sir Nevill) Mott FRS and later by the physicist and soldier Brigadier B.F.J. (later Sir Basil) Schonland FRS. For some months, David was ‘resident scientist’ at the headquarters of Anti-Aircraft Command at Stanmore, Middlesex.

In the summer of 1942, the possibility of dropping strips of aluminium foil (‘Window’) from aircraft to confuse enemy radar was raised, and Schonland was asked to investigate its effectiveness against our radars if used by the German air force. David wrote a report on this question, showing that it would be very effective. Its use by our bombers was therefore
postponed in case of its adoption by the Germans, and it was not used until the heavy raids on Hamburg in July 1943, when it was highly effective.

In September 1942, David was moved to the War Office in Whitehall, London, as a member of the team of some 10 scientists and mathematicians under Sir Charles Darwin FRS, Scientific Adviser to the Army Council, who was succeeded in 1943 by another physicist C.D. (later Sir Charles) Ellis FRS. With the prospect of being sent abroad, David was commissioned with the rank of Major (General List), thus losing the inestimable advantage given by wearing civilian clothes, that one is able to answer back to senior officers.

In December 1942, David was sent single-handed to explore the possibility of doing operational research with an army in the field, in this instance the British First Army in North Africa (Algeria and Tunisia). He joined up with others of the Operational Research Group who had been in Egypt, including the mathematician J.M. Whittaker (FRS 1949). David was not able to make any substantial studies, partly through a lack of resources but also because the capitulation of the German forces in North Africa was complete within two months of David’s arrival. Some useful technical intelligence emerged, however: for example, they found an abandoned German anti-aircraft predictor capable of predicting the forward track of an aircraft flying on a curved course. This was something that had not been attempted in Britain.

David did not remain with the First Army when they embarked for the invasion of Italy in the summer of 1943, but returned to the UK. He then spent about a year attached to an operational research group working with the Second Tactical Air Force in the UK.

In March 1944, Brigadier Schonland was appointed as Scientific Adviser to Field Marshal Montgomery, commanding the 21st Army Group for the invasion of France, and he got David appointed as his personal assistant. David spent a year in France, Belgium and Germany, taking part in the work of Operational Research Groups, collaborating in particular with M.M. Swann (later Baron Swann; FRS 1962). They analysed, and reported on, the performance of both Allied and German land and air forces. David obtained information about German weapons intended for bombarding the UK from mainland Europe, including some enormous static emplacements for barrel-launching of ballistic missiles, which were never used. David visited Caen shortly after it had been taken, to report on the effectiveness of the Allied bombing of the city. Schonland’s biographer (Austin 2001, p. 281) relates that David was horrified by the sheer devastation and loss of civilian lives but saw little evidence of the enemy or of the enemy headquarters that had been the focus of Montgomery’s attention; a bullet from a German sniper went through the shoulder of David’s jacket. In his report to Schonland, David used the phrase that it was ‘a battle that had gone horribly wrong’. Mr Austin also told me that in a letter David had expressed surprise at having been allowed, shortly before the invasion of France, to carry around a volume containing the complete plans for the invasion.

David and Schonland got on very well together throughout this period, and when Schonland was recalled to South Africa in December 1944 he gave David his personal copy of the Oxford Book of Quotations (Austin 2001, p. 300).

POSTWAR RESEARCH

David returned to Cambridge in September 1945 to take up the Research Fellowship to which he had been elected in 1940. He was also appointed to a demonstratorship in the University Department of Physiology (a five-year appointment equivalent to an assistant lectureship). He
was a member of an informal group within the department led by Alan Hodgkin; I also became a member of that group when I returned to Cambridge in January 1946, and so did R.D. Keynes and P.R. Lewis a little later. E.D. Adrian was Head of the Department and our research was funded by a generous grant that he had obtained from the Rockefeller Foundation, no doubt on the strength of the impression that Hodgkin had created during the year that he had spent there in 1937–38.

David’s first investigations after the war were a continuation of his prewar work on the oxygen consumption of muscle. Estimating the oxygen tension in a respiring muscle is difficult because of the resistance to diffusion and because the oxygen consumption seemed to be independent of oxygen tension down to very low values. David devised three ingenious methods for overcoming these difficulties and found that, in frog muscle at 15–20 °C, the oxygen consumption did not decrease until the oxygen tension was reduced below 0.5–2.0 mmHg (10, 11).

David’s next piece of work was the first of many that depended on optical measurements, although he recorded later that he could not remember why he became interested in optical changes. Preliminary experiments in collaboration with his cousin R.D. Keynes on nerve trunks from crustaceans showed an increase in light transmission on stimulation (13). In muscle there was a decrease in light absorption that started simultaneously with the latency relaxation and an increase in scattering that developed more slowly and persisted partially for a matter of minutes (14). David was not able to give physical explanations for these phenomena. Their interpretation was considerably altered by later experiments in which changes in the amount of light diffracted by the striation pattern were taken into account (19, 20).

In 1948 David left Cambridge on appointment as Physiologist at the Laboratory of the Marine Biological Association at Plymouth. He continued his investigations on the scattering of light by nerve, at first using leg nerves of crustaceans (15) as he had done in his preliminary experiments at Cambridge. The main effect was a decrease in light scattering that seemed to be due to an increase in diameter of the individual nerve fibres, because a similar change was produced by diluting the surrounding fluid. A small early increase in scattering was seen in many cases and became much more marked if the surrounding liquid was diluted, but no explanation was found for this phenomenon. Subsequent experiments on isolated giant fibres from cuttlefish (16) showed directly that stimulation caused an increase in diameter, attributed to the entry of ions with water following to cancel the rise of internal osmotic pressure.

In 1949, on the initiative of E.J. King (Professor of Chemical Pathology) and J. McMichael (Professor of Medicine), David was appointed as Senior Lecturer at the Postgraduate Medical School at Hammersmith Hospital, a School of London University, where he had worked for a short period in 1940. His prime duties were to promote the techniques of biophysics, medical electronics and medical engineering in the rapidly developing School, but he had time to continue his own research. He was promoted to Reader in 1962 and to Professor of Biophysics in 1975.

Soon after his move, David wrote two reviews, a general one on nerve (17) and a more detailed one on muscle (18). The latter is a reminder of how confusing things were before the appearance of the sliding-filament theory in 1953–54.

David’s next research was a continuation of his measurements of the optical properties of muscle. He was now including measurements of the intensity of light diffracted by the striation pattern, which he had not taken into account in the previous work. He showed first that a sudden stretch of resting muscle caused an immediate increase in scattering and a
delayed decrease in the intensity of diffracted light (19). The next paper (20) described the changes that occur when the muscle is stimulated: a decrease in diffracted intensity begins simultaneously with the latency relaxation; later changes were attributed to changes of scattering. Discussion of the physical interpretation of the changes is inconclusive; even in terms of sliding filaments it is not at all clear at present how the changes are to be interpreted.

David then turned his attention to the localization of nucleotides in muscle. The predominant nucleotide is ATP (adenosine triphosphate) and there was already evidence that hydrolysis of its terminal phosphate group was the immediate source of the energy for muscle contraction, though it was debated whether the actual utilization of ATP took place during the contraction phase or during relaxation, restoring the muscle’s ability to contract. His first paper in this field (21) dealt with the method of introducing tritium-labelled adenine into muscle for autoradiography on sections of quick-frozen, freeze-dried preparations, but gave only preliminary results. The final results of this series of experiments, in which only light microscopy was used, were presented in two papers (23, 24), which showed nucleotide localized at the Z line and near the A–I boundary. Much more detailed results were given in a later paper (27) in which electron microscopy was used as well as light microscopy. A substantial fraction of the adenine nucleotide was shown to be localized in the outer parts of the I bands but in interfibrillar space, not within the fibrils. No evidence was presented about changes on stimulation; later work on living fibres (Lännergren 1977) confirmed that part of the nucleotide is localized in the I bands and shows no change on stimulation or on treatment with 50% glycerol, which causes the unlocalized nucleotide (presumably ATP) to diffuse out of the fibre. It seems likely that the localized nucleotide is in RNA.

David also investigated the state of bound nucleotide by an optical method, namely measuring the dichroism of muscle in the region of ultraviolet absorption (22). (Dichroism is the difference in optical density according to whether the electric vector of the light is parallel to or perpendicular to the long axis of the preparation, its sign being positive if the former is greater than the latter.) David found weak dichroism in the regions of absorption both by protein and by nucleotides, the former being positive and the latter negative. The nucleotide dichroism remained when most of the nucleotide was extracted by treatment with 50% glycerol, showing that 90% or more of the acid-extractable nucleotide was not oriented and that the dichroism was attributable either to bound nucleotide or to nucleic acid. This agrees with the present-day view that most of the nucleotide absorption is due to ATP in free solution. Attempts to measure changes of dichroism on stimulation were not successful because of movement and change of thickness of the muscle.

David also examined the localization of tritium-labelled phosphocreatine by light microscopy (26). If the fixative did not contain a nucleotide precipitant such as a salt of lanthanum, all the phosphocreatine was lost. With lanthanum present, most of the phosphocreatine was retained and was localized in the outer part of the I bands.

David also used autoradiography to investigate the space within muscle fibres that is accessible to solutes that cannot penetrate the cell membrane. Tritiated plasma albumin was found to enter the transverse tubular system (29); the same conclusion was reached at the same time by others using different methods (Endo 1964; H.E. Huxley 1964; Page 1964). David’s autoradiographs also showed that the space between adjacent fibres varied greatly, in many cases being less than 0.1 μm in width. In these cases, the striations of the adjacent fibres were often exactly aligned with each other (30). David suggested that in these cases the two fibres had developed from a single fibre by longitudinal splitting.
David’s final experiments on isolated muscle were concerned with the mechanical properties of resting muscle, in particular his discovery of the ‘short-range elastic component’ or SREC (31). When a frog sartorius muscle was slowly stretched without stimulation, the tension at first rose steeply but became constant when the extension reached about 0.2% of the muscle length. This clearly implied that connections between the thick (myosin) and thin (actin) filaments existed even in the resting condition. It had long been known that the resting tension of muscle is raised by increasing its temperature (‘rubber-like’ behaviour), and David found (32) that this rise of tension became much more marked as the temperature approached that at which heat-rigor develops, suggesting that the resting tension was at least in part an active process. Another phenomenon pointing in the same direction was that the effect of temperature change was altered by raising the osmotic pressure of the surrounding medium (33): the usual tension change was preceded by a transient change in the opposite direction. In rat muscle, lowering temperature below 15 °C caused a rise of resting tension and also a great prolongation of the twitch, that is, a delay in relaxation, possibly implying a raised concentration of activator (34).

These observations and their implications for the nature of the resting state in muscle are probably the most important of David’s contributions to the understanding of muscle in isolation. All his later work was centred on human muscle in situ. This came about in 1971 through the opportunity to work with Dr R.H.T. Edwards, a lecturer in the Department of Medicine at the Royal Postgraduate Medical School, and his research assistant D.A. Jones. Edwards had recently returned from a year working on human muscle with E. Hultman and others at the Karolinska Institute in Stockholm. This collaboration continued until Edwards and Jones moved to University College Hospital Medical School in 1976.

Their first experiments of this kind were done on the extensor muscle of the knee (quadriceps femoris) (35–37, 39, 41) and were an investigation of the immediate causes of the slowing of relaxation that was known to accompany fatigue in amphibian muscle, together with parallel experiments on mouse muscle (40). Muscle tension and the internal temperature of the muscle were recorded continuously, and biopsy samples were taken before and after the contraction. The muscle was activated voluntarily to about half that in a maximum voluntary contraction, except in one subject in whom it was stimulated tetanically through surface electrodes. The rise of internal pressure stopped the blood flow through the muscle; in some cases a cuff was inflated round the upper thigh to make certain that blood flow ceased. Relaxation times increased up to five-fold (in a 2-minute tetanus). The rate of rise of temperature was proportional to tension and agreed with that calculated from the measured changes in metabolite concentrations. During prolonged stimulation, the rate of heat production per unit tension decreased to nearly half its initial value. Both this increase in economy of the contraction and the slowing of relaxation suggested that the underlying change was an increased cross-bridge cycle time.

By the end of the contraction, the concentrations of ATP and of phosphocreatine had fallen by about 15% and 90% respectively and the concentration of lactic acid had risen by about 50 mM. In the experiments on mouse muscles (40), both lactic acid production and oxygen consumption were prevented by poisoning with cyanide and iodoacetic acid, and the slowing of relaxation still occurred, so lactic acid accumulation was not the cause of slowing. There was, however, a strong dependence on ATP concentration, the rate constant of relaxation increasing linearly 2.8-fold as ATP concentration rose from 9 to 17 μmol/g dry weight. Together with the results from human muscle, this suggested that the cross-bridge cycle is terminated by a reaction with ATP.
A later investigation (38, 44) was concerned with the loss of muscle force that persists for up to 24 hours after a series of contractions sufficient to bring the force of a voluntary contraction almost to zero. When recovery was tested with tetanic stimulation at a high frequency (100 s⁻¹), it was complete in 1 hour, but if tested with a low frequency such as is used in voluntary activity (20 s⁻¹), recovery at 1 hour was only about 50%. Biopsies taken at 1 hour showed that the concentrations of ATP and phosphocreatine were fully recovered, and the electromyogram was not impaired at any time. The conclusion was that the long-lasting fatigue was due to the impairment of excitation–contraction coupling, as had previously been found in isolated muscles. This phenomenon is presumably the basis of the feeling of weakness that can persist for many hours after extreme exercise.

An additional collaborator in the work on long-lasting fatigue was P.A. Merton (FRS 1979) of Trinity College, Cambridge. David continued working with him after the departure of Edwards and Jones in 1976. They did a series of heroic experiments using high-voltage stimuli applied through the skin. They first stimulated the adductor pollicis muscle by shocks applied between large electrodes on the front and back of the hand (46). When a condenser of capacity 0.5 μF charged to a few hundred volts was discharged through the muscle, motor nerve twigs in the muscle were excited, but when the voltage was raised above 800 V the latency was much reduced, showing that the muscle fibres were being excited directly. The amplitude of the latency relaxation was then increased about sixfold because of the better synchronization of events in different parts of the muscle. When the condenser was charged to 2400 V, the peak force in a twitch was increased up to fourfold and was prolonged; the authors say that ‘shocks of this strength should not be used repeatedly: the hand may become swollen and painful’. More detail is given in a later paper (47), which is mainly devoted to stimulation of the cerebral cortex by electric shocks applied through the scalp. When this was done over the motor area, twitch-like contractions were produced and the muscle action potentials could be recorded. The latency was only a little greater than when the muscle was stimulated directly, indicating a high velocity of conduction. An interesting observation was that the stimulus strength needed to produce a maximal response was greatly reduced if the subject was voluntarily making a weak contraction in the same muscle. A surprising result was that the conduction velocity was still high when the muscle being activated was the external anal sphincter. They also produced muscle contractions by applying shocks over the spinal column; these responses were not affected by superposition on a voluntary contraction. Shocks over the occipital region caused the subject to see a localized but rather dim phosphene. They also used magnetic stimuli to the cerebral cortex (48).

David records that he and Merton intended to continue their collaboration after David’s retirement, investigating the latency relaxation. They did not in fact do so.

David’s research while he was at Hammersmith was supported by grants from the Medical Research Council, the Wellcome Trust, the British Heart Foundation, the Muscular Dystrophy Group of Great Britain and Northern Ireland (now the Muscular Dystrophy Campaign) and the Muscular Dystrophy Association of America.

**Administrative work**

As already mentioned, David was originally appointed at Hammersmith to promote the techniques of biophysics, medical electronics and medical engineering. For instance, when he
arrived there was a small mechanical workshop staffed by two mechanics. Ten years later, David had developed it into a department of its own, with a staff of 20 instrument makers. David speaks with great admiration of the head of the workshop, Cornelius Lordan, who ran it in an informal but extremely effective way. From 1970 to 1976, David was Vice-Dean of the Royal Postgraduate Medical School and served on all the main School committees. He was chairman of the Higher Degrees Committee for some years, looking after the interests of PhD, MPhil and MSc research students.

For several years until his retirement, David was Archivist of the School. He catalogued and organized the numerous documents that had accumulated in a haphazard way since before the opening of the School. He particularly enjoyed the task of recording on tape the reminiscences of as many of the existing and former members of staff as he could. He made transcriptions of the tapes and these are now included in the Archive.

David became a member of the Physiological Society in 1942, being proposed by L.E. Bayliss, with whom he was working in the Army Operational Research Group. He was a member of the Editorial Board of the Journal of Physiology from 1969 to 1976 and was Chairman from 1974 to 1976. From 1970 to 1974 he was Distributing Editor, with the time-consuming task of communicating with authors. This job is now done by paid staff at a centralized office. From 1976 to 1980 he was Chairman of the Editorial Board for the Physiological Society Monographs.

He was a member of several official advisory bodies, listed at the end of this memoir.

**Retirement**

David began taking a serious interest in photography after his retirement in 1982. He developed a process that gave large black-and-white prints from 35 mm negatives with an exceptional degree of smoothness, sharpness, richness of tone and absence of graininess. The process used extreme-contrast litho film, which was developed in a very weak, low-contrast developer. A disadvantage was that long exposures were needed, the effective speed of the film being 1 A.S.A.

After the family moved to Yorkshire in 1986, David had a large workshop equipped with tools and machines for working in wood. He made many very beautiful pieces of furniture with an excellent finish, using a variety of hardwoods and some superior varieties of pine.

He was troubled by osteoarthritis from 1992 and was operated on for stenosis of the lumbar spine (1993) and to replace one hip joint (1994) but was able to return for a time to his woodworking. Poor circulation in his legs led to ulcers and in September 2001 he was admitted to hospital and had both legs amputated high up. He became infected with an antibiotic-resistant bacterium (methicillin-resistant Staphylococcus aureus) but was able to return to his home where he was looked after by a team of devoted carers. My wife and I visited him in May 2002; his carers got him into a wheelchair and brought him into the garden for tea. He was cheerful but not able to speak much. He had to go into hospital again for a few short periods before his death on 18 August 2002.
PERSONAL CHARACTERISTICS

David was exceptionally kind, good-humoured, modest and generous. I became aware of this when he befriended me on my arrival at Cambridge as a shy undergraduate, and it was evident again in his good relations with Brigadier Schonland when they spent much time together in 1944. I never heard him speak in anger. In paperwork he was tidy and thorough, as was shown in his work as Archivist at the Postgraduate Medical School and in the exceptionally detailed notes that he left with The Royal Society for the benefit of whomever was to write his biographical memoir.

In his experimental work, he was highly ingenious and innovative in devising new methods, and he was ready to take great pains to get precise results. With one exception, his work on isolated muscle or nerve was performed alone, but in all his papers on human muscle he had one, two or three collaborators. He did not generally have in mind a specific hypothesis to be tested but expected that interesting results would emerge from the application of a new technique. An example is given by his most important discovery, namely the ‘short-range elastic component’ of muscle, which implies that there are attachments between the thick and thin filaments even in the resting state: he states in the introduction to his paper on this phenomenon (31) that ‘this form of elasticity had come to light, rather by chance, in the course of other work’. He wrote:

My progress in scientific research was always along practical lines; a visual, ‘hands-on’, ‘try-it-and-see’ approach was at the heart of my mode of progression. I resembled my father in this respect (‘thinking with one’s hands’ he called it, and recommended it). He was by nature an experimenter. In his field of study he was somewhat scornful of people who liked to generate elaborate ‘models’, to represent biological systems, out of purely theoretical precepts, though he could employ such mathematics and theoretical physics (e.g. thermodynamics) as were required to promote or substantiate his experimental results. He was well qualified to do so. I was not. I shared my father’s standards in using the English language correctly and succinctly when writing a paper, article or letter, but struggled more than he did in achieving fluency, and then it would be only by repeated re-drafting. We both wrote prose over which a reader would not stumble, mine was readable if lacking, maybe, the felicitous touch apparent, particularly, in my father’s non-scientific writing.

DEGREES (UNIVERSITY OF CAMBRIDGE)

1937  BA
1945  MA
1962  ScD

APPOINTMENTS HELD

1940  Elected to Junior Research Fellowship at Trinity College, Cambridge. Postponed residence until 1945–1948
1945–48  University Demonstrator in the Physiological Laboratory, Cambridge
1948–49  Physiologist on the staff of the Laboratory of the Marine Biological Association, Plymouth
1949–75  Senior Lecturer, and from 1962 Reader, at the Royal Postgraduate Medical School of London University, at Hammersmith Hospital
1975–82  Professor of Biophysics (personal chair) at the Royal Postgraduate Medical School
1970–76  Vice-Dean of the Royal Postgraduate Medical School
MEMBERSHIP OF ADVISORY BODIES

1953–55 Biological Warfare Advisory Board, Ministry of Supply
1955–82 Board of Studies in Biophysics, University of London
1975–82 Board of Studies in Physics, University of London
1974–78 Medical Sciences Research Committee, The Royal Society

ACKNOWLEDGEMENTS

David left with The Royal Society exceptionally full notes about his life. His daughters Mrs M.A. Bell and Miss K. Hill gave me other notes that he left, and gave me some additional information. I am also indebted to Mr Brian Austin for some pieces of information not included in his biography of Brigadier Schonland.

The frontispiece photograph was taken by Godfrey Argent and has been reproduced with permission.

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