ARCHIBALD VIVIAN HILL

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By Sir Bernard Katz, F.R.S.

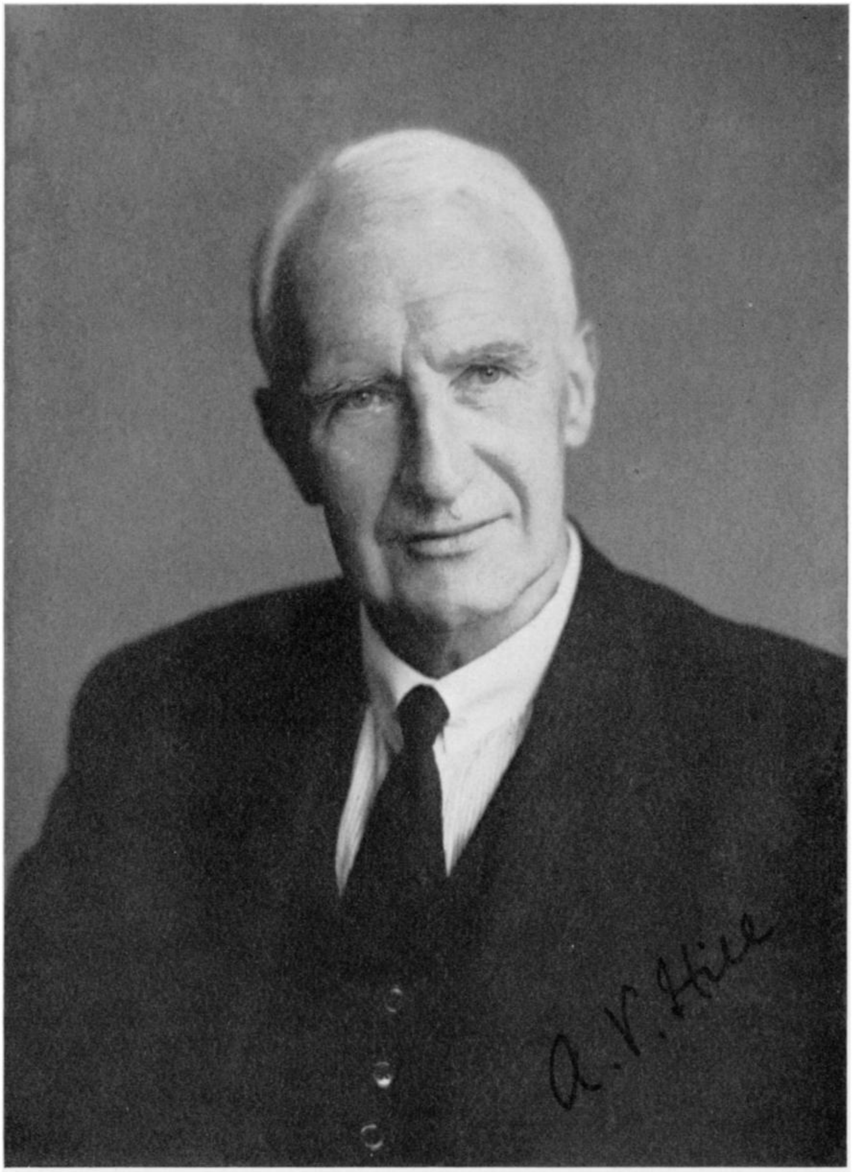
1. Origin

A. V. Hill was born in Bristol, the son of Jonathan Hill (1857–1924) and Ada Priscilla (*née* Rumney) (1861–1943). The father was the second of nine children; the mother one of four sisters. They were married in 1880, and had a son and a daughter, Muriel, who was born in February 1889. She became a biochemist and married Dr T. S. Hele, a colleague who worked in the same field and was later elected Master of Emmanuel College, Cambridge. Muriel died in 1941.

A. V. (as he became known to his family and all his colleagues) traced his ancestry to the middle of the eighteenth century. To judge by the family tree which he himself drew, the name 'Archibald Vivian' must have been a new departure. There were successions of Jameses and Jonathans, several Johns, an occasional Charles, George, Samuel, etc. among them, but apparently no precedent for Archibald or Vivian. A. V.'s forebears all lived in the West Country, mostly in Devonshire and Somerset. On the paternal side he was preceded by five generations of timber merchants at Bristol, carrying on the business which had been founded by James Hill in 1750. James had come from Ireland and later returned there to join a volunteer regiment. He is believed to have been killed during the Irish troubles.

The timber business died with A. V.'s father in 1924. A. V. himself might have become the 'sixth mahogany merchant at Bristol' (226) had there not been an irreconcilable break-up at home, in 1890, when he was only three and his sister just one year old. Eighty years later, A. V. wrote: 'Of that crisis I have only the faintest memory, as of a darkened room' (226). His mother and the two children apparently never saw the father again. A. V. was very conscious of the fact that he owed his start in life to the devotion and tireless efforts of his mother, a person of great character and determination who fortunately was able to overcome deprivation with resourcefulness and a powerful sense of humour.

A. V. had no memory of his father. He did not try to communicate with him and, until very much later, felt a compulsion of silence about him. It was not until after his father's death in 1924 that A. V. learned, from an old uncle, of



A. V. Hill

Jonathan Hill's continued interest and pride in his son's achievements.* And not until his mother died in a street accident in 1943, did he discover that she had kept throughout her life a golden locket containing Jonathan Hill's photograph. These rather touching revelations are all A. V. allowed himself to make in his autobiographical note; one cannot help regretting that the father died—a few months after learning of A. V.'s Nobel Prize—without seeing him.

His mother's family (the Rumneys, joined with the Hugginses and other Devonshire families) has also been traced back well into the eighteenth century. Their occupations were of a more varied kind than the Hills', with boat-builders and shipwrights, mariners (one of them drowned in the Bristol Channel in 1830), a successful apothecary and an unsuccessful wool merchant among them. The mother's father, Alfred Jones Rumney (1830–98), was apprenticed as a woollen draper, but might have done better as a scholar or a teacher. 'He had a lively sense of the ridiculous; this fortunately passed on to my mother who often needed it. His family were miserably poor, but his four daughters were people of character, originality and resource' (226).

2. School

Until the age of seven, A. V. received his elementary training at home. His mother taught him the three R's. In 1894 the family left Bristol and went to Weston-super-Mare where he entered a small preparatory school (Brean Villa) which did him a great deal of good. At 11, he was doing very well in algebra and geometry, and he reports that 'at twelve and a half I was gradually getting control of my temper'. His physical development must also have been progressing satisfactorily; he enjoyed playing hockey and going on long hikes, and he became very proficient in defending himself against other boys by 'learning to throw stones further and straighter'.

Soon after, at 13, the family doctor advised them to move to Tiverton in Devon, where the boy would have the opportunity of entering Blundell's School. This famous school was founded early in the seventeenth century by a wool merchant, Peter Blundell of Tiverton, whose object was to provide first-class education for the boys of his native town plus a limited number of 'foreigners'. The Hills set up house at Tiverton and stayed until 1909. A. V. went to Blundell's as a day boy in May 1900. He regarded this as one of the decisive steps of his life; 'once at Blundell's I was on a moving staircase to what happened later'.

He had been well prepared at Weston; mathematics was his strongest subject, and this was soon confirmed by his school reports at Blundell's. In 1901 he obtained a Foundation Scholarship; he joined the Classical VIth form in

* 'Though I never had any communication with my father, he took rather a pathetic interest in me. This I learnt, only after his death in 1924, from a kindly old uncle. For example, in 1921 when I had made a speech at my old school (Blundell's), on Speech Day, finding a report of it in the Tiverton newspaper he had copies printed to give to his friends. And, more remarkable, he included at the end in "thanks to the speaker" a tribute to my mother for her "sacrifice and devotion" paid by an old friend, a former medical officer at the school' (226).

which he stayed until 1903 when he specialized in mathematics. A. V. disclaimed any special gift for humanistic studies, but he seems to have enjoyed, and certainly remembered, his Classics and Scripture, sufficiently at least to acquire great proficiency in quoting from them in later life. Although he would have liked, in retrospect, to have had more opportunity for a wider range of study, particularly in the natural sciences, he never regretted the considerable time and effort he had spent on the Classics, realizing that the discipline of formal linguistic training helped him in the exact choice of words and phrases, and the expression of ideas. But the most important influence was that of J. M. Thornton, an outstanding mathematics teacher who not only inspired A. V. in the pursuit of his favourite subject, but who insisted relentlessly on clarity of thought and utmost precision in the use of one's language. The elegant simplicity and directness which are such characteristic features of A. V. Hill's writing must have owed a very great deal to his mathematics teacher at Blundell's School.

Though A. V. was a day boy and probably spent more time on study and homework than most of the boarders, he took a very active part in the school's life (and indeed continued to do so as a Governor for many years after). He joined the Debating Society (though he was always better presenting his arguments in writing than at debating or giving formal addresses in public); he excelled at rifle-shooting and was Captain of the VIII and a member of the Bisley team for four years—a major advance in his study of ballistics since the stone-throwing days at Weston. He was also an extremely keen runner (quarter-mile, mile, cross-country), winning many races, though admitting that 'I lost more races than I won'. His interest in running was one of the factors which attracted him later to the physiological study of athletic performance and of muscular activity in general.

A. V. had many friends at Blundell's and he always remembered his school with gratitude and affection as 'a very happy community'. It is clear from all accounts that the early domestic crisis of 1890 had left no visible mark or 'complex'; already in his days at school A. V. seems to have impressed his fellows as the same attractive and straightforward person imbued with vigour and a boyish sense of fun, whom his co-workers and scientific pupils came to know and appreciate later on.

3. Cambridge

At 18, A. V. sat the Scholarship examination for Trinity College, Cambridge. He could not have gone to Cambridge without it. Fortunately examinations, even as important as this one, did not unduly worry or upset him; the things that would rattle him were preparing for a mile race or for a speech at the Debating Society. He went to Trinity in 1905 and stayed there until the outbreak of World War I.

A. V.'s career as an undergraduate is interesting in several ways. Mathematics had been his favourite line at school; he had been taught by an inspiring master, who had already produced a number of high 'wranglers' in the Mathematical

Tripos at Cambridge. So it seemed only natural that he should pursue this subject, and indeed he finished as third wrangler in 1907, having spent two instead of the more usual three years on this course. He learned most of his mathematics from R. A. Herman, attended lectures by G. H. Hardy, E. W. Barnes and A. N. Whitehead to whom he was much indebted personally; he had gained by the kindness and hospitality received at the Whiteheads' home. But on the whole, he was disappointed with the mathematical teaching and became rather bored with the subject so that he seriously thought of abandoning it in his first year. He wrote later that he was 'better fitted to engineering' and that he soon lost interest in pure mathematics and 'some of the things that seemed rather remote from reality' (224a).

Perhaps it is not unusual for a student of inquiring mind to become dissatisfied with a straight continuation of work which he found most stimulating at school. Having been attracted to a special subject under the influence of a first-class teacher at school, one may—more often than not—find the university course uninspiring and rather an anti-climax. This is an almost inevitable risk of too early specialization! A. V. himself thought the trouble was with too much pure, rather than applied mathematics, but he was really looking for something fresh and more exciting. Nevertheless, his early training in mathematics was not wasted; although he got 'very tired of it as a full-time study', he 'continued to think mathematically all his life and frequently used (rather elementary) mathematics in later work'.

The decisive contact which A. V. made as an undergraduate was his tutor at Trinity, Walter Morley Fletcher.* Just as 'Joey' Thornton had guided him earlier on into mathematics, so Walter Fletcher opened the door for him now into physiology, the study of living engines and in particular of the mechanism of muscle. When A. V. came to Fletcher for advice, what to do and where to go after his dull first year of study, Fletcher told him to stick it out and take his Tripos, but he also mentioned the work that he was pursuing together with F. G. Hopkins in the Physiological Laboratory, on the chemistry of isolated frog muscle, and the production and oxidative disposal of lactic acid. Walter Fletcher had already done important and highly original research 10 years earlier, under Michael Foster at Cambridge, studying the metabolism of surviving muscle tissue. Frederick Gowland Hopkins joined the Physiological Laboratory in 1898, and with his chemical expertise greatly helped to improve the methods of analysis. At this stage, Hill and Fletcher had already found many points of common interest and formed a close personal friendship. Both were keen runners, with Fletcher apparently the superior performer, and when A. V. had taken his Mathematical Tripos and wanted further advice, Fletcher strongly encouraged him to become a physiologist. W. M. Fletcher stayed at Cambridge until 1914 when he was appointed the first Secretary of the new Medical Research Committee (later to become the Medical Research Council).

In October 1907, A. V. Hill started on his new course, studying for the Natural Sciences Tripos, this time taking physiology, chemistry and physics.

* 1873–1933, *Obit. Not. R. Soc.* **1**, 153.

To people outside the Cambridge environment, this must have seemed an unorthodox avenue of entry into physiology. Traditionally, it would have required a medical training as a preliminary qualification. The great pioneers of nineteenth-century physiology, persons like Hermann Helmholtz, Emil DuBois Reymond, Claude Bernard, Carl Ludwig and many others, though well grounded in the physical sciences, started almost without exception as medical graduates. But one wonders whether this rigid prerequisite of a medical degree, in practically all centres of physiological science, did not in the end prevent a more vigorous development of the subject, and in some places actually lead to a decline in its growth, and of its biophysical aspects in particular. At Cambridge, no such restrictions were imposed; J. N. Langley, who succeeded Michael Foster in 1903 as head of the Physiological Laboratory, had started as a mathematician and followed it up with a natural science degree in 1875, and Keith Lucas who had begun as a classical scholar and might have become an engineer, had recently take to physiology, like A. V. himself, under the guidance of W. M. Fletcher. The Cambridge tradition, producing physiologists without medical qualifications, some of whom acquired a Nobel Prize and honorary doctorates in medicine, gradually led the way to the general abandonment of the narrow entrance requirement for physiology that used to be almost universal less than 50 years ago.

After two years of quite hard work, A. V. took a first in Part II of the Natural Sciences Tripos in 1909 and emerged as a keen, though still rather green physiologist, very much aware of his lack of experience and the gaps in his knowledge (224a). But the personal atmosphere in the Cambridge laboratory made up for his deficiencies. He describes the laboratory itself as 'pretty awful by present (1970) standards'. However,

> 'there were probably more great physiologists there to the square yard than in any other place, before or since; and not only because there were so few square yards. A list of those who worked there between 1909 and 1914 follows:
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> J. N. Langley, W. H. Gaskell, L. E. Shore, W. B. Hardy, H. K. Anderson, F. G. Hopkins, S. W. Cole, W. M. Fletcher, J. Barcroft, K. Lucas, T. S. Hele (A. V.'s brother-in-law), V. H. Mottram, G. R. Mines, A. V. Hill, J. R. Marrack, H. Hartridge, G. Winfield, Ff. Roberts, J. C. Bramwell, E. D. Adrian, C. R. A. Thacker, D. Dale (Mrs Thacker), R. A. Peters, A. N. Drury, J. H. Burn, A. M. Hill (Mrs Hele, A. V.'s sister), C. G. L. Wolf, and L. Orbeli (St Petersburg), M. Camis (Parma), H. Piper (Berlin), H. Straub (Tübingen), F. Müller (Berlin), Alex Forbes (Harvard), F. Verzar (Budapest), V. v. Weizsäcker (Heidelberg), J. K. Parnas (Strasbourg), C. L. Evans (U.C.L.).'

In 1910, A. V. was elected a Fellow of Trinity, not long after embarking on his first research in the Physiological Laboratory where he had obtained a George Henry Lewes studentship the year before. The informal spirit prevailing there has been described by L. A. Orbeli in some priceless reminiscences (translated from the Russian). Orbeli (1882–1960), a distinguished pupil of I. P. Pavlov, was visiting German and British universities together with his wife, and spent the year 1909–10 in Cambridge; he was evidently very impressed by the free and easy manners of his English colleagues and the way in which they managed to maintain their 'amateur status' while at work. He wrote:

> 'The English method of working is greatly different from the German. Laboratories in those days were still housed in old buildings and were rather homely and modest. Langley was the head.
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> 'At that time the great scientist Barcroft was working there. He was already a fully qualified worker with his own assistants. Then there was Keith Lucas, also a qualified scientist. A young man called Archibald Hill also worked there. He had only just written his thesis and was a mathematician who had somehow done two subjects at the University, mathematics and physics, but he had had no previous connexion with biology or medicine. ["This is rather an exaggeration" (annotation by A. V. H.).] He was a great enthusiast for various sports, particularly running. Once while he was running the thought occurred to him, "How does the muscle machine work?" and this led him to the physiology laboratory where he he has worked ever since.
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> 'They all came in to work just when they felt like it. Only when they were to teach students did they arrive punctually.
>
> 'Lucas arrived. I was sitting and working. "Good morning, Sir! I am Lucas. Would you like to come out in my motor boat?" "Thank you." He sat down. "So, tomorrow, if it is good weather I'll go out and I would like to invite you and your wife to come. If it rains, I shall come to work at the laboratory. Perhaps you would like to see my experiments?" "Thank you, I would be very pleased to see them." "Well then, good-bye."
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> 'In the laboratory, each person had his place—in truth, his corner. The conditions were very modest. Gradually I got to know people. A man with a pipe appeared: "I am Hill. What are you doing?" I said, "I am operating on a frog." "Then why are you sterilizing the instruments?" "So as to make the operation aseptic." "And can frogs really have microbes?" I replied: "Of course they can. The microbes can live in the skin." "Can they hurt it? I know nothing about bacteriology or medicine. I am a physicist." He invited me to see his experiments. Then he disappeared somewhere. I asked: "Where is Hill?" "He is reading at the moment." So it seemed that he read for a week at a time, appearing in the laboratory to smoke his pipe and drink a cup of tea. The next week arrived. "Where has Hill got to?" "Hill is at an instrument factory watching the making of his galvanometer." In other words, Hill knew every detail, made specific requests, and himself tried out the range of instruments. Then they said: "Hill has got his galvanometer."
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> 'After this, Hill got to work. Where? In the basement. The galvanometer was set up on a special mounting. Hill shut himself up and nobody saw

him for a week. Suddenly he finished, came out again, and the motor-boats, running and all sorts of fun started up again.

'In England, it is absolutely necessary to drink tea at five o'clock. A small table was set up in the library of the laboratory and a servant brought in a tea-pot with hot water, made some tea and set out the cups. Suddenly everyone appeared from whatever they were doing, reading or working, and for thirty or forty minutes the whole laboratory drank tea and exchanged the latest news. Then everyone disappeared into his own corner and got back to work.'

FIRST RESEARCHES 1909–10

In November 1909, J. N. Langley wrote to A. V. suggesting that he might settle down to investigate 'the efficiency of the cut-out frog's muscle as a thermodynamic machine' and pointing out that the presence of Fletcher and Hopkins who had already made important contributions on a closely related subject would be an obvious advantage. To start him off, Langley was also able to produce from his cupboards a nice little instrument, a thermocouple plus mirror galvanometer which had been designed for just this purpose by the late Professor Magnus Blix of Lund. It is not clear who had used the instrument; somebody must have done so, for essential parts of the galvanometer were missing. At any rate, Hill managed to put it together and found it a useful piece to begin with. However, before setting out on what became his personal line of research, he was engaged on several more theoretical exercises helping to underpin mathematically the work of his more senior friends and colleagues in the laboratory. It is obvious that J. N. Langley, J. Barcroft, K. Lucas and G. R. Mines were glad to employ the mathematical 'whizz-kid' and his special talents to provide theoretical foundations for their experiments and to make their ideas more testable in quantitative terms.

The results of this period are as interesting as the somewhat depreciatory comments which A. V. made on those early efforts later on (224). The first paper, in 1909, on 'The mode of action of nicotine and curari' he describes, 60 years later, as 'a subject suggested by Professor J. N. Langley from among his current interests' and adds: 'The results look quite unimportant today . . . .' In fact, it contains the first kinetic description of drug/receptor interaction and the first appearance of the 'saturation formula' which Hill thus introduced several years before the Michaelis–Menten treatment of enzyme/substrate

* Hill's equation for the reaction-rate limited form of the contraction curve is

$$y = \mu\left(\frac{kNX}{k'+kN} - M\right)\{1-\exp[-(k'+kN)t]\},$$

where μ is a constant, X the total number (free and combined) of receptor molecules, M the minimum ('threshold') number of compound molecules needed for contraction; k and k' are the rate constants of the bimolecular reaction $N+A \underset{k'}{\overset{k}{\rightleftharpoons}} NA$, where N is the number (or concentration) of drug molecules, and A that of free receptor molecules ($X = A+NA = \text{const.}$). The saturation formula $y' = kNX/(k'+kN)$ is usually written in the form $y'' = S/(S+K)$ (or $1/(1+K/S)$), where y'' is fraction of maximal response, S the agonist concentration and K the dissociation constant k'/k.

reactions, and Langmuir's derivation in the case of molecular adsorption at surfaces.* The basic idea was to test Langley's view that specific drugs like nicotine and curare combine in a reversible manner with 'receptive substances' in the cells before producing their effect. A. V. used a simple apparatus which Keith Lucas had designed for Langley's work to record contractions of the frog's rectus abdominis muscle elicited by various concentrations of nicotine. An analysis of the size and time course of development and decline of the response, and of the effect of temperature changes showed that it was consistent with a reversible bimolecular chemical reaction whose rate constants and Arrhenius coefficient could thus be determined. Historically, this is a very interesting and instructive paper, but it is easy to understand A. V.'s apologetic comments, made at a later time when he must have considered the myograms he had recorded in 1909 as too indirect a type of response to allow quantitative inferences to be made about the molecular kinetics of the drug action.

The saturation formula, which subsequently became known as the Langmuir or Michaelis equation, had been introduced in Hill's first paper, but it was submerged among less important details and so escaped notice. This certainly did not happen to his next two publications, on the nature of oxyhaemoglobin and its dissociation curves. The first of these was a joint effort, with Joseph Barcroft supplying the experimental results and A. V. contributing the mathematical theory and thermodynamic reasoning. There remains a minor mystery about the data which show 'rectangular hyperbolae', with a linear start of the oxygen saturation curve of dialysed salt-free haemoglobin. When similar measurements were made in later years (for example, by Adair, Barcroft and Bock in 1921), this type of relation was not confirmed and sigmoid saturation curves were almost invariably found, a matter which caused much concern to Joseph Barcroft (see *Obit. Not. R. Soc.* **6**, 315). Hill used the 1909 results, together with a study of the effect of temperature, to decide between the possibilities of physical adsorption and chemical bond formation between O_2 and haemoglobin. Assuming it to be a simple bimolecular combination, he proceeded to derive the heat of reaction and found that the value was reasonably consistent with direct heat measurements. The theory, of course, needed revision in the light of the later data.

Much more influential was a short note in 1910 on 'The possible effects of the aggregation of the molecules of haemoglobin on its dissociation curve.' (Such aggregation was thought to occur in the presence of salts and carbon dioxide.) The paper contained the first kinetic model for a 'cooperative' reaction, in which several (n) substrate or agonist molecules interact with a macromolecular receptor. Hill introduced the equation $y = Kx^n/(1+Kx^n)$, sometimes rewritten as $y = 1/(1+K_1/x^n)$. Sigmoid saturation curves result if $n > 1$. In the current literature, n is generally referred to as the 'Hill coefficient' and is used as a characteristic index of 'cooperativity'. It is generally realized that the Hill equation is strictly applicable only if all n molecules react simultaneously (which is unlikely), and it is theoretically unjustified if intermediate steps cannot be ignored. Nevertheless the formula has been widely used by many investigators. It has been a typical case of a useful theoretical 'half-truth', cutting corners and oversimplifying the real situation, but still enabling one to gain some insight and to make practical, if only approximate, calculations. In the case of oxy-haemoglobin, although Hill's theoretical formula fitted and coordinated many of the observed results very nicely, it was left to Adair to find the correct value of n in dilute solutions ($n = 4$), and to F. J. W. Roughton and his colleagues very much later to explore the sequence of intermediate steps and to cover the ground which had been elegantly skipped over in the little 1910 paper.

There were two more 'auxiliary' theoretical contributions: one was a short note supplementing an ingenious method devised by G. R. Mines for measuring 'the relative velocities of diffusion in aqueous solution of rubidium and caesium chlorides', the other an elaborate mathematical extension of Nernst's theory of electrical excitation undertaken at the suggestion of Keith Lucas who was one of the leading experimenters in this field. Nernst had become interested in the stimulating effects of different forms of electric currents, noting that high-frequency alternating current was much less effective as an excitatory stimulus than in producing heat. He had developed a theory according to which excitation results from the ionophoretic build-up of a concentration change at a semi-permeable membrane, the effect of the current being opposed and dissipated by thermal diffusion. The theory explained the relation between the time course of a current and the intensity needed for excitation, but it was applicable only to a limited range of pulse durations and of alternating current frequencies, and it could not account for the complete failure of slowly rising currents or of weak currents of very long duration. A. V. Hill modified the Nernst theory in two ways. (i) By placing two membranes close together within the path of the current, so that the ion concentration change could not go on growing indefinitely as the duration of the pulse was lengthened and a minimum intensity was required even for very long pulses. (ii) He introduced a new 'threshold' requirement, namely that the 'rate of breakdown' of some substance (the breakdown being initiated by the concentration change) had to exceed a certain value. Thus, if the current intensity grew too slowly, the critical substance inside the membrane-bound compartment would become gradually depleted without the excitation threshold ever being reached. The paper was probably quite impressive at the time, not only because of its formidable mathematical content, but because it tried to produce more than just 'curve-fitting' formulae and present physico-chemical concepts in extension of Nernst's hypothesis. However, the ideas were not fruitful, and most neurophysiologists agree with A. V.'s own comment (224) that 'this paper is of no interest now, except possibly historical, though it was an unconscionable time dying; which, like Charles II, I hope that people will excuse . . .. Probably I was the only person who profited by it, for it taught me about the equations governing diffusion, which were useful later . . ..'

It would be quite wrong to regard these early theoretical papers as merely the commissioned effort of a 'tame mathematician'. Their writing bears the hall marks of A. V.'s clear personal style, they are alight with new and sometimes brilliant ideas, and already show signs of A. V.'s main contribution to physiological science, the introduction of physico-chemical concepts and the emphasis on quantitative, numerical treatment which became the distinguishing features of his particular brand of physiology, usually called 'biophysics'.

5. The start of the myothermic work

The last paper to appear in 1910 is also the first of the long series of Hill's myothermic studies. In it he describes the Blix thermocouple recorder which Langley had given him and which he improved sufficiently to put it to work showing that thermal responses could be obtained during single twitches as well as during prolonged contractions of isolated frog muscle. This was followed by a more substantial paper under the heading 'The position occupied by the production of heat, in the chain of processes constituting a muscular contraction'. This paper is of interest, not so much for its experimental results nor for the discussion which is adorned with some overconfident interpretations, but because it shows the start of a development of methods and constant adaptation and improvement of techniques which A. V. went on pursuing throughout his working life. Instead of a single thermocouple, he arranged five thermojunctions in series which enabled him to work for the first time on the thin parallel-fibred sartorius muscle. To improve time resolution and survival of the preparation, experiments were made at low temperature. Electric heating of muscles, rendered inexcitable at the end of the experiment, was introduced for calibration purposes.

Hill was impressed by the fact that under varying external conditions there was an approximately constant relation between tension and heat developed during an isometric muscle twitch.* He regarded the isometric tension as of more fundamental significance than the process of shortening or the performance of work, both of which depend on the load the muscle has to lift. The conclusion was that 'the muscular machine is concerned with the transformation of chemical energy into the potential energy of increased tension' (the output of mechanical work being thought of as merely a secondary consequence of the release of elastic tension). Later A. V. described this as 'unfortunate' and a 'false trail which led to a lot of confused thinking' (224) which is in marked contrast with the somewhat exuberant flourish in the last sentences of the 1911 paper that 'a complete investigation of these facts will give us more real insight into the nature of the muscular machine, and therewith of all living tissues, than any theories of contraction ever founded by ingenious mind upon insufficient knowledge'! Very shortly afterwards, A. V. seems to have had the sobering experience of discovering Otto Frank's excellent, 167 pages long article in *Ergebnisse der Physiologie* reviewing all the earlier research on thermal phenomena in active muscle. This paper impressed A. V., probably more than anything, with the need to learn more about the pioneering efforts that had been

* 'Isometric' refers to active muscle kept at constant length; 'isotonic' to active muscle shortening under constant load or tension.

made by the nineteenth-century German physiologists and to acquaint himself with current techniques used in the few places in Germany where such work was still being pursued. In the search for useful alternative methods, in particular for measuring slowly developing and prolonged heat production, A. V. had already started to design an ingenious differential calorimeter (8) and to experiment with it, but he decided early in 1911 to interrupt his work, and went to Germany for four months. He visited Leipzig and Jena, and then proceeded to Tübingen, where he spent several weeks in the laboratories of Karl Bürker, a physiologist who had published a detailed review on myothermic techniques and was able to advise A. V. on methods of constructing thermopiles, and of Friedrich Paschen the distinguished infrared spectroscopist who taught A. V. about the design of galvanometers and supplied him with one of the rapid and sensitive instruments which he had built in his own institute.

The instructive interlude in Germany had a few side-effects. In addition to making new friends and improving his knowledge of the language, A. V. also had the opportunity of witnessing at Jena some of the notorious duels in which members of the student corps were accustomed, or were required, to demonstrate their virility. It gave him a foretaste of what was to happen 3 years, and again 22 years later.

On returning from Germany, he carried on with the development of the calorimeter and, using it in conjunction with his new Paschen galvanometer, produced a number of interesting results. There is an amusing paper on 'The total energy exchanges of intact cold-blooded animals', measuring the temperature coefficient of resting heat production in whole frogs, snakes, newts and worms which he placed in his standardized Dewar flasks.

This was followed by his first and unsuccessful attempt to measure heat production during the passage of nerve impulses (10). For this he made his first thermopile, more or less following Bürker's instructions. He gives a full description of the method, explaining how he soldered 30 pairs of thermojunctions, from very fine constantan and iron wires, and presenting a formidable list of necessary precautions. Lest anybody should remain unconvinced, he informs the reader that 'it needs some acquaintance with the literature, and experience with the method, before one is able to avoid all the pitfalls which beset the observer'. (Fortunately, in one of the subsequent papers (14), A. V. is able to reassure us that some of the elaborate measures prescribed by Karl Bürker can be dispensed with.) The experiment on nerve heat failed because the thermal insulation and stability of the nerve chamber were inadequate. Also, as A. V. later commented, he had overestimated the sensitivity of his instrument about fivefold. He had not yet adopted the procedure which he later introduced, of a direct heating control made on the preparation at the end of the experiment. Even so, the 1912 attempt was a near-miss; with a relatively small improvement in stability, he should have been able to detect the temperature rise, which he indeed found 14 years later in the same type of experiment. In the summary of the paper he discarded some of the caution which he had displayed earlier on. His negative results were taken to 'suggest very strongly that the propagated nerve impulse is not a wave of irreversible chemical breakdown, but a reversible change of a purely physical nature.' It is probably apparent by now that A. V. loved to make provocative statements and did not mind 'sticking his neck out', sometimes to inflict the punishment himself later on! If one reads his commentary in *Trails and trials in physiology* (224), it is clear that he regarded errors in interpretation and the 'built-in obsolescence' of scientific theories as an inevitable and indeed necessary part of progress, and the more provocative the statement, the better it was in jollying progress along. A. V. did not return to the problem of heat production in nerve for many years. Instead he now redoubled his efforts to throw light on the energy exchanges in muscle.

It is instructive, especially with hindsight, to analyse A. V.'s argumentation in some of the early muscle papers. Like Helmholtz, 65 years before, he approached the subject of muscle along the avenue of energy and thermodynamic considerations. Thermodynamics, though only providing a 'framework for the chemical picture', had, to A. V., the advantage of 'allowing him to deduce certain characteristics of a system without a knowledge of its detailed machinery' (224). Biological processes such as muscle contraction are driven by chemical engines, and it should be profitable to apply the laws of thermodynamics to them. His aim was to measure the physical products of the reactions in terms of heat and mechanical work, taking advantage of the relatively good time resolution which could be achieved by recording the physical changes, and to relate these quantities to what was known or being discovered about chemical changes in muscle.

Two of his papers (11, 14) are particularly revealing. The first one, on 'The heat production of surviving amphibian muscles, during rest, activity and rigor', took off directly from the important work of Fletcher and Hopkins, who had measured the rate of CO_2 and lactic acid production under these different conditions. By placing isolated frog limbs into his improved micro-calorimeter, Hill found an initial peak of heat liberation in the resting muscles which was approximately equal to that measured *in vivo* and which gradually, over a period of several hours, fell to a much lower, but long maintained plateau. The time course roughly paralleled that of the CO_2 output determined by W. M. Fletcher. A quantitative comparison under various conditions enabled him to conclude that the early phase of relatively intense metabolic activity coincides with oxidative processes which gradually subside as the residual oxygen dissolved or stored in the tissue is consumed. The ensuing low plateau corresponds mainly to anaerobic production of lactic acid, the heat output resulting from the breakdown of a lactic acid precursor, and the CO_2 production from the neutralization of the acid with bicarbonate. The 'precursor' must be something other (more 'energy-rich') than dextrose because the experimentally obtained heat rate associated with the formation of lactic acid is too great to be accounted for by a breakdown of dextrose. In discussing his results, A. V. makes some very interesting observations. He emphasizes that the heat measurements by themselves do not tell one very much; what is really important is to know the free energy change of the chemical reactions, and this is generally not an easy thing to determine. He suggests that, during muscle activity, the breakdown of the 'lactic acid precursor' may liberate energy and provide mechanical work more than equivalent to the total energy loss occurring in the formation of lactic acid, and that subsequent oxidation may be a recharging process returning the lactic acid to its original state. 'When much work is done in a twitch, there might be for a short period a cooling of the muscle, but to the thermoelectric methods at present possible this initial cooling would be entirely masked by the rapidly ensuing process of restoration.'*

The reader will be struck by a number of things which are interesting as well as puzzling. A. V. clearly realized that drawing up an energy balance sheet without knowing the detailed items of 'income and expenditure' would not help very much in understanding biological processes. Why then did he continue to devote a tremendous and lifelong effort to the measurement of heat production? The reasons presumably changed as time went on and as he discovered an increasing number of interesting and successful applications for his ever-improving thermoelectric methods. But during the decisive early period, what he probably had in mind was that there could no longer be any reasonable doubt that the only relevant chemical reaction step during contraction had already been identified, that it *was* the formation of lactic acid from a precursor and nothing else, and that its free energy could be equated with the maximum mechanical work which an active muscle is able to deliver. That he regarded the matter as practically settled becomes apparent in the next paper (14) in which he says: 'Certain it is that lactic acid and CO_2 are produced by excitation, and apparently nothing but lactic acid and CO_2.' This belief persisted with minor modification until the advent of 'The revolution in muscle physiology' (129) in 1927–32. In fact, this was neither the first nor the last revolution in the course of which substance A was deposed and replaced by substance B as the king-pin of muscle contraction. After all, the work of Fletcher, Hopkins, Hill and later Meyerhof had raised lactic acid to the exalted position previously occupied by 'intramolecular oxygen' which was thought of as being utilized directly for the production of energy in muscle and other biological systems. Now, oxygen was demoted from the 'action ' to the 'recovery' phase. The same thing happened later when lactic acid was displaced by creatine phosphate, and soon after creatine phosphate lost its position to ATP (adenosine triphosphate). At present we are still uncertain of the exact rôle of ATP in the cyclic interaction between actin and the myosin cross-bridges, and it remains to be

* In the same paper, he states: 'At present I hold no brief that lactic acid *is* responsible for the muscular contraction; but until we know exactly what the precursor of lactic acid is, and what the "free energy" of its breakdown into lactic acid is, we cannot adduce considerations of energy to disprove the hypothesis that the sudden liberation of lactic acid causes a contraction, whether by a change of surface tension or by some other means.' In the Summary of the paper, he is less reserved and suggests 'that the lactic acid precursor contains a large store of "free energy", and that it may be able to account for the mechanical work done by a muscle simply by the process of breaking down into lactic acid.' And finally: 'Considerations of total energy are not sufficient . . .. The estimation of the "free energies" of the chemical reactions possibly involved in muscular metabolism is of fundamental importance.'

discovered whether the hydrolysis of ATP and its free energy is directly coupled to the forward, working stroke of the cycle or to its immediate reversal. In every case, with the possible exception of ATP, the substance which was thought to be the 'direct cause' of contraction was subsequently found to be one of the links in the recharging or repriming process. (In Hill's paper (11), it was the *formation* of lactic acid, the breakdown of its precursor, which was thought to provide immediate energy for contraction. However, in the next paper (14), and in others following it, lactic acid *itself* is said to cause contraction, and relaxation follows its oxidative removal or resynthesis. This can be confusing, for the same substance seems to fulfil two different and not obviously related rôles, and it is not always clear whether the author assigns one or both rôles to it; it is the kind of obscurity which is found not only in the early literature on lactic acid, but also on more recently fashionable substances.)

The work on prolonged heat production of surviving muscle tissue (11) was done with Hill's differential microcalorimeter. The instrument was further improved and the work extended with more accurate results by R. A. Peters (*J. Physiol., Lond.* **47**, 243). For his next experiments in which he set out to examine the rapid temperature change during a muscle twitch, Hill constructed special thermopiles and introduced the direct heating control on dead muscles for time and absolute amplitude calibration. The response of the recording system (thermopile and galvanometer), though being constantly improved in speed and sensitivity, was too slow to give a direct and faithful registration of the time course of the thermal changes. This had to be derived by a laborious step-by-step analysis of the records based on the effect of instantaneous heat control pulses.

Hill paid special attention to differences in size and time course of the myothermic response when the muscles were exposed alternatively to an atmosphere of oxygen and nitrogen, and he concluded that in the presence of oxygen there is a delayed production of 'recovery heat', after the mechanical response was completed, which amounts to at least 50% of the total heat production accompanying and following a muscle twitch. Exposure to nitrogen reversibly removes this second component. In conjunction with the earlier work, these results reinforced the view that 'anaerobic' heat (the initial phase) is due to lactic acid formation, while subsequent oxidation recharges the system to its initial state. In another paper on 'The absolute mechanical efficiency of the contraction of an isolated muscle', Hill determined the tension-length diagram, that is the tension developed after varying amounts of initial free shortening during a twitch (actually a short tetanus). From this, he concluded that the excited muscle behaved like an elastic body whose potential mechanical energy (i.e. the maximum work it would deliver under optimal conditions) was given by $Tl/6$ (T is the maximum isometric tension, l the resting length of muscle). The 'initial heat' H during an isometric twitch (under optimal conditions, when all the potential energy was ultimately dissipated as heat in the muscle) was found to be only slightly less than $Tl/6$, so the 'mechanical efficiency' $Tl/6H$ during the contraction itself was nearly unity. If the chemical energy expenditure during the recovery phase is included, the mechanical efficiency is of course reduced, but can still reach a value of 50%.

Among the work A. V. completed just before the outbreak of war, there are two papers published together with his sister, A. M. Hill, developing his calorimetric apparatus so that it could be applied to mammals, and even used for automatic recording on large animals (15, 25). More important, a young German physiologist from Heidelberg, Viktor von Weizsäcker,* had joined forces with A. V. Hill and demonstrated with a specially adapted myothermic method that the 'initial heat' during contraction is quite unaffected by oxygen withdrawal or cyanide poisoning, thus strongly confirming the concept of two separate, anaerobic activity and oxidative recovery, phases. He presented his results to the British Physiological Society in June 1914, an interesting early case of the international collaboration which A. V. was to attract throughout his life.

Rather less happy was the outcome of J. K. Parnas's stay in A. V.'s laboratory during the same period. Parnas had come from Strasbourg just before the outbreak of war and had been able only to spend a short time on a difficult experimental project. He was trying to decide—by measuring heat production and oxygen consumption of muscles which had been stimulated to exhaustion and then exposed to hyperbaric oxygen—whether their lactic acid was removed by oxidation or by resynthesis to the precursor. He concluded—on what later proved to be inadequate evidence—that the O_2 consumption was sufficient to burn the lactic acid completely, but was left with a large deficit in the accompanying heat production. To explain this, he postulated that the oxidative process had been utilized to restore some other form of potential energy in the muscle.

Unfortunately, this left the problem of the nature of the oxidative restoring process in a puzzling and unsatisfactory state, because this whole line of muscle research had to be abandoned 'for the duration'. For the time being, Parnas's conclusions had to be accepted, and A. V. later recorded with obvious displeasure that Parnas's work misled all his colleagues until it was rebutted by Otto Meyerhof's much more decisive experiments after the war. However, this judgement was perhaps a little hard; the trouble seems to have been that, in discussing the fate of lactic acid and its oxidative removal, all the protagonists, and that includes A. V. Hill, Fletcher, Hopkins and Parnas, were adopting a simple 'either – or' attitude, *either* that lactic acid was rebuilt into a precursor, at the expense of the oxidation of other material, *or* that it was burnt up and the energy so liberated utilized for a restorative pathway of a different kind. The answer provided by Meyerhof's experiments suggested that this exclusive line of argumentation may not be justified, and that the combustion of some 20% of the lactic acid (or of the equivalent amount of glucose) may be utilized

* V. v. Weizsäcker (1886–1957) had already published valuable studies on oxidative metabolism in the frog's heart and decided to pursue them and test his conclusions by myothermic measurements in Hill's laboratory. Weizsäcker later became a distinguished clinical neurologist and, as a moral and social philosopher, he was widely known and respected for his freely expressed liberal views.

to resynthesize glycogen from the remainder. Even this story was found to be too simple in later years when complicating factors, such as creatine phosphate, ATP, the 'Cori-ester', 'alactic' contraction, oxidative phosphorylation and resynthesis of glycogen without lactic acid formation, appeared on the scene and had to be taken into account.

6. Marriage to Margaret Keynes

In June 1913, A. V. married Margaret Neville Keynes, daughter of Dr John Neville and Florence Ada Keynes, of Cambridge, and sister of John Maynard (Lord Keynes), the economist, and (Sir) Geoffrey Keynes, the surgeon and author. A. V. records the event (226): 'Our friends, and many descendants, agree that this was the cleverest thing I ever did.'

Margaret describes some amusing incidents from the period before marriage in letters to her friend Eglantyne Jebb (the founder of the 'Save the Children' Fund). A. V. had evidently decided that a promising line of advance was to assist Margaret Keynes in her social work, concerned at that time with finding suitable employment for teenage boys. A good deal of the courtship was of the 'motorized' variety, with Margaret riding in the side-car of A. V.'s motorbike (in mid-January!). On one of those occasions, still recovering from a cold, she was wearing no fewer than 'five coats and two sets of boots'. Their conversation centred not only on Margaret's work, but she comments on the trials and tribulations experienced by A. V. who, as Junior Dean at Trinity, had to take time off from his Science 'to reprimand badly behaved undergraduates'. Margaret and A. V. became engaged early in February 1913; in March the motorbike took them all the way to Salcombe in Devon where they spent a short, but most successful holiday.

Margaret's father, Dr J. N. Keynes, was Registrary at Cambridge University and had published two well-known treatises on formal logic and political economy. His wife gave great public service; in 1932, during the year of their golden wedding, she was elected Mayor of Cambridge. In 1950, at the age of 89, she published a biographical history of the Keynes family (*Gathering up the threads*, Heffer, Cambridge). Margaret Hill herself was very active in social welfare work; she formed the Hornsey Housing Trust for the needy and later devoted herself particularly to the problems of old age. During World War II she started an organization providing shelter for old people whose houses had been destroyed in the bombing, and this work expanded later and led to the establishment of a series of Old People's Homes in the Highgate area of London, quite near their own family home in which they lived for 44 years, from 1923 on. The hospitality at their home and at the little summer house in Devonshire which they acquired in 1927 will have been among the most pleasant experiences of many of A. V.'s friends and colleagues.

Margaret Hill had many talents: bookbinding and gardening were among her favourite hobbies, and in later years she took up still life and landscape painting and became an accomplished amateur artist. During the 1960s her many-sided activities became progressively restricted by a crippling form of

Parkinson's disease, and after the tragic death of their younger son Maurice (*Biogr. Mem. R. Soc.* **13**, 193), A. V. and Margaret returned to Cambridge in 1967 to share the house with Maurice's widow, Philippa Hill. Margaret Hill died in Cambridge in 1970. They had four children, born during the years 1914 to 1919, Polly, David, Janet and Maurice. Polly (Mary Eglantyne Hill) became an authority on African rural economy (Smuts Reader in Commonwealth Studies at Cambridge), David (David Keynes Hill) a physiologist and Professor of Biophysics (F.R.S. 1972), Janet (Janet Rumney Hill), who married Professor John Humphrey, the immunologist (F.R.S. 1963), qualified in medicine and practised as a psychiatrist, and Maurice Neville Hill became a geophysicist and an authority on exploration of the ocean floor (F.R.S. 1962, died 1966). A. V. had 14 grandchildren, and at the time of his death 4 great-grandchildren.

7. War service 1914–19

Hill's physiological research was completely interrupted in August 1914 when, on the outbreak of war, he joined the Cambridgeshire Regiment. He did not return to the laboratory until demobilization in March 1919. In a roundabout way, this period of wartime service may have saved him for muscle physiology, for he reports (70 and 226) that 'in 1914 I was tending to drift away from physiology and had actually been appointed University Lecturer in Physical Chemistry at Cambridge . . . but after 4½ years absence I returned in 1919 to my first love'.

The first 18 months cannot have been very inspiring. A. V., who had been in an Officers Training Corps for many years and held a commission in the Territorial Army since 1909, entered as a regimental Captain, but was soon transferred to the position of Brigade Musketry Instructor for which he indeed had special aptitude.

In 1916 several changes took place. When the tenure of his Research Fellowship at Trinity came to an end, A. V. accepted a Fellowship at King's College, Cambridge, which he held until 1922. In January, he was asked to investigate several urgent problems of anti-aircraft gunnery. The persons responsible for this move were Sir Alexander Kennedy and Sir Horace Darwin of the Cambridge Instrument Company with whom A. V. was collaborating in the invention of a mirror position finder. Hill was given the task of forming and directing an Anti-aircraft Experimental Section within the Munitions Inventions Department. He assembled a distinguished group of young mathematicians and physicists who became known in the Services as 'Hill's brigands'.* The first to join him were R. H. Fowler (*Obit. Not. R. Soc.* **5**, 61) and E. A. Milne (*Obit. Not. R. Soc.* **7**, 421), both having started as pure mathematicians who after their wartime experience turned into great leaders in more applied branches of science, R. H. F. as a mathematical physicist and E. A. M. as an astronomer.

* The members of the 'brigands' included G. T. Bennett, W. R. Dean, R. H. Fowler, W. J. Goudie, D. R. Hartree, W. Hartree, A. C. Hawkins, R. A. Herman, B. Lockspeiser, E. A. Milne, H. W. Richmond, T. L. Wren.

The three started conducting field tests on the position finder at Northolt Aerodrome, then moved to Teddington in May 1916, and a little later to Whale Island, Portsmouth. By now the staff of the section had been considerably enlarged, A. V. was made a Brevet Major, and a number of investigations were under way, for instance on accurate localization of high-angle shell bursts, and on the failure of shell fuses at high trajectories (which was eventually traced to a peculiar failure of the compressed gunpowder to burn at the required rate, occasioned by a combination of high spin velocity and reduced air pressure!).

An interesting light on A. V. Hill's rôle in these activities, and on his personal leadership and the influence he exerted on the future careers of his friends, is contained in E. A. Milne's biographical memoir of R. H. Fowler (*Obit. Not. R. Soc.* **5**, 61): 'Hill was the inspirer of most of the researches that were conducted, whilst Fowler executed them in the field.' There were awkward moments, according to Milne, when Fowler's abrasive criticism of signs of inefficiency created an uneasy situation, but this did not survive long and was promptly dissolved into laughter by A. V.'s intervention. E. A. Milne continued about R. H. F. and A. V. H.:

> 'At directing research, both were superb. . . . to behold the way they set about a new problem, often in a new terrain with new material, to see the way they made inferences and came to conclusions and sound judgments and to take part in it all, was far better training than most Universities can offer to aspirants in research. The present writer (E. A. M.) desires to put on record his realization that his three years' period under Hill and Fowler, at the most formative period of his life (age twenty to twenty-three) was a most vivid, enjoyable and valuable experience; to both of them he can never be sufficiently grateful for that schooling in research.'

A fine comment, which I imagine meant more to A. V. than orders or decorations (he received an O.B.E. in 1918).

The work of the anti-aircraft section was later incorporated in several important textbook volumes (*Theory and use of anti-aircraft sound locators*, 1922; *Textbook of anti-aircraft gunnery*, 2 volumes, 1924–25, London: H.M.S.O.). In addition to directing the Anti-aircraft Experimental Section, A. V. became a member of several related wartime committees concerned with Air Inventions and Anti-aircraft Equipment, and an Associate Member of the Ordnance Committee.

8. Return to Cambridge and muscle physiology

One of the results of A. V. Hill's wartime occupation was that he met William Hartree, a former lecturer in engineering at Cambridge, who so much enjoyed working with A. V. and his 'anti-aircraft brigands' that he followed him back to his Cambridge laboratory in 1919 and at the age of 49 became a muscle physiologist for the next 14 years (213, p. 173, and *Memories and reflections* (*M. & R.*)). His friendship and close collaboration with Hill resulted in rapid improvements of the myothermic technique and the numerical analysis of data, and in a larger output of joint, and later—after A. V.'s departure from Cambridge—also separate publications.

In 1918, while still with the anti-aircraft section, A. V. was elected to the Fellowship of the Royal Society, and presumably this recognition—as well as reminding him of what was expected of him as a physiologist—made him eager to 'get back to his cellar' and to research in the Cambridge laboratory as soon as possible. After an interval of five years during which his publications consisted of a long (and long delayed) review in German translation of the myothermic work, and of reports of various pieces of applied research in other fields (including measurements of infrared transmission in the eye and in various glasses, done together with H. Hartridge for the Glassworkers' Cataract Committee of the Royal Society), he lost little time now in setting up again and improving his myothermic equipment with the eager help of W. Hartree. Within a few months, presentations of the renewed efforts started at the meetings of the Physiological Society. In July 1919, Hill and Hartree demonstrated their improved and more sensitive thermopiles; in December they showed their new methods of photographic recording of the myothermic response, the analysis of its time course by numerical superposition of successive 'heating blocks', and discussed the 'relaxation heat' which they observed at the end of an isometric contraction and correctly attributed to a dissipation of mechanical energy within the muscle substance. A month later, observations on thermoelastic effects in resting muscle were reported, and A. V. Hill described an inertia-type of ergometer, whereby the stimulated muscle was made to accelerate a suitably balanced mass (inertia lever) so as to extract the maximum mechanical work during a twitch, instead of allowing it to be degraded into heat during relaxation.

A full paper followed on 'The four phases of heat-production' in which Hill and Hartree separated the myothermal response, during a prolonged isometric contraction, into (i) initial heat associated with excitation and the development of tension, (ii) maintenance heat which accompanied the period of maintained tension, (iii) relaxation heat at the end of stimulation and (iv) oxidative recovery heat which continued for several minutes thereafter. During the same period several papers on related subjects appeared, by A. V.'s Japanese pupil, Yasukazu Doi.

9. Manchester 1920–23

During the post-war months of intense activity, important academic offers started to arrive, including the invitation to succeed W. H. Howell in the Physiology Chair at Johns Hopkins. It must have been unsettling and difficult to make up his mind whether to remain in Cambridge and continue at full speed with his flourishing research, or face another disruption with new administrative and teaching duties. In the end he decided to take the Brackenbury Chair of Physiology at Manchester University. He left Cambridge in 1920;

W. Hartree carried on in the cellar at Cambridge until 1933, with financial support from the Medical Research Council and in close consultation with A. V. with whom he continued to publish a series of joint papers.

In Manchester A. V. was faced with the task of resuscitating a derelict department and reorganizing the teaching course with a student population reinforced by about one hundred ex-servicemen. However, before accepting the Manchester post, he had prepared his ground by obtaining special funds from the University and much help from his friend W. M. Fletcher, who was by now the Secretary of the Medical Research Council. So he was able to equip his new laboratory satisfactorily and to attract staff and research assistants around him. A. V. was joined in 1920 by A. C. Downing, an outstandingly skilful instrument maker who worked with A. V. until his retirement and was responsible for some very important improvements in design and construction of galvanometers and thermopiles. Among his scientific colleagues at Manchester were W. K. Slater, a biochemist who later became Secretary of the Agricultural Research Council (*Biogr. Mem. R. Soc.* **17**, 663), H. Lupton and C. N. H. Long (later heading the Physiology Department at Yale) with whom he extended the study of muscular movement from frogs to man, W. E. L. Brown with whom he continued his research on the physical chemistry of blood, and J. C. Bramwell, an old friend from the Cambridge laboratory who was now working as a cardiologist at the Royal Infirmary at Manchester and who joined in applying A. V.'s hot-wire sphygmograph to a study of arterial elasticity and pulse wave velocity.

Hill had shown his organizational talents when he built up and directed the anti-aircraft section during the war. That experience stood him in good stead at Manchester where he managed, by extremely efficient planning of his timetable, to carry out his departmental and teaching duties, to prosecute his main line of research on muscle activity, and to apply his biophysical concepts and techniques to several 'peripheral' problems. His great facility in presenting his work and ideas, at scientific meetings and in print, helped a great deal, of course; nevertheless, the output of papers, immediately after the move to Manchester, remains a source of amazement to me. The following is only a short selection of the various contributions he made during the year 1921–22.

In a note on the temperature coefficient of the velocity of nerve impulses (40), he points out that the propagation velocity of a combustion wave in a gun-powder fuse was found to change hardly at all with temperature. He explains this arises because the rate-limiting step is not the local chemical reaction which proceeds very rapidly, but the much more time-consuming physical mechanism, namely heat conduction, by which the process is passed on from point to point. Conversely, the relatively high temperature coefficient of the conduction velocity in nerve does not by itself enable one to tell whether excitation is passed on, from one region to the next, by a 'physical' or 'chemical' mechanism.

There followed several short papers on the use of a resistance thermometer (a 'hot-wire sphygmograph') to detect pulsatile vibrations and to time them accurately. The hot wire was mounted effectively at the end of a 'stethoscope', acting like a microphone in response to sudden air pressure changes. The method was applied to measure arterial pulse wave velocity and to display the rhythmic contractions of motor units in human muscles during voluntary movement (48a, 56, 57).

As a by-product of the regular heating controls, made at the end of myothermic experiments on chloroform-treated dead muscles, Hartree and Hill determined the specific resistivity of frog muscle with alternating current and found it to correspond to that of a 0·36% NaCl solution (half the salinity of frog Ringer).

The pre-war experiments on the different phases of heat production were repeated with greater accuracy and improved time resolution (36, 47). The heat production in a single muscle twitch is greater at low than at high temperature; conversely, maintaining tension during repetitive stimulation is accompanied by greater heat dissipation at high temperature. Both phenomena are explained by the fact that the elementary unit of contractile activity, that is the cycle of rise and fall in a single twitch, is greatly prolonged at low temperature. As a consequence, there is more time for energy to be liberated and for contractile force to develop in a twitch, and because of the slower relaxation it becomes more economical, and less energy is needed to *maintain* tension at low temperature.

The most important work on isolated muscle was a detailed re-examination of the 'recovery heat' (54). Hartree and Hill once again confirmed the existence of two separate phases of heat production, the 'initial heat' which accompanied the contraction–relaxation cycle and was independent of oxygen, and the 'recovery-heat' which started to develop after a definite delay and went on long after the twitch was over. In quantitative respects, some of Hill's earlier results were revised. They found that the total recovery heat production amounted to 1·5 times the initial heat, and that it consisted of two discrete components which differed in size and exact time course, the major and prolonged portion being removed by cyanide or by oxygen withdrawal, while a small 'delayed anaerobic heat' remained which had previously escaped recognition.

By this time, Otto Meyerhof had entered the field and taken up the question of the fate of lactic acid where it had been left by Parnas in 1914. In a series of convincing experiments, Meyerhof refuted Parnas's claim that the whole of the lactic acid was burned after contraction and showed that at the most one out of three or four molecules is oxidized, while the rest of the lactic acid is resynthesized to muscle glycogen from which it was originally derived. In discussing the significance of his results, Meyerhof draws extensively on Hill's myothermic measurements whose guiding influence on his own research he acknowledges. Similarly, Hartree and Hill were now able to make full use of Meyerhof's complementary work, including his determinations of the heat of combustion of glycogen and of the calorimetric values of the formation and neutralization of lactic acid.

In this way, Hartree and Hill were able to draw up a 'balance sheet' for the heat evolution accompanying the cyclic liberation and removal of lactic acid during and after the twitch. They concluded that the initial anaerobic heat could be ascribed to the formation of lactic acid and its reaction with protein buffers, indeed they considered the calculations to provide strong evidence that formation and neutralization of lactic acid are all that happens during the initial cycle of contraction and relaxation.

Furthermore, if one accepts that the heat production during the muscle twitch, in the absence of oxygen, is accounted for by the formation of n grams of lactic acid (from $0.9n$ g of glycogen), then the total heat (anaerobic plus oxidative recovery phase) which accompanies and follows the twitch is only sufficient to account for the combustion of $0.17n$ g of glycogen, which indicates that only one out of every five or six molecules of lactic acid is oxidized during recovery and the remainder restored in an endothermic process. Quantitatively this differs somewhat from the estimate given by Meyerhof, but Hartree and Hill point out that the myothermic results were obtained from fresh muscles with much less fatiguing stimulation, and the efficiency of the oxidative process tends to decline in the course of a prolonged experiment.

The impact of this work can be gauged from the fact that a year later, in 1923, it was taken up by the Nobel Committee and awarded a prize (curiously for the year 1922, in which no award had been made). The brilliant exploitation of an ingenious and precise biophysical technique, the exact convergence of the results with those of an outstanding biochemist working quite independently in another country, the new light this was throwing on a fundamental process, namely the production of work by a cycle of chemical reactions in a living cell, all this represented a real triumph in experimental physiology, and it is easy to appreciate that the discoveries of Hill and Meyerhof were regarded as an exciting 'major break-through' by the scientific community.

What was perhaps even more impressive, Hill started immediately to test his conclusions on human muscles and to apply the new concepts of anaerobic activity and oxidative restoration to muscular movement in man. Some of his most enjoyable and entertaining papers stem from this period and are concerned with the physiology of muscular exercise and energy exchanges during athletic performance.

In the first paper on human muscle, A. V. describes an inertia ergometer consisting of a heavy flywheel with a set of eight pulleys, which he used to extract the maximum work from a flexion of the arm and to measure the relation between speed of shortening and mechanical efficiency. He found that at high speeds of movement, less work is done and mechanical energy appears to be dissipated due to some viscous resistance in the muscle fibres themselves. Similar observations were made later on isolated frog muscle by H. S. Gasser and Hill. Furthermore, as in the frog, additional energy expenditure is required to maintain muscle tension during a prolonged or slowly proceeding contraction; hence there is an optimum speed at which the mechanical 'efficiency' of a muscular movement attains a maximum value. This was verified by H. Lupton (*J. Physiol., Lond.* **57**, 68), both in elbow-flexing and in a 'stair-mounting' exercise in which he measured his extra oxygen uptake at various speeds of climbing.

A short note, with H. Lupton (55), describes the first experiments on 'oxygen consumption during running'. At high speeds, the athlete goes 'into debt', that is to say during the period of exercise oxygen intake is insufficient to prevent accumulation of lactic acid and running down of glycogen stores, and the deficit has to be made up by a large oxygen consumption during the subsequent rest period. The 'Douglas bag' method was used to measure the extra O_2 used. In a short period of severe exertion, a rapidly increasing 'oxygen debt' was incurred (a phrase coined by Hill and now in common usage), reaching in one subject 5.5 litres in 20 s; at low speeds of running, a steady state was reached with an overdraft of 2.5 litres. There was, however, 'no doubt that a champion runner in training could attain considerably higher values, especially if not subjected to the inconveniences of valves and bag'. The paper gives us some interesting vital statistics (presumably of A. V. himself): 'The subject is of athletic build, 11½ stone (73 kilos), fairly fit, 35 years of age, and used to running; he is not, however, and never has been, a first-class runner . . ..'

At about this time, A. V. recruited a young graduate in chemistry, C. N. H. (Hugh) Long, who later became a distinguished endocrinologist and one of the leading physiologists in the United States (*Biogr. Mem., U.S. N.A.S.* 1975, p. 265). His own description of his encounter with A. V. gives us a vivid picture of the Manchester atmosphere.

> 'One day in 1921, I was asked to see A. V. Hill, the newly appointed Professor of Physiology at the University. He told me that he was working on the physical and chemical changes underlying muscular contraction, and that the latter was associated with the breakdown of glycogen to lactic acid. He needed the assistance of a chemist to follow the changes both in animals and in the blood of humans who were exercising. I must say that my first reaction was not too enthusiastic, I had had but little experience in biology, and in those days the efforts of the so-called biochemists were not held in too high regard by many of their colleagues in pure chemistry . . . Nevertheless, as Professor Hill talked about the enormous possibilities for the understanding of living processes that the methods of chemistry and physics were able to offer, I began to be caught up in his enthusiasm and vision. I accepted the great opportunity he offered me and in due course wondered why I had not had the sense to see for myself the challenge and excitement . . . offered to young students of chemistry and physics . . ..
>
> 'When I began my work with Hill and his colleague Lupton, I soon began to suspect that their interest in me had not been entirely due to my extensive training in chemistry. I was at that time an enthusiastic player of football, field hockey, and cricket and this interest was soon put to practical use by my superiors for I found myself running up and down stairs, or round the professor's garden while at intervals healthy samples of blood were withdrawn from my arms. When I had recovered from my exertions I was asked to sit down and analyse these for lactic acid.'

The chief results of this work were published in 1924 in a series of joint papers by Hill, Long and Lupton.* The method consisted of measuring O_2 intake and CO_2 output during exercise and recovery periods, using a series of Douglas bags and analysing the expired air, and determining the amount of lactic acid which had 'spilled over' into the blood during severe exertion, and its final rate of removal. They found large transient changes in the 'respiratory quotient' (CO_2 expired/O_2 consumed) during the early recovery phase, first an increase well beyond unity, then a more prolonged drop below the final level of about 0.8. These phenomena are attributed to fluctuations in the acid/base balance brought about by the appearance and later the removal of lactic acid. Its accumulation in the muscles and subsequent diffusion into the blood stimulates the respiratory centre and leads to excessive elimination of CO_2; but once the lactic acid in the blood has reached its peak and been neutralized, the process becomes reversed, and the gradual removal of the lactate liberates alkali and causes a corresponding retention of CO_2, accompanied by a subnormal respiratory quotient. On this basis the authors used the measured 'CO_2 retention' during the later part of the recovery phase to calculate the amount of lactate which was being removed. At the same time, the O_2 consumption was used to calculate the amount of lactate that was oxidized. The ratio came to about 1 : 5, much the same as in isolated frog muscle. This striking result was confirmed by direct measurements of lactic acid elimination from the blood, again comparing it with the oxygen usage during the same period. There were important differences in the time course of oxidative recovery, depending on the degree of exertion: during moderate exercise, there was little 'overspill' of lactic acid into the bloodstream; most of it was apparently eliminated within 5 min inside previously activated muscles themselves. During severe exertion, lactic acid accumulated and overflowed into the blood, with the result that the recovery now took hours to complete, for the lactate had to diffuse back to the tissues before being restored to glycogen or oxidized, and the oxygen debt was now being settled by cells, most of which had not been involved in the exercise at all.

The concept of intensive muscular activity being carried out 'on credit', by running up an oxygen debt which could be paid off at leisure later on, was a new and exciting idea, and there was something very satisfying about the elegant way it all seemed to fit into the lactic acid cycle. It is hardly surprising that 10 years later, when creatine phosphate had appeared on the scene, some of Hill's interpretations of the oxidative recovery process were also questioned; thus Margaria, Edwards and Dill (*Am. J. Physiol.* **106**, 689) concluded that only in the most strenuous forms of exercise could the oxygen debt be related to the lactic acid cycle, and that during more moderate exertions an alternative 'alactic' mechanism comes into play and is used for oxidative restoration of phosphagen.

* In a postscript to papers (76), Hill and Long pay tribute to Hartley Lupton who had died, after a sudden illness, two months before the paper appeared.

Towards the end of A. V.'s Manchester period, he was joined by Wallace Fenn who published two important papers on the relation between mechanical work and total energy (work plus heat) liberation in isolated frog muscle. Fenn acknowledged the great help given by A. V. and his wife in not only offering him all the facilities of the laboratory, but letting him do some experiments in the cellar of the Hills' house at Altrincham which was apparently free from the electrical disturbances prevailing in the university laboratory. Fenn's main conclusions, which acquired great significance in later years, was that there is some internal 'feedback' in active muscle fibres whereby their total energy liberation is regulated by the mechanical conditions during the contraction process. When a muscle lifts a load in shortening, extra energy is liberated in proportion to the mechanical work done. When an active muscle is forcibly extended, the total energy output (that is heat production minus work applied to the muscle) is less than during isometric contraction. The results were very relevant to Hill's work and, as he pointed out in *Trails and trials* (224, p. 84), they should have deflected him from proposing internal 'viscosity' as a dominant factor in governing the energy liberation by active muscle. A. V. emphasized the importance of Fenn's observations in his Nobel Lecture in 1923, but he did not fully appreciate their significance until his own work, 15 years later, on the 'heat of shortening' and the relation between tension and energy production in active muscle.

10. University College London

In the autumn of 1923, several important events took place. E. H. Starling, who had held the Jodrell Chair of Physiology at University College London since 1899, became the first Foulerton Research Professor of the Royal Society, and A. V. Hill was appointed as his successor.* The Hill family moved to London and settled in a large and very pleasant Victorian house at Highgate,

* In his Inaugural Lecture at University College, with Starling in the chair, A. V. told his audience that a few years earlier he had asked Starling for advice 'whether he should venture to accept the Chair at Manchester or remain in the pleasant seclusion of Cambridge', especially as he was conscious of his profound ignorance of classical physiology. Starling's instant and reassuring advice was, 'My dear Hill, you don't know a word of physiology, but I think you ought to go there.' The medical students remembered this, and shortly afterwards when the Nobel Prize was announced, A. V. reports (213) that during an informal, though rather violent, celebration in which 'I was carried round the College on their shoulders, they finally took me to the top of the building where Starling was working. When Starling appeared, they loudly demanded, "Who says he doesn't know a word of physiology ?" to which Starling retorted, and insisted, "I did—he doesn't know a damned word". After which they let us go.'

Of course, it was Starling who had been principally responsible for attracting A. V. to University College. The following is an extract from a letter written by Starling to his married daughter, Muriel Patterson, in Australia (10 December 1922): 'I think I shall get A. V. Hill to succeed me—(now at Manchester) a tall vigorous personage—35 years old—who will be the most important person in the physiological world—and likes to be in the scrum. A good fighter! Foster [Sir Gregory Foster, Provost of U.C.L.] had heard about him—& asked me. I said "Yes, I think he is the right man. But of course he is not a medical man, he is not even a physiologist. He is a physicist and a mathematician". Poor old Foster, it was as if the bottom had dropped out of his Universe. He gasped "But he is a professor of physiology". I said "Oh yes—he will do very well as head of this Institute".'

adjoining Kenwood and Hampstead Heath. Their house in Bishopswood Road will be remembered by many of their younger friends and colleagues who enjoyed A. V.'s and Margaret Hill's hospitality. The diverse difficulties and worries which normally beset a move of this kind must have been happily dissolved by the news, in October 1923, that A. V. was awarded one half of the 1922 Nobel Prize in 'Physiology and Medicine', 'for his discovery relating to the production of heat in the muscle', the other half going to Otto Meyerhof 'for his discovery of the fixed relationship between the consumption of oxygen and the metabolism of lactic acid in the muscle'. This was the fourth time the prize had been given for a physiological discovery—the previous winners were Pavlov (1904), Barany (1914) and Krogh (1920)—and the first time a British and German research worker had been selected. If one reads the presentation and acceptance speeches, it is apparent that, quite apart from the scientific merit of the work which was very fully brought out by Professor Johannsson's address, the Committee was delighted to have the opportunity of dividing the prize between colleagues from former enemy countries. This seemed particularly apposite as there has been delays and difficulties in re-establishing full and amicable relations at the post-war International Congresses in Physiology. At Paris, in 1920, Meyerhof and other German scientists had been unable to attend, and consequently A. V. who had protested against such exclusion also refused to take part. At Edinburgh in 1923, the Congress was open to everybody, but with the military occupation of the Ruhr, political feelings on the Continent had been further aggravated, and many colleagues from France decided not to attend. The festivities in Stockholm presented therefore a happy contrast.

One of the first visitors to arrive in A. V.'s laboratory in London was Herbert Gasser. Their joint work led to a very influential paper on 'The dynamics of muscular contraction'. Several important findings emerged: isolated frog muscle showed the same inverse relation between velocity of shortening and contractile force (or work delivered during activity) as had been observed in voluntary movement of human arm muscles. Even more interesting, when a frog sartorius was stimulated repetitively and had developed its full isometric tetanus tension, a quick mechanical release (during continued stimulation)—allowing the muscle to shorten suddenly by a few millimetres—caused the tension to drop momentarily to zero and then to re-develop gradually, with a time course similar to that observed at the beginning. Gasser and Hill concluded that the ordinary development of isometric force does not provide an index of the basic change which occurs in active muscle, and that appearance of tension must be delayed behind the fundamental change which is responsible. This involves a sudden increase in rigidity and apparent viscosity. They showed that very soon after the stimulus, and long before the tension reached a plateau, the muscle fibres became very inextensible. Most of their observations could be interpreted in terms of a 'visco-elastic' model; this was later discarded by A. V. and indeed deplored by him as misleading (see also p. 112), but it had the merit of offering a simple and graphic analogy and for didactic purposes has been found useful for many years. The realization that the isometric contraction gives only a distorted picture of a more rapid primary response was new and has retained its value. It is still worth quoting the clear terms in which the 'visco-elastic theory' was originally introduced:

> 'It appears that on stimulation there is a sudden production of a much more rigid and viscous element in the muscle . . .. This element then tends to shrink, and so to extend other elements; but its own viscosity . . . prevent(s) this from happening immediately, and the external tension is developed only as the readjustment, under the influence of elastic-viscous forces, is completed. In a twitch the new state of the active elements passes off rapidly, the tension manifested externally rising . . . and falling more slowly than the fundamental internal mechanical change on which it depends.'

In October 1924 A. V. visited the United States where he gave the Herter Lectures at Johns Hopkins Medical School (78). This was the first of many transatlantic excursions, in the course of which he strengthened the very close scientific and personal contacts with his colleagues D. W. Bronk, W. O. Fenn, A. Forbes, H. S. Gasser, R. W. Gerard, L. J. Henderson and many other friends, and, last but not least, with the Officers of the Rockefeller Foundation which became, next to the Royal Society and the Medical Research Council, one of his most loyal and generous supporters.

During the first two years at University College, Hill and his colleagues went on exploring in greater detail the metabolic effects of muscular exercises in man, the relation between heat and mechanical force produced during contraction of frog muscle and, together with A. C. Downing, improving the design of their galvanometers. One notices at the end of one of the papers the first of very many acknowledgements of J. L. Parkinson's contribution. Parkinson had joined the London laboratory as A. V.'s personal assistant, helping to make experiments, to construct equipment and to look after the technical needs of visiting scientists. Parkinson soon showed the qualities of a top-class laboratory manager; he made it his job to provide the newcomers with the apparatus and technical help they required, and to protect A. V. against trivial and unnecessary disturbances. During the following 15 years and again in the post-war reconstruction period, J. L. Parkinson was an invaluable asset to A. V.'s laboratory, and he established a close and lasting friendship with many of the distinguished scientific visitors whose papers bear witness to the indispensable help they had received from him.

At the beginning of 1926 the Royal Society offered A. V. Hill a Research Professorship, the second Foulerton Chair, which he was only too happy to accept as it relieved him of heavy administrative, teaching and particularly examination duties which he felt were interfering with his research. He held the Foulerton Professorship until his official retirement at the end of 1951. He was succeeded in the University Chair by C. Lovatt Evans.

The Royal Society invited him to deliver the Croonian Lecture in 1926. The lecture presented under the title 'The laws of muscular motion' (88) gives a clear and up-to-date summary of the myothermic experiments and of the viscous-elastic properties of active muscle. The relation between shortening and work had been subjected to an improved analysis, with an ingenious new ergometer invented by his colleagues A. Levin and J. Wyman. Though A. V. continued to describe contractile activity in terms of viscous and elastic changes, the term 'viscosity' appeared now in inverted commas and was no longer taken in its strict physical sense. Even more interesting is A. V.'s general survey in his Croonian lecture of what he considered to be the most promising lines of experimental attack on the mechanism of muscular movement. 'There are three chief ways in which it may be studied: the chemical, the mechanical and the thermodynamic'. The omission of any reference to studies of fine structure was no accidental oversight; A. V. was in fact not very interested in that aspect. This is understandable, for the interpretations at the time of the significance of cross-striations in skeletal muscle and of the changes in microscopic appearance during activity had been very controversial and confusing, and in view of the fact that A. V. had not been able to find any great difference between the behaviour of striated human and frog and of smooth holothurian muscle (89), one can sympathize with his attitude of not taking discussions about the significance of striation patterns very seriously. With hindsight, we know that this was actually a severe limitation, and that quite unexpectedly some of the most significant advances in our understanding of the mechanism of muscle activity did originate some 20 years later from a study of ultrastructural changes in striated muscle with the electron microscope and X-ray diffraction.

However, the most notable event in A. V.'s career during that year 1926 was the discovery of heat production during the passage of nerve impulses, making up for his earlier failure (and that of many others from Helmholtz onwards). Stimulating an isolated frog nerve at 15 °C at a rate of 280 Hz for 1 s produced an immediate ('initial') heat deflexion equivalent to 7.6×10^{-6} cal g^{-1} and a total ('initial' plus 'delayed') heat of 6.9×10^{-5} cal g^{-1}. These quantities were superseded in subsequent studies, and considerably larger values were found for the immediate heat liberation by working with small diameter non-medullated nerve fibres and improving the time resolution. Thirty years later, Hill and his colleagues found that the initial heat production is diphasic, a relatively large phase of heat liberation being rapidly reversed and followed by heat absorption; the earlier experiments only disclosed the net effect which is about one-fifth in amplitude. The positive results in the 1926 paper were themselves the outcome of a whole series of technical improvements, more suitably designed thermopiles with hundreds of junctions (fine constantan wires with silver-plated segments), 'thermal amplification' of the galvanometer deflexion (the moving light spot falling on a radiation thermopile—this was later replaced by a photo-electric relay), better electrical insulation and better thermal stabilization of the equipment, finally a direct heating calibration, all of which made it possible to follow the recovery heat production which went on for 10 min after the stimulus and accounted for 90% of the total heat liberation. Although the quantities had to be revised later, Hill based some pertinent suggestions on his findings which have remained valid, particularly 'that the process of transmission (of a nerve impulse) does *not* involve the whole surface of the nerve fibre, but only a small proportion of it'.

At the Royal Society Anniversary Meeting in November 1926, A. V. was awarded a Royal Medal. The President, Sir Ernest Rutherford, referred to Hill's work on muscle and nerve which 'in the past seven years' he had accomplished 'with a success beyond expectation'. So altogether, with a Croonian Lecture, a Foulerton Professorship, a Royal Medal and the discovery of the nerve heat, this was not a bad year! It ended with a series of superb Christmas lectures and demonstrations given before a 'juvenile audience' at the Royal Institution and resulting in a book *Living machinery* which became a famous popular science classic.

Early in 1927, A. V. paid his second visit to U.S.A. He had been invited to spend several months at the Cornell University campus at Ithaca, as the George Fisher Baker Lecturer in Chemistry. He used the opportunity to conduct further experiments on athletes, some of which were published in a monograph on *Muscular movement in man* and also in two joint papers with K. Furusawa and J. L. Parkinson.

He uses a 'dimensional' argument to show that, regardless of size, 'similarly' constructed animals would all have the same maximum speed of body movement (the time taken by a twitch in corresponding muscles would increase with their linear dimensions), and that the limitation is imposed by the permissible inertial stress on bones, tendons and other mechanically supporting structures. He produces some simple equations for the acceleration and final velocity in 'sprinting' and in up-hill running. The predictions are based on the previously found inverse relation between speed and mechanical work, and on the assumption that in 'flat running' the work is done mainly in overcoming internal muscle 'viscosity' and only to a negligible extent external air resistance. The experimental tests were made by letting the sprinters carry a magnet and recording successive current pulses induced in a series of coils placed along the track and connected to a suitable galvanometer. The papers are entertaining and contain interesting calculations on the limits of athletic performance, though in his later comment, A. V. found the theory and its inherent oversimplifications rather deplorable.

11. Devonshire interludes

After returning to England, A. V. and his family went once again camping on the Devonshire moors, and this time decided to look around for a holiday home in the vicinity. A. V. had been fascinated by Dartmoor and its surrounding scenery ever since he had moved with his mother to Tiverton in 1900, and he had spent many holidays walking and cycling in the area. There were other attractions nearby: in the winter of 1925 he had worked in the Plymouth laboratory on Holothuria (the sea cucumber) muscles; he was on cordial terms with the staff and the Director, Dr E. J. Allen, and he retained a close connection with the Marine Biological Laboratory and its work for 50 years. In 1926, after returning from an International Physiological Congress in Stockholm, A. V.

and Starling spent the early autumn in the laboratory on Plymouth Hoe 'to learn some Zoology', and the idea of settling more firmly in Devonshire probably arose on that occasion. So, in August 1927 when the 'six Hills' explored the area around Cornwood and Ivybridge, they discovered and acquired 'Three Corners', a secluded cottage with a small field, which in A. V.'s words 'provided a fairyland for the family and many guests until 1939', and was 'the nearest to heaven I shall ever get' (*M. & R.*). It was, as far as I know, the only place about which he ever allowed himself to become sentimental!

12. The Physiological Society and the Boston Congress

During the following year, a long series of papers appeared in the *Proceedings of the Royal Society* (99–107). It marked an interesting change in A. V.'s choice of journal for his own publications. In recent years he had submitted most of his work to the *Journal of Physiology*. From 1927 onwards he sent his papers for several years to the Royal Society, although other contributions from his laboratory, by his pupils and younger collaborators, continued to be published in the *Journal of Physiology*. There were probably two reasons for this change; having been appointed to the Foulerton Professorship, it seemed appropriate that he should submit the reports of his work to the Society's journal. But what was perhaps more important, in 1926 he became one of the chief editors of the *Journal of Physiology* and would naturally have felt inhibited from taking up a great deal of space for what might appear to be 'self-edited' papers. The *Journal of Physiology*, incidentally, which had been owned and run by J. N. Langley until his death in 1925, was now managed by the Physiological Society and edited by E. D. Adrian, A. V. Hill, J. N. Leathes and C. S. Sherrington, with A. V. taking charge of the editorial correspondence. He had been a member of the Physiological Society since 1912; he served it in one function or another from 1921 to 1945, on its Committee until 1926, as Chief Editor until 1935, as Secretary from 1927 to 1933 and as Foreign Secretary from 1934 to 1945. He had also been a very active participant in the International Physiological Congresses, at Groningen in 1913, Edinburgh 1923 and Stockholm 1926, and now, in 1927–28, A. V. took on the task of organizing transportation across the Atlantic of several hundred European physiologists to the next congress held in Boston in 1929. He made arrangements with the U.S. Atlantic Transport Line to use the S.S. *Minnekahda*, an ex-troopship which had been converted after the war to a single-class passenger boat. It was a most successful journey which has been vividly described and illustrated by Y. Zotterman in W. O. Fenn's *History of the International Congresses* (Amer. Physiol. Soc. 1968). Judging from Professor Johannsson's speech at the farewell dinner party, A. V.'s efforts earned him the friendship and gratitude of many colleagues who previously had little contact with him. A. V. became now a member, and before long Secretary, of the International Physiological Committee and was actively involved in the several congresses that followed, in Rome, Moscow/Leningrad and Zürich.

13. Thermal puzzles, artefacts and new discoveries

To return to the work published in 1928, this was a curious interlude in that it was productive only indirectly and in an unexpected way. With the discovery of creatine phosphate and of a 'phosphagen cycle' during muscle activity, and under the impact of Embden's critical, though not decisive attacks, doubt had been cast on the principal role of lactic acid in contraction, and on its exact position in the energy balance sheet. Hill decided to resume the myothermic experiments with improved equipment, but things started to go wrong and some of the new results and conclusions published in 1928–29 were beset with experimental errors. The most important outcome of this series of papers was connected with a peculiar thermal artefact which A. V. came to understand only some 20 months later. Once he had done so, he managed to turn it into a very useful and ingenious micromethod for measuring vapour pressures.

In order to follow aerobic and anaerobic heat production over long periods, the stability of the recording system was improved, new thermopiles were constructed, better thermostats designed and a better method for calibration was introduced (99). With this advanced technique, A. V. made the very puzzling observation that when muscles had been stimulated in the absence of oxygen, their subsequent 'resting heat-rate' (that is, the final level of heat production attained at the end of the usual recovery period) was enhanced and remained high for an almost indefinite period. This only occurred under anaerobic conditions; the effect was substantial and could not be attributed to continued lactic acid formation, nor could A. V. at that stage discover any experimental error to account for the phenomenon. He produced an amusing commentary (126 and 213, p. 148) on the various futile hypotheses and attempts to make sense of these observations. The fog was finally dispersed in July 1929,* when it had suddenly dawned on him that the effect must have been due to condensation of moisture on the muscle surface. The anaerobically stimulated muscle was left with the accumulated breakdown products of glycogen, which raised its osmolarity and reduced its vapour pressure relative to the Ringer solution on the walls and in the bottom of the moist chamber. This osmotic imbalance (though amounting to less than 1 part in 1000) gave rise to steady slow condensation of water vapour and thus to the observed rise of temperature which persisted for hours after the end of the stimulation period. A. V. and his colleagues, particularly Dr E. J. Baldes, went ahead to exploit this 'useful artefact' and, by constructing suitable differential thermopiles, and later very small pairs of thermocouples, turned it into a differential micromethod of high sensitivity, for determining osmotic and vapour pressure of minute quantities of fluid (see also *Trails and trials* (224), pp. 108–112 for numerous applications of the method).

In 1928, however, before the discovery of its real nature, the puzzle created by the anaerobic experiments did not help to clarify the rôle of lactic acid

* A. V.'s explanation of the 'mystery' was sent to the Royal Society's *Proceedings* on 23 July as a postscript to one of his papers. It was published 5 weeks later, on 2 September, a remarkable speed even for those days.

against creatine phosphate, and the arguments deployed in the resulting series of papers (100–107) must have appeared unconvincing and confusing at the time, nor does A. V. recommend them to the reader in his later comments (*Trails and trials* (224), pp. 51–53). Many of the observations were superseded by A. V.'s work in 1937–38 (161–164) in which he pointed out experimental errors arising from the use of an 'unprotected' thermopile which must have vitiated some of the 1928 results, and errors in interpretation caused by a failure to realize that appreciable internal shortening occurs and work is produced even in an 'isometric' contraction.

A paper of an altogether different kind was the next one, on 'The diffusion of oxygen and lactic acid through tissues' (updated in *Trails and trials*, (224)). This was an important piece of applied mathematics, providing solutions of the diffusion equations in several cases of particular physiological interest and illustrating the examples with useful graphs and tables. The work has been of considerable practical help to many others concerned with the problems of diffusion of metabolites in various tissues, of different shapes and sizes. Pointing out the general proportionality between kt ('diffusion times') and x^2 (second power of distance), A. V. draws attention to interesting biological consequences, in cases of microscopic as well as large-scale dimensions. The main part of the paper was written during a holiday at 'Three Corners'. Handling the mathematics was made easier by A. V.'s early experience with similar equations which had led to the regretted 1910 paper on the theory of electric excitation.

A. V.'s concern with diffusion problems is evident from several papers published by his younger colleagues in the department at that period (e.g. G. Stella on phosphate; W. Dulière and H. V. Horton on potassium; P. Eggleton on creatine and urea). It also produced an interesting study which he did with P. S. Kupalov, shortly before setting off on the *Minnekahda* journey. This deals with the prevention of fatigue of isolated anoxic frog muscle by keeping it in an O_2-free Ringer bath (instead of a moist atmosphere of N_2), allowing lactic acid to diffuse away rather than accumulate in the tissue. In the bath, the muscle continued to respond to stimuli three times longer, apparently until its carbohydrate store had been depleted; and it would go on longer if glucose was added to the solution. In oxygenated Ringer's fluid, the muscle performed better still; more than 10 000 twitches could be evoked, equivalent (per gram) to the work done in 'a nine-mile walk by a man'. What seems a little surprising, though, is that no mention is made in this paper of the effect of potassium leakage, which was being worked on by Hill's colleagues at the same time, and which could have been partly responsible for the 'fatigue' ascribed to lactic acid.

The heat production in nerve had not been forgotten, as is clear from an important paper, also completed before A. V.'s departure for the Boston Congress. With Downing's help, the nerve thermopile was improved, to double the sensitivity, reduce heat losses and give better stability in following the recovery heat production. The experiments were made, for the first time, on isolated nerve bundles from the spider crab, composed of a large number of small, non-myelinated fibres. Previous observations by Levin and Furusawa had shown that in these nerves a period of electric impulse activity is followed by very slow recovery of the resting potential, and it appeared that oxidative metabolism was required to 're-charge the membrane battery' which provides the normal action current. Hill found that these non-medullated nerves, available from marine animals at the Plymouth laboratory, are much more suitable objects for heat measurements. The total heat, per gram tissue, produced by one second maximal stimulation was 33 times greater than in the frog's medullated nerve; the earlier investigators could have saved themselves a lot of time and trouble, had they thought of using crustacean rather than frog nerve for their experiments. There were, as in muscle, two phases of heat production, an 'initial' and a 'recovery' heat. But the relative proportions and time courses were quite different: in the crab nerve, the 'initial heat' (15 °C) was only about 2% (later revised to about 10%, see p. 130) of the 'total', and the 'recovery' heat production lasted for more than 30 min.

It looked at the time as though the conduction of the nerve impulse (including the immediate restoration of electric excitability) required no special chemical breakdown, such as lactic acid formation. Pulses of action currents are provided, in large numbers, by brief discharges of an 'accumulator' whose potential energy is stored in the form of ionic concentration differences across the cell membrane. 'In recovery, however, the ions have to be separated again, the initial concentration differences to be restored' (113). This is done at the expense of oxidative metabolism, with relatively large quantities of waste heat appearing as a by-product. Although A. V. re-emphasized here the smallness of the initial heat and expressed doubts about any 'special chemical reaction' being associated with the initiation and conduction of the impulses, he remained properly sceptical about such doubts, as he indicated a little later in his very readable, and influential, lecture on 'Chemical wave transmission in nerve' (128).

When the mystery of the thermo-osmotic 'artefact' was clarified, it led not only to the development of a new technique, but to an immediate attack on the perennial problem of 'free' against 'bound' water in muscle and other tissues. In collaboration with Kupalov, A. V. wrote two important papers on the state of water in muscle and blood. He emphasizes at the outset that a great deal of confusion and unnecessary controversy can arise because different authors use divergent definitions of the term 'bound' water as well as discrepant methods of determining it. For example, the fact that some of the water in a muscle cell, or for that matter in an agar gel, does not freeze at -20 °C is no indication that the same water would fail to act as a solvent above the normal freezing point. Its ability to dissolve added substrates with a normal depression of vapour pressure is Hill's definition of 'free' water. With Kupalov he proceeded to use his thermo-electric method to determine the osmolarity of frog's blood, with which the muscle is normally in osmotic equilibrium, and found that it corresponds to a 0.725% NaCl solution. They then made up a list of the known soluble constituents of muscle and concluded that it exactly balances the osmolarity of the blood, provided all constituents are 'freely' dissolved in the tissue's total water content. However, when the muscle was stimulated anaerobically to complete fatigue, a quantitative study of the 'thermo-osmotic change' revealed a large discrepancy. The osmolarity increased by as much as 0.35% NaCl. This was far too much to be accounted for by the formation of lactate from glycogen, and even after allowing for phosphagen and ATP breakdown, there remained an appreciable imbalance. Hill concluded that yet another unidentified breakdown must be going on, and 'it is indeed unlikely that, after the striking progress of the last few years, we should at this particular moment have discovered *all* the reactions involved in muscular activity' (117). A lot of water had flowed under the bridge since 1913 (14) when it seemed that 'nothing but lactic acid and CO_2' are produced by excitation of muscle. An interesting final suggestion by A. V. and Kupalov is that osmotic swelling of muscle fibres may occur during severe and prolonged exercise and be responsible for muscle stiffness.

With the use of thermal technique for a direct determination of the 'free' water fraction, A. V.'s procedure was to measure the change in vapour pressure, when a weighed amount of a hypertonic salt solution was added and allowed to equilibrate with a weighed amount of muscle. The resulting 'free' water fraction (defined as the weight of H_2O in 1 g of tissue which can dissolve added substances with the normal depression of vapour pressure) came to 0.77, which is only 4–5% less than the 'total' water fraction (0.8–0.81). The fact that the swelling or shrinking of isolated muscles in hypo- or hypertonic solutions gave results which apparently diverged from Hill's conclusion was attributed to a gradual deterioration of the cell membranes in the course of a prolonged experiment. While Hill's work left little room for 'bound' water in muscle, it is not surprising that a quantity which depends so much on definition and on method of measurement is still not free from controversy.

In October 1930, A. V. went to Philadelphia at the invitation of D. W. Bronk to give the Johnson Foundation Lectures, published under the title *Adventures in biophysics* (a theme on which variations were played subsequently by other illustrious scientists). In these lectures he describes very vividly the discovery of the vapour pressure technique and its scientific repercussions, and his latest views on nerve, muscle and the physical chemistry of blood. The book makes pleasant reading; the purpose of the lectures was to get away from the customary dry style of scientific reporting:

> 'In our journals we try, so far as we can, to present a concise and logical account of our alleged discoveries. The real reasons why we did the things we did, the delays and imperfections and perplexities which beset us, the misery of continual failure, the joy of occasional success, the faith that with patience and persistence we should find the unknown something we were sure was there—all these are unfitting in a scientific periodical, yet somewhere a hint at least of them should be recorded.'

14. 'The revolution in muscle physiology'. Return to studies on nerve, and various diversions

By now, the final act in the lactic acid drama had been performed, and the next papers were written under the impact of E. Lundgaard's discovery in 1930, that muscles treated with iodo-acetate can contract without forming lactic acid. This was followed by confirmation in Meyerhof's laboratory of Embden's earlier claim that some of the lactic acid is produced after the end of the contraction. The 'initial' heat was now interpreted as arising from at least three reactions, namely hydrolysis of creatine phosphate plus formation and neutralization of lactic acid, while the old puzzle of the 'anaerobic delayed' heat was now ascribed to the net thermal effect of delayed lactate formation coupled with endothermic rephosphorylation of creatine. It seemed, however, that the old days of drawing up a satisfactory thermal balance sheet, in terms of known chemical reactions, had gone for good.

This whole period of A. V.'s muscle studies ended with an interesting review on 'The revolution in muscle physiology', in which he traced the rise of the phosphagen story and the gradual displacement of lactic acid from its supreme position. For the next five years, A. V. Hill added no further personal contribution to the subject of muscle energetics, though a number of important papers appeared from younger members of his laboratory, notably from T. P. Feng who had joined A. V. in 1930 and made a number of major advances in the thermal studies of muscle and nerve. A. V. himself only returned to the muscle work in 1937, with a much improved technique and a refreshingly new approach, having devoted himself entirely to the problems of nerve activity during the interlude.

By the end of 1931, he and Downing had made further modifications in their nerve thermopile and introduced photo-electric amplification of the galvanometer deflexion. Renewed experiments on frog's nerve gave revised values for the different phases of heat production. In May 1932 A. V. Hill discussed his results in the Liversidge Lecture at Cambridge; this was published as a monograph on *Chemical wave transmission in nerve*, a remarkable little book full of stimulating ideas and speculations about the physical chemistry of the nerve impulse. It had a profound influence on the younger generation of neurophysiologists. A. V. considered the significance of the very small, but clearly positive 'initial' heat associated with the impulse. It is instructive to follow his arguments, first for and then against, the explanation of the thermal response as being due to the electric discharge of the membrane capacity. Some of his calculations, concerning the thickness, electric field and capacity of the axon membrane come quite close to values later established by direct measurement. He rejects the 'condenser discharge' hypothesis on the grounds that the net thermal effect should be zero at the end of the impulse when the membrane potential has been restored. Some 25 years later, A. V. and his co-workers had improved the technique sufficiently to show the almost equal positive and negative phases of heat production which he had predicted, but this does not affect the validity of his argument about the net heat, which was all he could observe in 1932.

In his Liversidge Lecture, A. V. shows a renewed interest in the laws of electric nerve excitation. His approach is now rather different from that used in the 'Nernst-type' theory of 1910. He adopts the view (originally proposed by Bernstein) that excitation is a sudden increase in ion permeability of the membrane when its resting potential has been reduced ('depolarized') by a critical 'threshold' amount. The resting potential is regarded, as in Bernstein's theory, as a diffusion potential across a potassium-selective membrane. Excitation makes the membrane permeable to other ions, possibly—A. V. suggests—to lactate. Electrically the resting membrane is equivalent to a charged condenser, and excitation to a sudden lowering of its 'insulation resistance'. The initial heat is the sign of an 'irreversible' process associated with the permeability change; the very much larger and later recovery heat has to do with chemical restoration of ionic concentration differences.

One can see that there is some connection between these thoughts and the work on 'electric excitation and accommodation' which Hill took up during the next few years (see papers 157–160). It is however, surprising that after the inspired and far-seeing physico-chemical speculations in his *Chemical wave transmission* he reverted to a rather formal, albeit successful and accurate, description of stimulation kinetics. It may have been the opportunity of making measurements of extraordinary precision and of fitting them elegantly with the simplest theoretical assumptions, that attracted him away from the more difficult problems of the underlying physico-chemical mechanism.

By now, however, other serious distractions appeared on the scene. In January 1933, Hitler took over in Germany, and very soon many scientists and public servants were dismissed from their posts on racial or political grounds. Others were forced to leave because they could not reconcile themselves to the degradation of standards of truth and decency which pervaded the academic atmosphere. To help refugee scientists, the Academic Assistance Council was formed and housed at the Royal Society in London, with Sir William Beveridge as the initiator and A. V. Hill one of its chief protagonists.

After the end of the 1914–18 war, A. V. had been foremost in advocating reconciliation, to bury feelings of national animosity and to welcome the return of German colleagues to scientific meetings. Now, however, he lost no time in attacking the new masters of Germany and their scientific henchmen. In his Thomas Huxley Memorial Lecture on 'The international status and obligation of science', published in *Nature* in December 1933 (also 213, p. 205), he poured scorn and derision on the philosophy and actions of the Nazi regime, and there is no doubt that A. V. could pursue his attacks with the same vigour and precision as his scientific arguments. He had previously demonstrated this in his running fight against deliberate distortion by 'anti-vivisectionist' and other 'anti-scientific' propaganda (213, p. 105, and *M. & R.*); now he was intervening, not just against a pseudoscientific doctrine, but on behalf of colleagues who had been unfairly treated and driven from their places of work.

That his attack was well aimed, became evident in an ensuing correspondence in *Nature* between Professor Johannes Stark and A. V. Hill. Stark was a well known physicist and Nobel Laureate (1919). While he had ceased to be active scientifically, he had been a strong supporter of the Nazi party for many years. In 1933, Friedrich Paschen, a good friend of A. V. since his stay in Tübingen in 1911 and a person of liberal views, was dismissed from the important position as Head of the Physikalisch-Technische Reichsanstalt (previous holders had been Helmholtz and Nernst), and Stark was put in his place, and became some kind of scientific 'Gauleiter' in Nazi Germany. When A. V. denounced the Hitler regime and its persecution of Jewish and 'dissident' scientists, Stark promptly took him to task and stated, in letters to *Nature*, that there was no factual basis for A. V.'s critical remarks, that the Nazi Government had been obliged to protect iteslf against the influence of disloyal persons and was only taking lawful actions as any respectable government would do in similar circumstances. A. V. Hill terminated the correspondence* with a brief note saying that gifts of money had been received in response to his appeal for assistance to colleagues who had been driven out of Germany. He added that he was uncertain whether the donations were the result of his own eloquence, or rather of Professor Stark's arguments, to whom he felt some thanks were due on this account. It was characteristic of A. V. to dismiss even the most vicious absurdities with a humorous touch: 'Laughter', he said, 'is the best detergent for nonsense.' I was at that time (summer of 1934) a medical student in Leipzig, about to take my finals and anxiously making plans to escape from a hostile environment. Hill's Thomas Huxley lecture and the correspondence in *Nature* —it was still possible to obtain it in unexpurgated form—made a tremendous impression on me. It gave me the first glimpse of A. V.'s personality, and I found it so attractive that I made every effort to go and work with him as soon as I could.

A. V. Hill's connection with the Academic Assistance Council and with its successor, the Society for the Protection of Science and Learning, continued long beyond the end of the 1939–45 war. He became its Chairman in 1946 and President in 1963, and there were several great occasions, the last one on his ninetieth birthday, when friends and colleagues, who remembered with gratitude his intervention on their behalf, joined in celebrating the event and sending him their messages of affection.

Meanwhile, in collaboration with T. P. Feng and L. Bugnard, A. V. went on with the neurothermal experiments, pursuing them with continuously improving recording techniques (133–135, 148). This work came to a halt in 1934, and A. V.'s interests gradually shifted to the field of nerve excitation and the efficacy of various forms of electric stimulation. Together with Bugnard, he

* There was another curious sequel. Professor Stark wrote to Lord Rutherford asking him to stop A. V. making dangerous statements. Evidently Stark regarded Rutherford as his British equivalent endowed with similar authoritarian powers! He probably did not realize that Rutherford was one of the signatories of the original appeal by the Academic Assistance Council and became its president.

published a series of papers showing that brief condenser discharges repeated at very high frequency had an 'inhibitory' effect, which was due to a lengthening of the refractory period by 'ineffective' depolarizing stimuli applied immediately after the initiation of an impulse. A. V. then developed a highly successful theory of 'excitation and accommodation' which was capable of coordinating a vast range of observations and putting them on an easily calculable basis. The fundamental assumptions were very simple: an electric current causes excitation if it displaces the membrane potential (in the depolarizing direction) by a critical amount ('threshold'); this is opposed by two processes of different 'relaxation times': (a) the potential change itself tends to decay with a brief time constant (k), (b) the 'threshold' rises slowly (time constant λ) so that the effect of a steady potential change maintained by a constant current is gradually neutralized. Although these were oversimplifying assumptions, they were sufficient to give an excellent quantitative description of a great variety of stimulation phenomena, they fitted most of the classical strength–duration curves obtained with constant current pulses and condenser discharges, the characteristic relation between intensity and frequency of sinusoidal alternating currents (with an optimum frequency whose value is determined by the two relaxation times), the reduced effect of slowly rising currents etc. Hill's theory was not the only one of its kind, nor did it explain the physico-chemical mechanism of excitation; but its great success in coordinating all kinds of stimulation data on very simple premises probably helped to put an end to half a century of similar, but less successful attempts. Having been personally involved in the experimental tests, I can say that I found the work very attractive and indeed fascinating for two quite different reasons. In the first place, it enabled one to make reproducible measurements of quite extraordinary accuracy with simple equipment. Secondly, although the verification of the theoretical equations was not, by itself, very fruitful, a number of discrepancies from the predictions of the simple theory gradually emerged which did have important consequences, for they led to the recognition of the 'non-linear' characteristic of the nerve membrane, and of the occurrence of a regenerative voltage change even in the sub-threshold range of membrane potentials ('local response'), which in turn provided a clue to the mechanism whereby an impulse is initiated.

I have a vivid recollection of that period, early in 1935, when I first met A. V. Hill. The welcome I received in his laboratory was probably similar to that experienced by many others who came to work with him, whether they were already well known and distinguished or—like myself—scientific freshmen with no credentials worth mentioning. I had, in fact, a recommendation from my former Professor of Physiology, M. Gildemeister, but little else. I remember climbing a narrow spiral staircase to the very top of the Physiology Department in Gower Street, and there I found A. V. discussing an experiment with D. Y. Solandt. I knew about A. V.'s reputation as a scientist and had been impressed by his outspoken comments on the Nazi regime; now, I was struck by his handsome, somewhat military appearance, very tall and youthful looking, with contrasting grey hair which he had acquired many years earlier. I was equally impressed by the friendly way in which he greeted me, interrupting his discussions to take me into his tiny office. There he told me after a short bilingual conversation that he was going to take me on 'as an experiment'. He then took me around the laboratory, introduced me to his colleagues, and showed me some special items on display, which had been imported from Germany. Among them was a little toy figure of Hitler, with a movable saluting arm, mounted on a Plasticine pedestal stuck against the wall. This was to make people like me 'feel at home', though I later heard him explain to a more official type of visitor from Germany that he kept the miniature statue in his laboratory as a sign of gratitude for the scientific workers Hitler had sent him. In successive years the number of these symbols gradually increased, and they caused varying degrees of amusement and occasionally embarrassment to casual visitors. For a young stranger like myself to be received in Hill's laboratory like a member of the family was a marvellous change. Coming from an academic environment in which the general attitude of most of my seniors as well as contemporaries had been cool and reserved, if not one of outright hostility, the contrast was almost unbelievable.

Apart from looking after his laboratory, studying the laws of nerve excitation and finding employment for the displaced scholars from Germany, further responsibilities were piling up and making increasing demands on A. V.'s carefully organized timetable. He had become Secretary of the International Union of Physiologists and was preparing to attend the 15th Congress in Leningrad and Moscow, in August 1935. After serving on the Council of the Royal Society from 1932 to 1934, he was appointed its Biological Secretary in November 1935, an office which he held for 10 years followed by a further year as Foreign Secretary. To accept this considerable task, he decided to relinquish the editorship of the *Journal of Physiology*.

15. The Tizard Committee

But the most important new commitment was in joining an Air Ministry Committee, together with P. M. S. Blackett and with H. Tizard in the chair, 'to consider how far recent advances in scientific and technical knowledge can be used to strengthen the present methods of defence against hostile aircraft' (quoted from Sir Bernard Lovell, *Biogr. Mem. R. Soc.* vol. 21, p. 50). There are several published accounts concerning the influence of the Tizard Committee (its full title was Committee for the Scientific Survey of Air Defence) and of A. V. Hill's part in setting it up.* Its principal rôle was in initiating a new system of aircraft detection and location by reflexion of radio pulses (radar) and developing its operational capability before the outbreak of war. In October 1934, the Director of Scientific Research at the Air Ministry, H. E. Wimperis, had been in touch with A. V. Hill and consulted him on the possibility of scientific countermeasures against enemy air attack. R. W. Clark describes it as follows:

* See Sir Charles Snow, *Science and government* (1961); R. W. Clark, *Tizard* (1965); R. V. Jones, *Biogr. Mem. R. Soc.* vol. 7, p. 331 *seq.*; Sir Bernard Lovell, *loc. cit.*

> 'Wimperis wrote to A. V. Hill of University College, proposing that they should meet at the Athenaeum. Hill was a physiologist with a long record of pure research, but during the First World War he had also, as Director of the Anti-aircraft Experimental Section, Munitions Inventions Department, helped to devise the rudiments of what was later called Operational Research. He had a facility, as had Tizard, for perceiving what scientific principle might best be utilized by the Services. And he had a reputation for straight-speaking as great as Tizard's own.'

As a result of this discussion, Wimperis approached the Secretary of State for Air, Lord Londonderry, and suggested the formation of the Committee of three (Tizard, A. V. and Blackett) with Wimperis and his assistant A. P. Rowe representing the Air Ministry. The Committee had its first meeting on 28 January 1935. By that time, according to Clark (1965, *loc. cit.*, see also Jones, *loc. cit.*), Wimperis had already been corresponding with R. A. Watson Watt at the National Physical Laboratory, who hinted that it might be feasible to detect and locate aircraft by reflected radio waves. The Committee decided to give it a trial which happened at the end of February. This early investigation in 1935 was the start of the development of radar with its enormous military and technical consequences. The further history of the Tizard Committee had its ups and downs; it was beset with the much publicized intervention by Churchill's powerful adviser, Professor F. A. Lindemann (Lord Cherwell), the friction and disputes that developed between him and the others followed by Hill's and Blackett's resignation in July 1936, and the reconstitution of the same Committee (with the addition of E. V. Appleton and omission of Lindemann) under the new Secretary of State, Lord Swinton, in October.* The Committee examined many other problems and projects, but continued to ensure that the highest priority was given to the development of the coastal radar chain in readiness for the war. After 1939 the Committee lost its influence; it was finally dissolved in 1940 when its members found themselves employed on other war-time missions.

* This unfortunate episode has been fully described by R. W. Clark (1965, *loc. cit.* chap. 6) who has published Hill's comments and his letter of resignation to the Secretary of State, dated 15 July 1936. The trouble was not just a disagreement on certain measures which Lindemann advocated, but that Lindemann regarded his ideas as of overriding national importance and could see no reason for sticking to what other members of the Committee considered to be the normal rules of the game. He had explained to Tizard that he would use every means at his disposal 'to accelerate progress'. He did this in a way which induced A. V. not simply to resign, but to write to Lord Swinton that 'instead of being frank and open with his colleagues and the Chairman, [Lindemann] went behind their backs and adopted methods of pushing his own opinions which—apart from anything else—would make further cooperation with him very difficult'. The outcome is well known: the Tizard Committee was quickly re-established without Lindemann and retained great influence until 1939, but then the pendulum swung the other way, and Lindemann now acquired the dominant rôle as Churchill's personal adviser.

16. Back to muscle

After the completion of his papers on the 'laws' of electric excitation and accommodation in nerve, there was a short gap in A. V.'s research activities. It would have seemed only natural if the years 1936–37 had marked a permanent transition to administrative duties at the Royal Society, and to his concern with anti-aircraft problems, with the defence of the country, and with the deteriorating international situation and the plight of refugees. While all this continued to occupy him and absorbed an increasing amount of his time, the year 1937 saw a remarkable revival of his interest in muscle energetics, resulting first in greatly improved methods of myothermic measurements and analysis, and the year after, in the publication of a paper on 'The heat of shortening and the dynamic constants of muscle' which represents one of his most important contributions to the subject. With A. C. Downing's help, very thin thermopiles of small heat capacity were built, giving a much better time resolution than the older instruments and permitting a simpler and less time-consuming analysis of the records. But more important, a source of error was discovered which must, to some extent, have affected all earlier experiments in which a muscle was allowed to shorten on a thermopile. This arose because the precautions previously taken had not been sufficient to avoid temperature gradients along the muscle, which would give spurious deflexions when a warmer part of the muscle moved on to the thermopile during contraction. 'It had not been realized that the heat production of the muscle itself, either the resting heat, or the recovery heat and the undissipated remainder of the initial heat of previous contractions, might make parts of the muscle not lying on the thermopile appreciably warmer than parts lying on it.' The matter was investigated with a thermopile divided into two segments, so that during shortening only one of the segments would come into contact with a portion of the tissue that had not been on the thermopile while the muscle was fully extended. The tests showed that thermal measurements from this segment were faulty. By using only the other, 'protected' portion for experimental measurements, this error was eliminated.

In the subsequent paper the recording system was further improved by using two galvanometers, with photo-electric amplification of the primary deflexion and sufficient negative feedback from the photocell to obtain the required speed and satisfactory baseline stability. The experiment consisted in measuring the rate of heat production and of mechanical work when a stimulated muscle was allowed to shorten against various loads, and comparing this with the energy liberated during an isometric tetanus. The observations were made at 0 °C on pairs of frog sartorius muscles. Hill confirmed that, during a maintained tetanus, extra energy is liberated when the muscle shortens. He found some very simple and intriguing quantitative relations: (i) Extra heat is produced, in proportion to the total change of length. This is called the 'heat of shortening' $H = ax$ (x being the amount of shortening and a a constant). (ii) Over a limited range the muscle lifts a given load P at constant speed v ($v = 0$, when $P = P_0$, this being the isometric tetanus tension). Hence, the *rate* of extra energy liberation (mechanical work plus heat) during active shortening is $v(P+a)$. (iii) The value of this total energy production was found to be directly proportional to (P_0-P), i.e. to the difference between actual and isometric force. In other words, $v(P+a) = b(P_0-P)$, where b is a velocity constant for the particular muscle. This is also the 'characteristic equation' which relates the speed of isotonic shortening of active muscle (v) to the load, or force, P, to which the active muscle is subjected.

Thus, the surprising outcome of the experiments was that the value of a (the 'shortening heat constant') could be determined directly from the mechanical force–velocity relation, without any thermal measurements at all. In Hill's interpretation, the meaning of the 'characteristic equation' was that the power output of active muscle was in some way governed by the longitudinal force acting on the contractile elements; the greater the force, the lower the rate of energy liberation, hence the lower the speed of shortening. The old 'viscosity' model was abandoned and superseded by the new concept which had, in fact, been anticipated by W. O. Fenn in 1922. If one assumes that the contractile part of the muscle, which obeys the characteristic equation, is normally in series with a passive elastic portion, then the gradual development of isometric tension (and its slow redevelopment after a sudden release) is a direct consequence of the 'internal shortening' which must take place in extending the elastic component, at first at relatively high speed and low tension, the speed gradually falling to zero as the tension P approaches P_0. From the isotonic measurements and an additional determination of the elastic compliance, Hill was able to calculate the correct shape of the isometric tension curve. A thorough re-examination of older experimental results showed that most of the earlier work on muscular dynamics could be explained, or at least satisfactorily coordinated by the new formulation, and it appeared that the characteristic relation with its parameters a and b was going to be of fundamental importance for any theory of muscle contraction.

Since then the subject has developed in a different direction, and with the emergence of the sliding-filament theory the main interest has shifted, away from the thermodynamic approach to the molecular mechanism of contraction. Hill's force–velocity relation, and his concept of a quickly established active state preceding the development of isometric tension, have retained their empirical usefulness, and the data can be accommodated in kinetic models built on the sliding filament theory (A. F. Huxley, 1974, *J. Physiol., Lond.* **243**, 1). However, the precise significance of the shortening heat is still uncertain, and when Hill re-examined it in 1963 (219), he found that the relation between heat and the amount of shortening departed from the simple linearity which had been the basis of the 'characteristic equation' of 1938. The equation could be modified to fit the new data, but of course it lost its original attractive simplicity.

The 1938 paper was followed by the Guthrie Lecture to the Physical Society (164) and by three short publications in *Proceedings B*, in which the new relationships were applied to a study of the mechanical efficiency of isolated frog muscle and, finally, to obtain an estimate of the dynamic constants (a and b) in human muscle. These were the last experiments A. V. made, 'in a shed during the early days of the "phoney war",' before the second major interruption of his physiological research.

17. The 1939–45 War

The Central Register

Soon after the outbreak of hostilities, University College was evacuated, Hill's laboratory closed and the staff dispersed to different wartime assignments. But already the year before, Hill and A. C. (Jack) Egerton, who had joined him as Physical Secretary of the Royal Society, had taken steps in consultation with the Ministry of Labour to ensure 'that scientific and technical manpower was properly employed in the war that loomed ahead' and to avoid a repetition of their experiences in 1914, when 'human scientific and technical resources instead of being husbanded . . . had at first been squandered and neglected' (*M. & R.*, see Appendix I). A minute of the Council meeting on 12 January 1939 records:

> 'The Secretaries reported that they had discussed with representatives of the Ministry of Labour details of proposed arrangements by which the Royal Society would approach the other scientific societies with a view (a) to completing the register of scientific persons available in the event of a national emergency, (b) to ensuring the more effective utilization of scientific personnel and of existing scientific organizations.'

A. V. and Egerton thus became responsible for preparing the Central Register of Scientific and Technical Personnel, a heavy and very important task which they effectively completed during the summer of 1939. When Dr J. B. Conant, the President of Harvard, came to England on a scientific mission in 1941, he reported on his return:

> 'It seems clear that the British were wise beyond measure in establishing a list of reserved occupations, carrying through their scheme of enrolment of students under Joint Recruiting Boards, and establishing the Central Register. If these steps had not been taken, many physicists, engineers and chemists desperately needed in the war effort might to-day be dispersed throughout the armed forces and their talents wasted' (*M. & R.*, p. 332).

During the war, the Scientific Register was eventually turned over to the Ministry of Labour who were assisted by two members of the Royal Society's staff. To operate the scheme effectively, it required of course a certain amount of 'form-filling' on the part of individual scientists. Most of them were helpful and gladly cooperated, but there were exceptions as is illustrated by the following correspondence in *The Times* (dated 23 May 1941).

'Sir,

I have been in Government service for 30 years: I am a Knight of one Order and Companion of another: my last salary in Government service was about £5,000 a year; my history is recorded in most books of reference. Though I have no greed for remuneration, I thought I ought to offer my services to the Government. I gave the Central Register of the Ministry of Labour and National Service a full account of my qualifications. After a considerable delay I have been asked in a letter measuring 9 in. × 7 in. to fill in two forms, each measuring 8 in. × 5 in. The request is contained in an envelope $8\frac{1}{2}$ in. × 5 in., and an envelope $8\frac{1}{2}$ in. × $5\frac{1}{2}$ in. is enclosed for reply. The form is singularly ill-adapted for my case or for anyone who is not expert in writing the Lord's Prayer on a threepenny bit, and it asks for no information which I have not already given. It is sent in order that "particulars of my qualifications may be available in a standardized form".

'All this is very reassuring. Clearly there can be no scarcity of paper and no shortage of man-power. The Central Register are amassing the most magnificent collection of "standardized forms": but they must be careful lest they should be beaten by the Government Department which asked me to state on a standardized form what were the birthdays of the dozen chickens that I keep.

Yours faithfully,

Ignotus.

A. V. records,

'This was "asking for it", and I replied as follows next day:

'Sir,

Unlike Ignotus, writing in *The Times* of to-day, I am neither a Knight of one order nor a Companion of another, my salary has never been £5,000 a year, and I have not been in the Government service for 30 years. In spite, however, of these disadvantages, having been connected with the Central Register since its inception, I venture to point out that it is impossible, in any orderly system, to make special provision, or to supply special forms, for ex-Government officials who may have recorded their histories in most books of reference, but whose qualifications for more ordinary jobs may not be so obvious.

'When the Royal Society undertook to construct the Scientific Section of the Central Register the president, then Sir William Bragg, O.M., and a former president, Sir Charles Sherrington, O.M., gladly filled up their two forms, 8 in. × 5 in. like Ignotus's; not because they can have supposed that they were unknown, but because their modesty demanded that they should be uniform with their colleagues. Sir William remarked to me that perhaps he might be able to teach physics to release a younger man. And, Mr William Thompson Hay, better known as Will Hay, the popular headmaster (B.B.C.) of St Michael's, whose salary may even have been comparable with Ignotus's, completed the same forms meekly as an amateur astronomer and instrument maker.

'Ignotus complains, about the size of the form, that his distinguished services could not be recorded on it unless he was capable of writing the Lord's Prayer on a three-penny bit. It may relieve him to know that extensive experience with the Central Register has shown that it is those of the least importance who write in the greatest detail of their qualifications.

Yours faithfully,

House of Commons, May 23. A. V. Hill.'

Member of Parliament 1940–45

An ancient tradition, which had begun early in the seventeenth century and continued until 1951, allowed the Universities to elect representatives ('burgesses') to Parliament. In November 1938, a small, but influential group at Cambridge which included F. Gowland Hopkins, proposed that the University should be represented by Independent Members, elected on the grounds of personal distinction and not of political party affiliation (see Appendix II). At the beginning of 1939, A. V. was invited by this group to accept nomination as their candidate, but he declined as it would not have been compatible at that time with his Royal Society research appointment. When a further approach was made to him in December, after the closure of his laboratory, this objection had disappeared, and he accepted the nomination which came, this time, from the Cambridge University Conservative Association, on the understanding that he would describe himself as an 'Independent Conservative' with emphasis on 'Independent'. He explained his position in a letter to a 'discreet journalist' in the following terms:

'My position is that I have never been connected with a political party and am one of those who feel that University Representation loses its chief value if employed for party purposes; indeed it seems rather likely that University Representation will be abolished altogether in future unless the Universities find some better justification for it than to support one or other side by a party member.

'The Cambridge Conservative Graduate Association, or perhaps I should say a progressive and liberal minded section of it, has long had this consideration in view. When the party truce was agreed upon after the outbreak of war, and it was understood that the Conservatives (having the then member Sir John Withers) would be allowed to nominate his successor without contest if he retired, the Association looked round for a Candidate who would be agreeable to the other parties and fulfil the consideration referred to above. They tried to get Mr J. M. Keynes to stand and nearly succeeded, only considerations of health finally deciding against it; he is certainly not a Conservative, whatever he is. Other names including mine were then considered, of which Dr J. H. Clapham, Vice Provost of King's, a life-long Liberal so far as his politics go, was one. Their choice actually fell on me. The Conservative Association, therefore, did try to do the generous and broadminded thing in view of the party truce.

'The Labour Party are *not* putting up a Candidate, recognising that they are bound by the agreement referred to. Certain, however, of the Left Wing people in Cambridge, not liking the agreement, have evaded it by putting up an "Independent Progressive" candidate on their own.

'You will see from my Address the chief objects I should have, if elected. I have not elaborated them. You probably know, however, that I have been very concerned with such things as assisting academic refugees from Germany etc.; and that I am strongly in favour of improving public health by more attention to, and expenditure on, public health service, hospitals, nutrition, physical training, housing, etc. I hope to live to see some form of Universal Medical Service set up. I am a strong believer in international co-operation and have worked hard to achieve it in my own field of Science.

'This letter is not intended for publication, but if you wish to refer to the election you may make use of the information in it as you please.'

He was elected on 23 February 1940 and 'took the oath' four days later, but did not start effectively as a member of the House until June when he returned from his first war-time mission to America.

It was natural for a person of A. V.'s charm and complete integrity to gain many friends of all political colours in the House. This was mutual; as he put it in *Memories and reflections* (p. 548): 'Five years in Parliament, particularly in those heroic days, cured me—if I needed curing—of any vulgar prejudice against politicians. In fact, for most of my colleagues there I conceived a sincere regard and affection, not only (if I may say so humbly) for their fundamental humanity but also for their devotion to the institutions of Parliament and their sagacious realization that politics is the art and science of practical government.' Nevertheless, on balance, A. V.'s period as a Member of Parliament cannot have been a very happy experience. The type of manœuvre that is often necessary 'to get things done' in the political arena was clearly repugnant to him, and the failure or delay in having scientifically sound advice adopted, or in obtaining the release of highly qualified loyal colleagues from refugee internment camps, must have been frustrating. Speaking of the qualification of scientists in handling political affairs, he said in 1946 (*M. & R.*, p. 355): 'Indeed —and I speak with some experience—a dislike of misrepresentation and of compromise with the truth, makes them usually pretty inefficient politicians.' Some of his speeches in Parliament convey the impression that more than once he was driven to extreme exasperation. On the other hand, he assures us in his autobiographical sketch that 'after many years I came to the conclusion that it never (repeat never!) pays to lose one's temper; but that occasionally in a good cause it is useful to *pretend* to lose it. In that sense I lost it in 1936 with Lindemann [see p. 110] and in 1940 over the indiscriminate internment of refugees'.

I feel certain that this is the only form of deception he ever permitted himself to engage in!

Concerning his efforts in the House to secure the release and proper employment of scientists who had been kept interned on the Isle of Man, Professor H. O. Schild, F.R.S., told me an amusing story. He and the other inmates had been for a time without information about day-to-day events, and rumours were going around the camp about imminent attack and takeover by German forces. Then one day he saw a newspaper and read with amazement and immense relief a report of A. V. Hill's parliamentary intervention on behalf of interned refugees. It not only raised his hopes for the future, but he concluded the war situation could not be so serious, if Parliament had time to concern themselves with people like himself.

Transatlantic mission

In February 1940, A. V. went to Washington, as a 'supernumerary Air Attaché' of the British Embassy, technically on loan from the Royal Society. His task was to pave the way for establishing full scientific liaison and exchange of information between Britain, Canada and the United States, or in Tizard's words for 'bringing American scientists into the war before their Government'. A. V.'s mission was the result of discussions with Tizard and Egerton which had been going on for some months, and its outcome was that R. H. Fowler went from Cambridge to Ottawa, as liaison officer with the Canadian National Research Council, and Tizard proceeded to Washington via Canada in August 1940, at the head of a group which included J. D. Cockcroft and E. J. Bowen, with authority to disclose and exchange secret technical information. The various obstacles which had to be overcome before this stage was reached are set out fully by R. W. Clark in his biography of Tizard. A. V.'s preliminary work and his numerous friendly contacts with American scientists had been of immense value in preparing for what became full-scale technological cooperation across the Atlantic.

In June 1940, after three months in the United States, A. V. felt it was time to return to England, to be on the spot and agitate for more rapid progress, without which he feared the impetus and willingness of the Americans to collaborate would vanish. He proposed 'that we should offer any information desired [by the U.S. Government], *without condition*, since we realize that America is fundamentally engaged in the same struggle for civilization as we are. The exchange would follow naturally' (Clark, *loc. cit.* p. 254). In an even more forthright memorandum which was submitted to the Prime Minister, A. V. wrote:

> 'Our impudent assumption of superiority, and a failure to appreciate the easy terms on which closer American collaboration could be secured, may help to lose us the war. . . . An American said recently to Mr Casey, the Australian Minister in Washington, "Why do the English always hold their friends at arm's length?" There is a very strong desire to help us, but of course the same fetish of secrecy exists in the Service departments

in the U.S.A. as in Great Britain, it can be avoided in only one way, namely by a frank offer to exchange information and experience; without such an offer the resources of the U.S. will remain imperfectly accessible to us.'

It took another two months before the Tizard mission finally set off and was able to do its vitally important work.

Scientific Advisory Committee

Back in London, A. V. Hill intensified his attempts to make sure that the Cabinet was supplied with soundly based scientific advice. After his personal experiences on the Tizard Committee in 1935–36, A. V. had strong misgivings about the dominant position of Professor F. A. Lindemann and regarded it as undesirable that 'a scientific courtier . . . monopolized the grace and favour of the Prime Minister.' These are strong words,* and one feels that A. V., in spite of his refusal to become intemperate, was 'over-reacting' and may have failed to appreciate the very great importance of the personal and political trust which existed between the Prime Minister and his friend who was able to explain technicalities in intelligible terms and give him tangible advice. It seems inevitable that, on controversial issues, the Prime Minister should have listened to his personal counsellor; it was an unfortunate fact of life that Lindemann, instead of acting as a mediator, kept himself aloof from the scientific community and by his somewhat contemptuous attitude provoked the kind of reaction which is evident from A. V.'s remarks.

In an effort to redress the balance, the Officers of the Royal Society approached the Government and succeeded in forming a Scientific Advisory Committee to the War Cabinet, in which the President and Secretaries of the Society were joined by the Secretaries of the Research Councils (see Appendix I). The terms of reference were to advise the Lord President of the Council and appropriate Government Departments on scientific problems and selection of suitable persons when requested to do so, and also to draw the attention of the Lord President to promising new scientific developments (the use of atomic fission was the first problem that came up; the Committee recommended that the project of an atomic bomb be pursued vigorously, but that the development work be done in Canada and the United States). The Advisory Committee was the forerunner of other bodies with different names (Advisory Council on Scientific Policy etc.).

One of A. V.'s important actions, taken soon after his return from America, is described in Lovell's biographical memoir of P. M. S. Blackett (*Biogr. Mem.* **21**, 56). In early August 1940, A. V. visited General Pile at Anti-aircraft Command. Quoting from Pile's letter: 'I was not having much success in dealing with enemy aircraft. Professor A. V. Hill came to my command one day to discuss all the problems . . .. He invited me to attend a meeting at the Royal Society the next day. Patrick Blackett addressed the meeting and I was much

* The full strength of A. V. Hill's attack is apparent from a war-time memorandum 'On the making of technical decisions by H.M. Government' which he had drawn up and which is quoted in part by R. W. Clark (1965, *loc. cit.* p. 244).

impressed by him.' The outcome was Blackett's secondment to A.A. Command to improve the application of radar tracking to A.A. gunnery. He was assisted in this work by a group of young scientists some of whom had been collected by A. V., including his son David, Leonard Bayliss and Andrew Huxley.

During the next two years, 1941–43, A. V. continued to be active in many different fields, as a member of the University Grants Committee (1937–44), of the Advisory Council of the Department of Scientific and Industrial Research, of the Colonial Research Committee, the Interdepartmental Committee on Medical Schools, as Chairman of the Executive Committee of the National Physical Laboratory, and of the Research Defence Society. He played an important part in getting the London Medical Schools to increase their intake of women students. He intervened in the public press and in the House in his usual forthright manner, in his efforts to improve the utilization of scientific and technical advice at the highest level of command, and when other matters of scientific or medical concern were raised, or when the position and employment of refugee scientists came up for discussion, and he contributed actively to the working of the new Parliamentary and Scientific Committee.

Visit to India

But his most important contribution came in 1943–44 with his visit to India and his subsequent report to the Indian Government. In his presidential address to the Royal Society in 1968, P. M. S. Blackett described it as an 'event of historic significance . . .. A. V. Hill's 50 page report . . . gave a very comprehensive account of the state of science in India and made many wise and useful comments. Surveys of a country's scientific set-up are commonplace to-day, but they were not so then. So Hill's survey must have been one of the first of its kind.'

The undoubted success of A. V.'s mission was due to his simple and straightforward way of dealing with people. He came, not as a political observer, but as a colleague representing the Royal Society which was concerned with the development of scientific collaboration with the Commonwealth, especially during the imminent post-war period. A. V. already had close friends among his Indian colleagues, particularly S. L. Bhatia, the Deputy Director of the Indian Medical Service, H. J. Bhabha, of the Tata Institute, and S. S. Bhatnagar, later the Secretary and Director of the Indian D.S.I.R. A. V.'s visit arose from a request of the Viceroy (Lord Wavell), and in the summer of 1943 the Secretary of State for India wrote to the President of the Royal Society

> '. . . The most important matter to be discussed, I understand, is the organization of scientific and industrial research as part of the Indian post-war reconstruction plan, and its coordination with the corresponding activities here. But advice would also be welcome on current research problems and visits by a distinguished scientist to universities and other research centres would undoubtedly be much appreciated. I have now been requested by the Viceroy to convey an invitation to the Royal Society to

depute a distinguished scientist to visit India, and to enquire whether it will be possible for them to spare Professor A. V. Hill for this purpose . . .. Arrangements would be made for him to see as much as possible of India's scientific, technical and research work.

'I myself feel that such a visit would be of very great value both generally in regard to relations between this country and India, and specifically as a means of developing contacts with that country in the scientific and academic field.'

A. V. arrived in India on 16 November 1943 and stayed until 5 April 1944. During this time he visited a large number of centres and made many new friends all over the country. He was able to inspire confidence; when he gave advice, it was done with tact and evident sympathy, and one recognized that his purpose was to help improve standards of medical education and agricultural research and to further genuinely autonomous development. His report goes over the organization of science and technology in 24 detailed chapters; many of the suggestions were later adopted in one form or another. A particularly interesting example was the recommendation to establish an All-India Medical Centre, a kind of 'Indian Johns Hopkins'. A. V. had served on the 'Goodenough Committee' in Britain which furnished a well known report on medical education in 1944, and he found his experience on that Committee very useful in his present task. In commenting on deficiencies he saw in both the pre-clinical and clinical teaching, he hits the nail straight on the head:

'In all the subjects of a medical course, in laboratory as well as hospital, the crying need in India is for full-time workers, capable and well-trained, able to devote their lives to the advancement of the science and practice of medicine by education and research.'

'Under the present system there are very few full-time teachers and research workers in the clinical subjects, and there are no full-time medical, surgical or gynaecological units. Busy and successful practitioners usually control the teaching and stand out as the ideal to be aimed at by the medical student. Their hearts are bound to be mainly in their private practices. It seems to me imperative that full-time clinical units should be started in all Indian Medical Colleges, in medicine, surgery and gynaecology, as soon as teachers and research workers of a high enough standard are available . . ..'

The nucleus for creating such people was to be 'a great All-India Medical Centre', with highly selected students for whom adequate scholarships or bursaries should be made available. It should be established in the capital city, Delhi. He went on to consider the type of buildings and the capital cost required. A. V. commented later that he 'did not really expect much result' (*M. & R.* p. 640); but he kept hammering away at it, wrote to Wavell in 1945 and to Lady Mountbatten in 1947, and this may have helped in paving the way. The scheme was taken up on the recommendations of the Indian Health Survey and Development Committee in 1946, and it (the 'All-India Institute of Medical Sciences') started in earnest in 1947, with the offer of one million pounds by New Zealand to the new Independent Government of India.

A. V.'s report dealt with other matters, concerning the promotion of training facilities in Britain for Indian postgraduates, the development of adequate technological information services, the establishment of a central organization for scientific research, heading a group of research councils which would be similar to those in the United Kingdom (separate from, but complemented by, 'development councils' in the 'user' departments of Health, Agriculture, Industry etc.). Many of the suggestions in Hill's report acted as a stimulant and were put into practice after Independence in 1947.

An interesting sidelight on A. V.'s visit to India appears in Feldberg's biographical article on H. H. Dale (*Biogr. Mem.* **16**, 146). Some Indian scientists, who had been elected Fellows of the Royal Society, had not been able to come to London to be formally admitted and sign the Charter Book. The President therefore requested A. V. Hill to perform the Society's admission ceremony at a special meeting in India. A. V. was to take with him 'a sheet of suitable parchment on which the Fellow's obligation is inscribed, and on which signatures can be taken for eventual incorporation in the appropriate page' of the Charter Book. The ceremony took place at Delhi on 3 January 1944 in the presence of the Viceroy, and two Indian Fellows were duly admitted.

Post-war rehabilitation

Towards the end of 1944, A. V. started thinking seriously about his own scientific rehabilitation after the war. He had expressed doubts about being able to do so for a second time and at the age of 58. 'Unfortunately for 5½ years there has been no chance of working in a laboratory, my mind has become scientifically rusty and my hands have lost much of any cunning they may have had. I am not without hope, however, of being able to get back to research; and it is likely that all these connexions (established during the war with governmental and industrial research laboratories) with science on a wider stage would be useful in the plans one has in mind, particularly in getting younger people to work' (from a memorandum on 'The needs of biophysics', dated 21 February 1945). What had given him an enormous boost was a visit from J. L. Parkinson at about that time, who was employed during the war at the Royal Aircraft Establishment at Farnborough. Parkinson told A. V. that the war was won and it was about time to rebuild the laboratory, collect equipment and start proper work again!

In the aftermath of the war, it took A. V. some time to wind up his extramural commitments. He had already decided not to be a candidate in the 1945 parliamentary election; in November 1945 he completed his 10-year term as Biological Secretary of the Royal Society, but agreed to carry on the business of Foreign Secretary during 1946 when the first Commonwealth Scientific Conference was held at Burlington House. This was the fruition of a plan which A. V. Hill and A. C. Egerton had been preparing for a long time, and in a way was the natural outcome of the war-time efforts they had made to strengthen scientific contacts and exchange of information among English-speaking people.

The immediate post-war period brought A. V. high public honours, in recognition of the service he had given. In his *Memories and reflections* he makes some caustic comments about certain aspects of the 'Honours system' and quotes with approval T. H. Huxley's view that 'the sole order of nobility which becomes a philosopher, is the rank which he holds in the estimation of his fellow-workers'. It is clear that A. V. did not want a title (apart from other reasons, he was probably not enamoured of his forenames and preferred to be known by his initials). But he was glad to accept not only the many academic distinctions, honorary degrees, scientific medals, elections to foreign scientific societies which were offered to him, but also enjoyed being made a Companion of Honour in the New Year's list of 1946, and soon afterwards receiving the Medal of Freedom with Silver Palm from the United States (1947) and becoming Chevalier of the Légion d'Honneur in 1950. He was thrilled with the Copley Medal which the Royal Society gave him soon after he had ceased to be a member of its Council.

18. Return to the laboratory

The immediate prospects of rebuilding the laboratories were not too bright, and there were a number of problems. Although the Medical Sciences buildings at University College had not suffered serious bomb damage, the Faculty had been moved out to Leatherhead, and the Gower Street buildings were still occupied by Government Departments, the Ministry of Food and the Admiralty. Moreover, A. V. was hoping to use the period of post-war reconstruction to establish the whole subject of 'biophysics' on a firmer and more permanent basis. Already in November 1937 he had drafted a proposal to set up an institute for research and graduate teaching in which the full resources of physics and physical chemistry could be applied to biological and medical problems. He now wrote a memorandum elaborating on that idea.

> 'Much has happened since 1937 to strengthen the case for a special laboratory devoted to Biophysics. The use of radio-active and other isotopes for a great variety of biological purposes has already shown in America and elsewhere very great achievement and even greater promise, and a vast field of research has been opened up in which British Science has taken as yet practically no part. Apart from the war, this would have been discreditable. Developments have occurred in genetics which provide a challenge to theoretical physics well described in Schroedinger's recent little book (*What is life*, C.U. Press), as well as offering a wonderful field for fine physical technique.'

He points out that

> 'many physicists, some of standing and experience, others enterprising youngsters who have seen many strange new applications of physics during the war, have become interested in the exciting new scientific possibilities

and the probable practical importance of applying the latest resources of physics, theoretical and experimental, to biology. On the other side, many first-rate young biologists, during the last $5\frac{1}{2}$ years, have been devoting their talents very effectively to physical war-problems, and have acquired techniques and knowledge and shown initiative in experiment which could find undoubted scope in biophysics. Many of these, physicists or biologists, have from time to time in the last few years enquired of me what regular outlet might exist for this new potential interest of theirs.'

His answer had to be that there was little opportunity in 1945 in Britain.

'There is no University department of Biophysics; such equipment as is available in other laboratories is on a small scale, and there is no centre at which research can be done or experience gained in the general field of Biophysics. All this was formerly true also of Biochemistry—it is certainly no longer true: yet ultimately the importance of Biophysics may be just as great as that of Biochemistry.'

At the time he wrote this, A. V. Hill was looking into the possibility—suggested by Sir Henry Dale—that, instead of returning to University College, he might move to the Davy Faraday Laboratory at the Royal Institution and develop it into a much more substantial centre for Biophysics. However, this did not materialize, and A. V. had to confine his plans to what was possible within the much more limited space and facilities of his old laboratory. But he certainly continued to encourage young physicists to enter the biological field and to develop biophysical research, on nerve and muscle, on the mechanism of sense organs, and on molecular problems of genetics, in several other laboratories.

The contemplated transfer to the Royal Institution was not the first time that a suggestion had been made to move away from University College. In 1937, A. V. was invited to become Master of Peterhouse, Cambridge. However, that approach came at a time when he was fully preoccupied with exciting research in his laboratory as well as with many other activities centred in London, and the decision to decline cannot have been difficult. The situation was different in 1945 when he was faced with the formidable task of almost starting afresh at the age of nearly 60, and having to make his laboratory inhabitable again. The way in which he managed to return to his bench, roll up his sleeves and produce once again a large output of research during the next 20 years is remarkable and probably unique. It is true that much of it is an elaboration of detail, confirming or somewhat modifying his earlier results, but there are some important advances, both in technique and information, notably the new light which he and his co-workers were able to shed on the diphasic temperature change during the nerve impulse.

The success of his second post-war enterprise, in the face of the restrictions prevailing at the time, depended on many factors. There was no immediate possibility of establishing a university department with regular staff appointments, but with the help of the Rockefeller Foundation, and of the Royal

Society and the Medical Research Council, A. V. was able to offer appointments and scholarships to a small number of research workers and technical assistants. J. L. Parkinson saw to it that the laboratories were cleaned out, repainted and equipped with apparatus, some of it of pre-war vintage and taken out of storage, but many other items surplus from the services or 'liberated' from the enemy. By the late spring of 1946 most of the laboratory was back in functioning order, and experimental work was starting on a variety of problems, muscle energetics, membrane excitation, ion exchanges across cell surfaces and related matters. A. V. himself returned to the questions arising from his myothermic experiments in 1938 and, as usual, preceded it by redesigning equipment and making a number of important technical improvements. With Downing's help, even better and quicker galvanometers were made, reducing the recording time lag to about 2 ms, and with the assistance of V. H. Attree the recent developments in electronic circuitry were used to display temperature and mechanical changes conveniently on a twin-beam cathode ray oscilloscope. A. V. describes (*Trails and trials* (224), p. 66) how he celebrated his sixtieth birthday in September 1946 'by obtaining the first records ever made with a cathode ray tube of muscle heat'. But, with reorganizing the laboratories and helping others to get started, 'two years and a half elapsed before anything serious could be reported'. Demonstrations to the Physiological Society recommenced in March 1947, and the flow of full research papers gathered momentum in 1948 and continued unabated until 1964 (followed by the last two monographs, *Trails and trials in Physiology* in 1965, and *First and last experiments in muscle mechanics* in 1970).

Two short papers appeared in 1948, one considering the problem of the coupling between excitation of the surface membrane and the contractile interior. It seemed clear that, in a large muscle fibre, some process other than ordinary diffusion must be responsible for spreading activity from the surface to the centre, if the centre had to be reached during the short rising phase of the twitch. The answer to this problem was provided several years later when it was realized that excitation can propagate towards the middle of the muscle fibre along radial tubular infoldings of the surface membrane. A second paper dealt with a nice application of a thermal pressure recorder, using a thermistor to measure the temperature change due to adiabatic compression of liquid paraffin in a fine cannula. The probe was inserted into a frog's gastrocnemius muscle to determine the pressure rise during contraction of this 'balloon-shaped' muscle. The results were of interest in showing that the compression inside the muscle was powerful enough (a) to shut off the blood circulation and (b) to account for most of the transient volume constriction which had been recorded (and misinterpreted) by various authors for many years.

Another critical note appeared soon after, in which A. V. challenged biochemists to try to demonstrate ATP hydrolysis in a functioning muscle; he suggested the use of a tortoise muscle at 0 °C, to make the process slow enough to determine the time course of the chemical breakdown in relation to the contraction cycle.

This was followed, in 1949, by a whole series of papers in which he repeated the myothermic work of 1938 and re-examined the validity of the 'characteristic equation' of energy liberation, this time experimenting with twitches rather than maintained muscle contraction. He considered it preferable to investigate the transient single twitch, because—unlike the maintained tetanus—this is 'a simple elementary process.' Even before the birth of the sliding-filament theory, this must have seemed a curious and somewhat old-fashioned view; it was not very long before the concept of the 'elementary process' in contraction was transferred to the single cycle of cross-bridge interaction between myosin and actin molecules. Probably the real attraction to A. V. was that the improved time resolution of his instruments enabled him for the first time to make measurements during the brief rise of a single twitch. Anyway, he succeeded in making a large number of interesting observations. Confining the analysis to the ascending phase of the twitch, he found that the total energy liberation E consisted of three separate components $E = A+W+ax$, where A is the heat of 'activation' (independent of load or shortening, and corresponding to the heat of 'maintenance', i.e. of continued activation, during a steady tetanus), W is the work done in lifting a load or stretching an elastic body and ax is the heat of shortening. The 'activation heat' starts to evolve very soon after the stimulus (at 0 °C, in frog muscle, after a delay of 10 ms). During isotonic relaxation no thermal changes were observed, provided the lifted load had been held up or removed; otherwise the mechanical energy of the falling load was degraded as 'relaxation heat' in the relaxing muscle. In so far as it could be tested, the characteristic relation $v(a+P) = b(P_0-P)$ applied satisfactorily during the shortening period, and the parameters agreed well with those of the 1938 experiments.

The associated problems with which A. V. Hill was concerned at this time were the time course of contractile *activation* (rather than the development of isometric tension), in more detailed pursuance of the work started by H. S. Gasser and himself 25 years earlier. To ensure synchronous excitation of the whole length of the muscle fibres, an electric shock was sent through an array of distributed stimulating electrodes. By applying a quick stretch to the muscle during the latent period, Hill found that there is a rapid, almost abrupt, transition during which the muscle becomes 'stiff' and capable of *withstanding* the maximum isometric force, very early and long before it is able to *develop* maximum tension. The obvious interpretation was that in applying a stretch at the right time and of the right magnitude, one forcibly extends the 'series-elastic' component to the full tension, and so saves the 'contractile' portion of the muscle the work of having to shorten internally (which is believed to be the normal cause of the gradual and delayed rise of tension in isometric contraction). Hill estimated that contractile activation is complete within 10% of the rise time of the isometric twitch (in about 40 ms in frog sartorius at 0 °C). Later the figure was revised to 20%, and the transition was recognized to be rather less sudden than thought at first. Also the interpretation depended on a knowledge of the internal elastic compliance of the muscle, which later turned out to be less than was realized at that time.

Another question which exercised him was whether 'relaxation is an active process'. He found that an initially slack muscle, which was stimulated to shorten to much less than its normal extended resting length, showed no apparent 'slackness' after the stimuli. This indicated that the muscle fibres did not actively extend themselves during relaxation. More recent work on isolated muscle fibres (H. Gonzáles-Serratos, 1971, *J. Physiol., Lond.* **212**, 177) shows, in fact, that relaxing myofibrils are thrown into folds within the fibre if this is kept at short length, but this may be brought about by elastic forces and does not conflict with A. V.'s conclusion that relaxation is 'passive' and simply a cessation of the 'active state'. However, with the new concept of rapidly repeated cyclic interactions between actin and myosin cross-bridges, the whole problem of 'relaxation' has shifted to the molecular level and to a different time scale, and if one considers the detachment of cross-bridges, this is very likely an 'active' process.

Following his recipe of working on the slowest muscles that can conveniently be placed on a thermopile, A. V. used tortoise muscle at 0 °C to check the precise time relation between the thermal and mechanical responses, and found that the temperature rise began some 30 msec before any tension development could be observed. He concluded that the early start of 'activation heat' is a sign of a chemical change which precedes and initiates the contractile process.

In November 1949, A. V. devoted an Evening Discourse at the Royal Institution to his old hobby, the influence of bodily dimensions on muscular performance and metabolic expenditure. It was published in *Science Progress* (186) and presents many interesting calculations on a great variety of animals, explaining why a whale can remain submerged and do without breathing for half an hour, why the jumping records of kangaroos are not much superior to those of men, and why—among similar creatures—large and small animals have the same linear speed of propulsion, but the muscles of the larger animal take a longer time for the same kind of movement, which is more 'economical' and makes their muscles less fatiguable and their efforts more enduring.

During the next few years, Hill continued to examine the dynamic properties of muscle and the changes which occur during the earliest onset of contraction. But the series of papers on this subject (189–192) were somewhat repetitive in substance and concerned mainly with the elaboration of further detail. Of much greater interest is his study (193) of the thermal effect which accompanies *forcible extension of contracting muscle.* This is a problem which arose directly from the 1938 experiments and from the 'characteristic equation'. The question was whether the extra heat production ax (and the underlying chemical process), associated with the *shortening* of active muscle, can be reversed and turned into heat absorption by causing a stimulated muscle to lengthen under a load which exceeds the normal isometric tension. The experimental test is complicated because it necessitates the 'injection' of mechanical work into an active muscle where some or all of it may be degraded into heat, and so obscure the looked-for reversal of the shortening heat. The result which Hill and his colleagues B. C. Abbott and X. M. Aubert obtained was a clear deficit in the total energy liberation, and often also in the net heat production, during a period of enforced lengthening. The authors regarded this as evidence suggesting that the chemical reaction which underlies the characteristic relation $v(a+P) = b(P_0-P)$ and gives rise to the heat of shortening is reversed in direction and leads to cooling, when v and (P_0-P) are made negative, that is during lengthening of active muscle. Hill and his co-workers realized that this interpretation lacks finality, for it depends on the unproven assumption that other factors, such as 'activation' or 'maintenance' heat rate are not altered during the enforced lengthening, and that the isometric heat rate can be taken as the standard baseline in evaluating the results.

During 1950–52, A. V. Hill organized two Discussion Meetings at the Royal Society to which he contributed substantial introductory papers (180, 195). In the first one, he summarized his views on muscle contraction; at the second meeting he presented an extensive account of the 'thermo-elastic' properties of unstimulated muscle. When resting muscles are stretched, or released from initial tension, small temperature changes occur whose direction, amplitude and time course depend on the muscle length. A. V. tried to analyse these complicated phenomena in terms of two different types of elastic behaviour ('rubber-like' elasticity at short length, 'normal' elasticity at greater length), but the physical or chemical basis of the thermal effects remains obscure.

19. 'Retirement' to the laboratory

In 1951, A. V. Hill was faced with important personal decisions. More than five years had elapsed since the end of the war, and there was still no assurance that his research unit would acquire the status of a university department, with an established staff and regular budget. There was, in fact, no obligation for him to relinquish his Foulerton Research Professorship when he reached the statutory retirement age of 65 for university appointed teachers.* But he must have felt that as long as he held his research appointment, there would be little prospect of forcing a decision about the future of the research unit, and so he announced that he would retire from his Royal Society post and leave the laboratory at the end of 1951. It was not clear immediately whether this was going to lead to a continuation or a dispersal of his group. All this happened before the end of a financial 'quinquennium' which formed the basis of the academic budget, and there were undoubtedly administrative difficulties for the University and the College in funding the necessary transfer arrangements. To its great credit, University College treated the matter as an obligation of the highest priority and decided to set up a Biophysics Department at the beginning of the 1951–52 Session. A. V. became its first head, until 31 December when he officially retired and, again entirely on his own, decided to move into new quarters which had been offered to him by Lindor Brown, two floors below in the 'old' Physiology Department. As A. V.'s bibliography testifies, 'retirement' meant anything but cessation of work; it was in fact a generous

* Retirement regulations for Royal Society Research Professors were made in December 1951.

manœuvre to bring to fruition a long-standing plan for the strengthening of his favourite subject.

Although A. V. had shed many of his outside commitments after 1945, he had maintained and indeed increased his international scientific contacts, attended the Physiological Congress in Copenhagen (1950), where he gave a keynote address, and paid several visits to U.S. and European centres. In 1952, following his official 'retirement', he travelled extensively and accepted new and quite heavy tasks. He had become President of the British Association and was preparing a very important address for the Belfast meeting in September 1952 (213). Earlier, in March, he went together with H. T. Tizard to Pakistan to attend the meeting of the Pakistan Association for the Advancement of Science in Peshawar, and also visited several other scientific centres, in Lahore, Rawalpindi, Quetta and Karachi. Later in the year, he proceeded to East Africa and Rhodesia as a member of a Commission on higher education for Africans, chaired by A. M. Carr Saunders, whose report led to the foundation of the University College at Salisbury. A. V. became President of the Society for Visiting Scientists which for a number of years fulfilled a much needed social function and provided a meeting ground in the centre of London. Finally, he became Secretary General of the International Council of Scientific Unions, a heavy commitment which he took on for the next four years. That he should be chosen for this appointment seemed natural, in view of his earlier experiences in international scientific relations, in the field of physiology, also through his war-time activities, as Biological and Foreign Secretary of the Royal Society, in establishing closer liaison with America and the Commonwealth. However, he had never attended the General Assembly of I.C.S.U. (which, in his absence, elected him at the Brussels meeting in 1952). He accepted the appointment at a time when he had not yet settled into his new laboratory and possibly under-estimated the extent of his personal involvement in research during the coming years. It seems, from his brief reference to his I.C.S.U. activities that he was glad to give them up in 1956 and go back full-time to his experiments and his papers. Nevertheless, he scored one success which gave him great and lasting satisfaction: through his personal intervention he secured the accession of the Soviet Academy, in June 1955, and its active participation in the work of the International Council. He managed to achieve this largely through his contacts with V. A. Engelhardt, the distinguished Russian biochemist, with whom he had maintained very friendly relations, quite unruffled by Engelhardt's public attack on A. V. after his famous address to the British Association.

20. The ethical dilemma of science

On 3 September 1952, A. V. delivered his presidential address on 'The ethical dilemma' to the British Association for the Advancement of Science. It was an important speech in which he brought into open discussion human problems which had weighed heavily on his mind for many years, especially after his war-time visit to India. He maintains that 'the fundamental principle of scientific work is unbending integrity of thought, following the evidence of fact wherever it may lead'. But scientists, like other people, had to face newly created world problems, the gravest of all being uncontrolled population increase which was accelerated by recent advances of science. He goes on to examine 'the consequences of scientific discovery in human affairs', and continues: 'The dilemma is this. All the impulses of decent humanity . . . insist that suffering should be relieved, curable disease cured, preventable disease prevented.' But 'in many parts of the world . . . the fighting of disease, the lowering of infantile death rates, and a prolongation of the span of life have led to a vast increase of population'. He quotes statistical examples from his experiences in India and refers to the report of a recent Indian Government Planning Commission which pointed frankly to the dangers of 'increasing pressure of population on natural resources' and to the immediate need for introducing effective measures of birth control.

A. V. discusses and questions privileges one tends to take for granted, including the 'sacred' rights and freedom of the individual. 'Do human rights extend to unlimited reproduction ? . . . These problems must be faced not only with goodwill and humanity, but also with integrity and courage, not refusing to recognize the compulsion of simple arithmetic.' And referring again to the progress of science and technology and summarizing our ethical problem in one sentence: 'Are we justified in doing good when the *foreseeable* consequence is evil ?' He concludes

> '. . . There seems to be no simple answer to the riddle. All knowledge can be used for evil as well as good; and in all ages there continue to be people who think its fruit should be forbidden. Does the future welfare, therefore, of mankind depend on a refusal of science and a more intensive study of the Sermon on the Mount ? There are others who hold the contrary opinion, that more and more of science and its application alone can bring prosperity and happiness to men. Both of these extreme views seem to me entirely wrong—though the second is the more perilous, as more likely to be commonly accepted.'

What is needed is a middle way, an attitude of conciliation not conflict between the two ideas. The ethical dilemma, in reality, is not one concerning scientists alone.

> 'It is true that integrity of thought is the absolute condition of our work, and that judgments of value must never be allowed to deflect our judgments of fact. But in this we are not unique. It is true that scientific research has opened up the possibility of unprecedented good, or unlimited harm, for mankind; but the use that is made of it depends in the end on the moral judgments of the whole community of men. It is totally impossible now to reverse the process of discovery: it will certainly go on. To help to guide its use aright is not a scientific dilemma, but the honourable and compelling duty of a good citizen.'

Much public discussion followed. In subsequent years, the problems of overpopulation, and disputes and attacks on the rôle of science became fashionable and top items of public interest, but in 1952 this was not so, and much of what A. V. had to say was new and provocative. He later made some wry comments on the reactions to his address: he noticed that denunciation followed 'alike in Pravda and the Vatican Press, so it might be concluded it was about right!'

21. More work on muscle and nerve

During the 1950s, Hill's research on muscle continued and he published papers dealing with the 'thermo-elastic' properties of resting and active muscle, the effect on contraction of replacing chloride with foreign anions, further studies of the effect of enforced lengthening on energy liberation, and of the time relations between the thermal and mechanical response.

In 1955, A. V. was elected President of the Marine Biological Association, an office which he held for five years and which was a fitting culmination of his very close relationship with the Plymouth laboratory and the powerful encouragement he had given over many years to the study of comparative physiology on marine animals.

Of his subsequent work, the most noteworthy event was his renewed attack, with quicker and greatly improved technique, on the thermal changes during the nerve impulse. At the age of over 70, he produced two first-class papers, together with B. C. Abbott and J. V. Howarth, showing that in non-medullated crustacean nerve, the impulse is accompanied by a diphasic thermal response. At 0 °C, a positive phase of heat production (amounting to 9 μcal/g) is followed by a slower phase of heat absorption (7 μcal/g), whereas the older experiments had only been able to disclose the small net effect. Hill calculated that because of temporal dispersion of impulses in the different nerve fibres, his new result gives only an attenuated value; the initial transient temperature rise in each fibre is probably nearly twice as large. The physico-chemical interpretation of the energy exchanges remains uncertain: the time course seemed to be incompatible with the simple 'condenser theory' according to which one might expect a brief heating during the depolarizing phase, followed by cooling while the membrane is recharged to its resting potential. The thermal response seemed too slow, though it was of approximately the right magnitude for this type of explanation to hold. Alternative suggestions were that the initial heat liberation might be due to the mixing of external sodium and intracellular potassium ions, and the cooling effect due to a chemical recovery reaction. When Hill and Howarth repeated the experiments on frog's medullated nerve, the thermal response was much smaller, and no second phase was observed, though it was not certain whether the temporal resolution of the instruments was sufficient in this case.

Having found a genuine phase of cooling during the nerve impulse, Hill resumed his myothermic studies, remembering that W. Hartree as well as D. K. Hill had many years earlier obtained evidence for a small heat absorption after muscle contraction. In a paper in 1961, A. V. confirmed this effect with his new equipment, though its chemical correlate could not be identified.

His last research papers on muscle form a curious group; it almost seems as though he felt compelled to go on pointing out real or possible sources of error, to save others from making mistakes. He discusses at length a series of complicating factors, a 'thermo-elastic' phenomenon (a physical side-effect whereby rise of tension in a passive component of the muscle is associated with a small, but not negligible heat absorption), artefacts due to non-uniform distribution of heat in the muscle itself or to irregular surface contact between muscle and thermopile, calibration errors which he thinks have affected some of the pre-1932 determinations of absolute isometric heat values and made them between 10% and 50% too large. To one who is not directly concerned, all this is a little confusing, though reading A. V.'s own comments in his monograph *Trails and trials*, one gets the impression that he enjoyed this last minute burst of corrections and revisions!

I have already mentioned the paper in 1964 (219), in which he showed that the constant a of the force–velocity relation can no longer be identified with a constant coefficient of the heat of shortening; the latter was now found to vary with the load P. While he was making these revisions, A. V. was faced with a more serious dispute, when F. D. Carlson queried the real existence of the shortening heat. This arose from the finding that in after-loaded isotonic twitches the total initial heat production seemed to be constant, regardless of the load and the extent of movement. A. V. pointed out, however, that this constancy is not observed if the heat production is measured during the shortening phase of the twitch, nor if the load is removed at the end of the shortening. Unless this is done, the situation becomes much more complicated; the retained load influences the kinetics of decay of the active state and so alters the associated heat production.

At this stage, A. V. took some time off actual experimenting in order to complete an unusual 'pot-pourri' of a book, *Trails and trials in physiology*, a mixture of annotated bibliography of his work, from 1909 to 1964, 'with reviews of certain topics and methods and a reconnaissance for further research'. It forms a scientific counterpart to a monograph (*The ethical dilemma of science*) which contains a selection of A. V. Hill's writings and comments on general topics. In *Trails and trials*, one finds very useful chapters combining previously published and recently added treatments of the theory of moving-coil galvanometers, of the diffusion of oxygen, of the flow of heat from muscle to thermopile, and of obtaining corrected time relations by numerical analysis of records, with an extensive discussion of various sources of error and their probable magnitudes. Intermingled with these chapters are reprinted review articles, popular scientific lectures, numerous anecdotes concerning various mishaps in the laboratory and even a 'spoof' paper. For my present task, I have found A. V.'s comments on his own early papers particularly useful and entertaining.

In 1964, after putting the final touches to his monograph, A. V. resumed experimental work, but now he confined himself to a study of the mechanical response, a more detailed investigation of the force–velocity relation, the dynamics of contraction, the elastic properties of muscle, and the onset and duration of the 'active state'. He vacated the myothermic laboratory in the Physiology Department and moved back to Biophysics, his old home which had, by now, acquired new and larger territory. For the next three years, A. V. amassed a great deal of experimental material until he and Margaret Hill decided to return to Cambridge in 1967. There were many loose ends, and A. V. incorporated his final research work in a small book, *First and last experiments in muscle mechanics* (1970), starting with the famous Gasser and Hill work of 1924, writing about the new experiments in a leisurely and discursive way, 'thinking aloud' about the puzzles he was leaving others to tackle, and in his own words 'letting oneself go in a way that editors of scientific journals quite properly forbid.'

In September 1965, A. V. paid his last visit to an International Congress of Physiological Sciences in Tokyo. It was a happy reunion; A. V. gave the principal address at the opening session, reminiscing about earlier congresses in other parts of the world, about his friendship with the great leaders of physiology, with Pavlov and Sherrington, Barcroft, Cannon and Dale and many others, and recalling his happy association in the past with Japanese colleagues and pupils, in particular Dr R. Azuma who, by the time of the Congress, had become Governor of Tokyo and who was now able to present A. V. Hill with the 'keys of the city'.

During his last 10 years, A. V. kept himself busy and entertained, collecting and reviewing old observations, reminiscing and writing sketches about himself and Margaret, preparing an anthology of epigrams and poems, of serious and humorous speeches and addresses, in three informal, privately circulated volumes (*Memories and reflections*). Though one discerns in his notes an occasional tone of pessimism, when he meditates on the decline in influence and standards of the democratic society he used to cherish, he continued to see fun and derive enjoyment from many small events in life, and his friends found him as receptive as ever to a good and slightly mischievous joke, and as ready to produce them. He bore personal misfortune with great courage; the severe physical disability of Margaret who died in 1970, the tragic illness and death of Maurice in 1966, and the slow but progressive loss of motile power in his legs from which he was suffering during the last 13 years of his life. This disability started in 1964 and gradually deprived him of his out-door recreations —walking, running, archery, game-shooting—of which he used to be fond. Fortunately, it did not interfere with his principal 'hobby' which remained his experimental work and scientific writing. It did, however, put a stop to his daily run before breakfast: the early morning run had been a regular part of his daily routine, which always began at 7.15 a.m. and finished at 10.30 p.m. A. V.'s timetable was extremely well organized; it had to be to allow him to combine so much intensive research with public service. The day's work was completed with reading and writing after dinner. A. V. was thoroughly proficient in the use of his dictaphone, and manuscripts resulting from his dictation usually needed very little change. He had the habit of answering all letters promptly, almost by return of post. Until his last few weeks he kept himself well informed of public affairs; reading *The Economist* from cover to cover was part of his weekend occupation. With other spare-time pursuits he had little patience; card games, television and similar 'artificial aids to recreation' did not appeal to him.

In an attempt to present a detailed account of A. V.'s scientific work, his personal character and the great intellectual and moral impact he made on his friends and pupils may tend to get obscured. In fact, committed though he was throughout his life to work in the laboratory, it was his concern for others, the encouragement he gave to young colleagues, his upright defence not only of the cause of science, but of scientific men who had been driven from their places of work and needed help, in short it was his devotion to such wider issues, outside the boundaries of his own research, through which he exerted his most important influence on other people's lives and on the course of events.

From a distance, A. V. may on occasions have given the impression of being a somewhat formidable and even intolerant person, but closer acquaintance quickly dispelled this impression. It is true that he had little time for small talk, and one risked a cool reception or even a sharp rebuff if one approached him in a tactless or provocative manner. But he was intolerant and scornful only of pretentiousness and intellectual snobbery. In general, his manner was easy and relaxed, whether he was dealing with scientists or politicians, with private soldiers or generals; he readily formed, and was able to inspire, bonds of friendship and understanding, and he particularly admired those who, though much less gifted than himself, would do a simple job honestly and well, without complaint or boasting. Many who had personal contact with him, and especially those in difficulties, learned that he would promise little, but give much, and often one had to discover the magnitude of his support from someone else.

A. V. was held in the greatest affection by more than a hundred scientific descendants all over the world, both for the scientific help and inspiration he had given them, and for setting them an example of uncompromising integrity in personal and social relations. He was unrelentingly critical and never ceased to probe for flaws in his own methods and deductions. 'To be uncritical', he said, 'particularly of oneself and one's ideas and motives, is the first long step towards dishonesty' (213, p. 39). Yet he never permitted his intellectual austerity to damp his enthusiasm, and I do not believe he ever allowed the slightest doubt to arise in his mind about the importance of the work he was engaged in. This buoyancy transmitted itself to those who were associated with him and helped to carry them over periods of failure and possible frustration. A. V. was a person of old-fashioned tastes and virtues, addicted to simple commonsense and straight dealings, and very allergic to pomposity. His literary preferences were for the Scriptures, the Classics and for Kipling (in moderation) and Mark Twain. Though he lacked appreciation of music and the fine arts, he was a good judge of fine craftsmanship; and above all, while he was given to direct and downright speech, he remained always sensitive to other, especially younger, people's feelings. Until the end, he retained an intense interest in the progress of his friends; he liked writing to them and greatly enjoyed the messages he received from them. On the last great occasion, his ninetieth birthday, over a hundred of his colleagues, among them many whom he had helped to escape from political and racial persecution, had sent him a handsome volume containing their greetings and reminiscences of earlier years, and he derived much pleasure from browsing through it during the last months of his life. Although his legs were paralysed, he retained great mental agility and his sense of humour until the last weeks when he succumbed to the after-effects of a virus infection.

He died on 3 June 1977; a Memorial Service was held in the Chapel of King's College, Cambridge, on 17 June 1977.

I have been helped by many friends and colleagues in preparing this biographical memoir, and I am particularly indebted to Professor David Hill, F.R.S., and Professor Sir Andrew Huxley, F.R.S., and to the Master and Archivist of Churchill College, Cambridge.

The photograph is by W. Stoneman.

HONORARY, FOREIGN, CORRESPONDING, OR ASSOCIATE MEMBERSHIPS

1924 Pathol. Soc. *Philadelphia*
1924 Acad. Med. *Rome*
1925 Deutsche Akad. d. Naturforscher, Leopoldina. *Halle/Saale*
1927 Soc. of the Sigma-Xi, *U.S.A.*
1927 Soc. Argentina de Biol. *Buenos Aires*
1929 Saxon Acad. Sci. *Leipzig*
1929 Accademia Nazion. dei Lincei, *Rome*
1930 Soc. Biol. *Paris* (certificate 1937)
1932 Soc. Ital. Biol. Sper. *Naples*
1934 Amer. Acad. Arts and Sciences, *Boston*
1934 Indian Acad. Sci. *Bangalore*
1934 Acad. Med. *Paris*
1935 Roy. Acad. Sci. *Sweden*
1936 Amer. Ass. Adv. Sci.
1937 Med. Soc. *Budapest*
1938 Acad. Sci. *Budapest*
1938 Amer. Philosoph. Soc. *Philadelphia*
1938 Amer. Acad. Physical Education
1941 Nat. Acad. Sci. *Washington*
1941 Soc. Argentina de Biol. *Buenos Aires*
1944 Indian Sci. Congr. Ass. *New Delhi*
1944 Nat. Inst. Sci. India, *New Delhi*
1944 Indian Assoc. Cultiv. Sci. *Calcutta*
1944 Asiatic Soc. *Calcutta*
1944 Physiol. Soc. *India*
1946 Roy. Danish Acad. Sci. and Letters, *Copenhagen*
1946 Norwegian Acad. Sci., *Oslo*
1946 Amer. Physiol. Soc. (repeated 1950!) *Washington, D.C.*
1946 Flemish Acad. Sci. *Brussels*
1947 New York Acad. Med. *New York*
1952 Roy. Acad. Belgium, *Brussels*

1955 Brazilian Acad. Sci. *Rio de Janeiro*
1960 Acad. Med. *Buenos Aires*
1965 Acad. of the Socialist Republic of Romania, *Bucharest*

Honorary degrees

1929 Edinburgh LL.D.
1930 Louvain M.D.
1930 Pennsylvania D.Sc.
1933 Bristol D.Sc.
1934 Manchester D.Sc.
1934 Oxford D.Sc.
1944 Algiers D.Sc.
1949 Brussels M.D.
1949 Toulouse M.D.
1950 Liège D.Sc.
1950 Johns Hopkins D.Sc.
1952 Belfast LL.D.
1953 Brazil D.Sc.
1954 Columbia D.Sc.
1959 Rochester, N.Y., D.Sc.
1962 Rockefeller D.Sc.
1963 Exeter D.Sc.

Membership of British societies

1912 Physiological Society
1918 Royal Society
1922 Biochemical Society
1925 British Association for the Advancement of Science
1926 Marine Biological Association
1933 Society for the Protection of Science and Learning
1936 Royal Institution
1942 Society for Visiting Scientists
1942 Junior Institution of Engineers (hon.)
Ergonomics Research Society (hon.)
British Biophysical Society (hon.)

Prizes

1912 Gedge (Cambridge)
1914 Rolleston (Oxford)
1923 Nobel (Stockholm)
1926 Croonian Lecture (Royal Society)
1928 Actonian (Royal Institution)

Medals etc.

1910 Walsingham Medal (Cambridge University)
1918 Order of the British Empire (O.B.E.)
1926 Royal Medal (Royal Society)
1927 Baly Medal (Royal College of Physicians)
1937 Coronation Medal (King George VI)
1946 Companion of Honour (C.H.)
1947 Medal of Freedom (U.S.A.)
1948 Copley Medal (Royal Society)

MEDALS ETC. *cont.*

1950 Légion d'Honneur (France)
1965 Key of Tokyo Metropolis
1966 Cothenius Medal (Leopoldina, Halle/Saale)

HONORARY FELLOWSHIPS

1927 King's College, Cambridge
1941 Trinity College, Cambridge
1948 University College London

APPENDIX I

This is an excerpt from an unpublished account written by A. V. Hill about A. C. Egerton ('Jack'), covering some of his and Egerton's joint activities as war-time Secretaries of the Royal Society. The quoted sections are taken from A. V.'s *Memories and reflections*, Chap. 12.

> 'We had served together as ordinary members of Council in 1933, and I was appointed Biological Secretary at the end of 1935. Three years later he became Physical Secretary, at a time, shortly after Munich, when it was already quite evident, to people who were not blind, that war was coming. We served together as joint Secretaries of the Society till 1945, when my term ended; but after that I was Foreign Secretary for a year.
>
> 'When Jack joined me as Secretary in 1938, and indeed some time earlier in anticipation, one of our first activities was, with the warm approval of Sir William Bragg, then President of the Society, to do everything we could to make sure that scientific and technical manpower was properly employed in the war that loomed ahead. In the 1914–18 war, human scientific and technological resources, instead of being husbanded and properly employed, had at first been squandered and neglected. We proceeded to urge the Ministry of Labour to take this matter seriously. The action of the Ministry of Labour was to ask the Royal Society in consultation with other scientific societies and institutions, to prepare a register of scientific and technical personnel available in case of war (referred to of course as an "emergency"). Council minute 12 of 12 January 1939, under the heading "Scientific Service in a National Emergency", is worth quoting:
>
> > "The Secretaries reported that they had discussed with representatives of the Ministry of Labour details of proposed arrangements by which the Royal Society would approach the other scientific societies with a view
> >
> > (a) to completing the register of scientific persons available in the event of a national emergency,
> >
> > (b) to ensuring the more effective utilization of scientific personnel and of existing scientific organizations.

"Further proposals from the Ministry of Labour were expected shortly. The opinion was expressed that the register should include those younger members of the universities or other scientific institutions who, although of first-class scientific calibre, were not yet members either of scientific societies or of the staffs of their institutions; and that the best way to secure their inclusion would be a direct approach to the heads of scientific departments.

"Council recognized that although the early completion of the register was an essential step, its use would be comparatively limited without far more critical and expert supervision than was possible by any non-scientific organisation. The Royal Society could provide the machinery on the one hand and could obtain the expert advice on the other which, in consultation with various Government Departments, were essential if proper use was to be made by the nation of its scientific personnel and organization; and it could undertake the task forthwith. The Secretaries would have the full support of the Council in bringing these considerations to the notice of the Ministry of Labour and of the Advisory Committee."

'By March 1939 the Ministry of Labour had agreed to all our proposals and the construction of the Scientific Register was beginning. For some time work was done in the quarters of the Royal Society, in London and after war had begun in Cambridge, and by the staff of the Society; but finally it was removed to the Ministry of Labour (on condition that they took care of it!) and two members of the Society's staff were lent "to assist in its operation" and see that it was used properly. The construction of the Scientific Register proved to be a very heavy task, but it was enormously important and throughout the operation Jack's wide knowledge and obstinate persistence helped it to success.

'Early after Jack's coming to the Royal Society we began to discuss the importance of having expert and distinterested scientific advice available to the Government at a very high level of policy. For a long time our continuing efforts, separately and together and strongly supported by the President, appeared to be fruitless; to a politician without any knowledge of science, science like plumbing was no doubt quite important, but what could it have to do with policy? In the end, however, our efforts (like those of the importunate widow, and perhaps for the same reason) were successful and Council minute 5 of 24 October 1940 recorded,

"It was reported that in order to ensure the fullest co-operation of scientific workers with the Government in the national war effort, the Lord President of the Council, after discussion with the Officers of the Royal Society, had, with the approval of the Prime Minister, appointed a Scientific Advisory Committee to the War Cabinet, the members of which were Lord Hankey (Chairman), Sir William Bragg as President of the Royal Society, Dr E. V. Appleton, Sir Edward Mellanby and

Sir Edwin Butler as Secretaries of the Research Councils and Professor A. V. Hill and Professor A. C. G. Egerton as Secretaries of the Royal Society. The joint secretaries are Group Captain (later Air Chief Marshal) W. Elliot and Professor W. W. C. Topley. The terms of reference of the committee are:

(a) To advise the Lord President on any scientific problem referred to them;
(b) To advise Government Departments, when so requested, on the selection of individuals for particular lines of scientific inquiry, or for membership of committees on which scientists are required; and
(c) To bring to the notice of the Lord President promising new scientific or technical developments which may be of importance to the war efforts."

'The War Cabinet Scientific Advisory Committee, under the Chairmanship initially of Lord Hankey and later of Mr R. A. Butler and then of Sir Henry Dale, continued till 1945. It was succeeded under the Labour Government of 1945–50 by the Advisory Council on Scientific Policy of which (1946–52) Henry Tizard was chairman. It has continued since in various forms.

'The War Cabinet Scientific Advisory Committee undertook in fact a number of important tasks; though it could have been much more useful, if a scientific courtier had not monopolized the grace and favour of the Prime Minister. Among the first problems which it considered, in the autumn of 1940, was that of the warlike development of atomic fission, a possibility just beginning to be realized. Its strong advice, after very close consideration, was that this should be handed over to Canada and the United States. Our scientific and technical resources in Britain were being so fully stretched by then, and the difficulties and dangers due to enemy bombing were potentially so great, that the task could not properly have been undertaken here. In fact this advice was taken and the Tizard mission to the U.S.A. in the autumn of 1940 passed over the information we had here to the other side.*

'Another matter which Jack and I discussed continually in 1939, before and after the war had begun, was the critical importance of keeping the British Dominions properly informed about scientific and technical developments here, and about our operational experience with scientific equipment and devices. We suspected that this task of scientific liaison had been grossly neglected, it seemed to be nobody's business; that was

* As was pointed out to me by Mr Ronald Clark, the Tizard mission had been completed before the Scientific Advisory Committee was formed. It was not until the summer of 1941 that this Committee was officially consulted on the question of the 'uranium bomb'.

the sort of neglect that could have been impressed on the Cabinet by a Scientific Committee, had one then existed. Later, in the spring of 1940, when I went to Canada, I found how damaging had been our failure to keep Canadian scientists in touch. By the later summer of 1940 that had begun to be put right, but precious years had been wasted. The trouble was that few responsible ministers had any acquaintance even with the most elementary scientific matters, nor any notion of the scientific and technological development and resources of the Commonwealth, particularly of Canada and Australia. In the end a variety of activities were started by the Royal Society, which have matured in the appointment of scientific liaison officers, and such organizations as the British Commonwealth Scientific Office (B.C.S.O.) in London.

'Analogous to this problem was another, obvious to Jack and me and even more vividly in Tizard's mind, of how to take advantage of the scientific and technological help potentially available to us in the United States. In February 1940, therefore, Tizard contrived (with Jack's warm support) that I should go to the British Embassy in Washington, disguised (very imperfectly) as a supernumerary air attaché, with the purpose (as he put it) of discreetly "getting American scientists into the war before their country". By May (when many Americans were beginning to fear that the Royal Navy might surrender and leave their eastern seabord naked (!)) it became evident to me that the President would react favourably to a suggestion from here that their scientists and engineers should share information with ours and cooperate in war research. But it took months here to get it settled. Finally, however, Tizard went with his mission to America and in the spring of 1941, nine months *before* Pearl Harbor (!), J. B. Conant came to establish a scientific liaison office in London. A British Central Scientific Office was set up in Washington, to which a year later Jack himself went for five months to reorganize its work and to try to improve scientific communication between Washington and London.

'In October 1941 the Royal Society set up a British Commonwealth Science Committee "consisting of United Kingdom and Empire representatives, to consider means of promoting cooperation between the several parts of the Empire (a) in scientific research and (b) in the application of science to technical, biological, medical and economic problems". The report of this Committee, after many meetings, is annexed to Council minutes of 15 April 1943. The recommendations in this report had far-reaching results, e.g. (a) the calling of an Empire Scientific Conference which met in June 1946 (and was followed by the international tercentenary celebrations of Newton's birth, deferred from 1942), (b) the calling of a Conference on Scientific Information in June 1948 and (c) the establishment of the British Commonwealth Scientific Office (B.C.S.O.) in London. In all these Jack took a very active part, indeed the Information Conference was always recognized as his "baby".

'It is interesting now to recall how all this started. During the summer of 1941 a young New Zealand scientist, Nevile Wright, came on his own initiative to Burlington House to talk to us. His suggestion led us to call a conference on 7 October 1941 at the Royal Society's rooms to discuss them; as a result the British Commonwealth Science Committee was set up. I doubt if one young man's suggestions could have had so considerable an effect had they been made to a Government Department! But Jack was always ready to consider a bright idea; it gave him no glow of satisfaction to turn anything down, and he was ready to take infinite trouble to give a good idea a chance.

'In 1943 and early 1944 various Fellows of the Society approached the Secretaries with proposals that the Society should set up organized inquiries about the needs of research in various branches of science after the war. As a consequence committees were appointed to look into the problems involved. I was in India from November 1943 to April 1944, and the brunt of all this work (and of much else) fell on Jack; and he wrote himself an admirable synopsis of the six reports received. Later his synopsis was adopted as a Report of Council and was widely circulated.

'My visit to India in 1943–44 led to a reciprocal visit to the United Kingdom, in October 1944, of a group of Indian scientists. In both of these activities Jack was extremely interested, and—as usual—helpful; and the visit here of the Indian Scientists provided contacts which led him in 1948 to visit India as chairman of a committee to review the working and development of the Indian Institute of Science at Bangalore.'

Appendix II

These are excerpts from notes written by A. V. Hill in his *Memories and reflections*, chap. 45, about 'How I became a Member of Parliament in 1940'.

'Early in 1939 I was invited by this group to be their candidate at the next election. This proposal I could not accept, since (apart from other difficulties) to be a Member of Parliament would not be consistent with holding a full-time Research Professorship of the Royal Society.

'But early in December 1939, after the war had begun, a private inquiry was made to me, on behalf of the Cambridge University Conservative Association, as to whether I would think of accepting their nomination if Sir John Withers retired; he was in fact very ill. I replied that my time was rather taken up with various matters connected with the war, and with being Secretary of the Royal Society, but that owing to the war my previous objection did not hold since it was now impossible for me to continue my normal work; and that if it were thought useful that I should be in Parliament during the war and if the invitation were made to me I would consider it.

'Early in January 1940, after Sir John Withers's death, further indirect inquiries reached me, and on 13 January I was invited by Sir Geoffrey

Ellis, the Chairman of the London Committee of the Association, to meet him to discuss the matter. In our conversation I said (1) that it was most unlikely that I should be able, if elected, to continue in Parliament after the war, and (2) that I had never been connected with any political party and could not properly be described as a Conservative. His Committee, he thought, would have no objection to this, provided that I was a supporter in general of the policy of the Government. I agreed that I would accept an invitation on that basis.

'If it were thought best, I wrote to him later, to describe me as an Independent Conservative, I should tell my friends "that I am really an Independent nominated by a broadminded Conservative Association".

'The London Committee met on 18 January and invited me to accept their nomination. This I did in writing on 19 January.

'I had understood that a contest was unlikely, since there was an agreement between the main parties to that effect.

'The poll took place on 23 February and I was elected by a good majority. I "took the oath" on 27 February but had only ten days before sailing to America on 9 March on an errand (arranged some months earlier) which has been described elsewhere (*The Times*, 17 June 1941). So, effectively, my membership did not begin till after 13 June when I got back.

'When I arrived in New York, on about 20 March, I was met by the British Air Attaché George Pirie, today (1971) Air Chief Marshal, then Air Commodore. We had not met before and he described his alarm and despondency when he discovered, a week or so earlier, that his (temporary) colleague at the Embassy was not only a Professor but a Member of Parliament. The R.A.F. in fact had by then adjusted itself pretty well to what it called professors, but Members of Parliament were a different kettle of fish. We tried to hush it up as well as we could. Anyhow we did quite a useful job together before I returned early in June. Then I really did become an M.P. Some people would say I have never been quite the same since.

'I did not stand for re-election in 1945 and, as expected, the large Labour majority of the 1945–51 Parliament abolished University Representation.'

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