The energy, enterprise and judgment he displayed during the difficult war years would be considered exceptional, even in one trained to important administrative tasks. That they should be found in a man of science brought up in academic seclusion and long confined to the narrow paths of fundamental scientific research may be thought a portent.

On this subject, the memoirs are singularly revealing and present an interesting psychological study. Perhaps the main characteristics of the author may be summarized as an abiding enthusiasm for scientific studies, a deep sincerity of purpose and abounding self-confidence. From that day in early youth when, with some trepidation, he waited upon the great chemist Mendeléeff and received from the lips of the sage an opinion that his knowledge was too meagre for experimental work, until the occasion some thirty five years later when he celebrated his scientific jubilee amid congratulations from the whole scientific world, no misgivings ever entered his mind as to his high destiny. Indeed we may attribute to this trait an impatience with mediocrity and a highly critical attitude towards his colleagues and associates, which form one of the less pleasing aspects of his character.

The Revolution of 1917 found Ipatieff a lieutenant-general in the Imperial Russian Army, chairman of the important Chemical Committee and one of the key men responsible for the organisation and conduct of the industrial war effort. From the first, he refused to interest himself in political affairs, but was prepared to work loyally with any party in power. There were moments in those turbulent days which ushered in the spring of 1917 when it seemed probable that he would share the fate of his distinguished predecessor, Lavoisier. The revolutionaries of the Kremlin had no greater respect for savants than had those of the Luxembourg; many of his colleagues perished in the first explosion of popular wrath. But Ipatieff had powerful friends and loyal subordinates. "During the first days of the Revolution," he says, "the soldiers of the Chemical Battalion were worried about me and repeatedly offered their protection in case of danger." He continued to be employed by the Provisional Government, and later by the Bolsheviks, under Lenin. Although an uncompromising individualist, he contrived to work with the People's Commissars and with the Party representatives on his various committees. But his opinion of his colleagues is outspoken and critical. Of Kuibyshev, chairman of the Supreme Council of National Economy, he says: "I knew no more narrow-minded, stupid man than he. His knowledge of industry was nil, and, since he had no opinions of his own, his superiors could easily persuade him to accept theirs. I did not like him, nor he me." Of another eminent colleague, Lobov, he states: "His stupid, unattractive face classified him at once as one fitted for only the most menial work".

Holding these views, which he was not always successful in concealing, it is not surprising that he encountered increasing political obstruction in his efforts to organise and develop the Russian chemical industry in the post-war years. While Lenin and Trotsky were in power his position was assured; but Lenin was a sick man, and after his death Trotsky's influence declined, and he was finally expelled from the Party and exiled in 1927. Of all the revolutionary leaders with whom Ipatieff came in contact, Lenin impressed him as being the only one with the high ideals and vision necessary to

build up the new Russia on sound and progressive lines.

Stalin succeeded Lenin and, under his leadership, the Soviet Government gradually assumed its present form. The State Political Administration, afterwards the G.P.U., was created in 1922, and rapidly grew to be a powerful instrument of Government policy. Ipatieff's position became increasingly dangerous. His refusal to join the Party, his outspoken criticism of his political colleagues and his frequent visits abroad served to arouse the suspicion of the G.P.U. Many of his contemporaries were arrested and imprisoned or executed. "I reckoned," he says, "that up to 1930, of all the military engineer-technologists who had completed their training at the Artillery Academy, only two or three were left in Soviet territory. The remainder had been arrested and their fate was unknown. Day by day, these facts confirmed my suspicions that I could not long escape the fate of most of my dear students and comrades of the Artillery Academy."

He resolved to quit Russia for ever. Fortunately, he had duties which necessitated frequent visits to Germany; and, in June 1930, he was able to obtain permission again to proceed there on Government business. It was with a feeling of relief and gratitude that, in company with his wife, he passed the frontier for the last time; and on this happy note the memoirs end. It is gratifying to know, however, that after so many years of trouble and danger, Ipatieff spent his declining years a distinguished and honoured guest of the United States. D. M. NEWITT

OBITUARIES

Sir F. Gowland Hopkins, O.M., F.R.S.

FREDERICK GOWLAND HOPKINS, the father of British biochemistry, and perhaps the last of our great pioneers of science, died on May 16, at the age of eighty-five. His death will be felt with a keen sense of loss by all those who have come under his inspiring influence.

Hopkins was born at Eastbourne on June 20, 1861, in a house now destroyed by enemy action. While still an infant he lost his father, who had been an enthusiastic amateur in science. This loss greatly affected his subsequent career. He was educated at private schools. He published his first scientific contribution—a brief note—at the age of seventeen. Shortly afterwards he was articled to a public analyst, from whom he received his first technical training, and in 1883 he was appointed assistant to Sir Thomas Stevenson, the eminent Home Office analyst, whose evidence played an important part in many sensational trials. His real scientific education, however, began five years later, when at the late age of twenty-seven he became a medical student at Guy's Hospital. The ordinary medical curriculum constituted his only academic training. During his medical course he did important research and was the first holder of the Gull Research Studentship. He graduated in science and medicine at the University of London in 1894, and was a member of the staff of Guy's Hospital Medical School.

In 1898 Hopkins married Jessie Stevens, daughter of Edward Stevens, of St. Lawrence, Kent, and was expecting to follow a clinical career. In the same year, however, Sir Michael Foster invited him to join the staff of the physiological department at Cam-

bridge, with the task of developing and extending the teaching of the chemical side of physiology in the University. Here he held a University lectureship in physiology for some years. He was elected a fellow of the Royal Society in 1905. During 1905–10 he was tutor of Emmanuel College. In 1910 Trinity College offered him a fellowship and appointed him praelector in physiological chemistry, and in the following year he was made University reader in chemical physiology.

Up to this time the physiological chemistry department at Cambridge had formed a section of the physiology department; but in 1914 a special chair of biochemistry was created for Gowland Hopkins and a separate biochemical department was formed. In 1921 a large bequest from the trustees of Sir William Dunn made it possible to provide a separate building and staff for the new department. The building, accommodating about forty research workers, was completed in 1924, and under Hopkins' leadership a large and active school of biochemistry rapidly grew up and has played an important part in the development of the subject. He was knighted in 1925, and shared the Nobel Prize for Physiology and Medicine in 1929 "for his discovery of growth-promoting vitamins". During 1930–35 he was president of the Royal Society, and in 1935 he received the Order of Merit. He received many other honours, including doctorates from more than twenty universities. He retired in 1943, having held the professorship of biochemistry at Cambridge for thirty years. Such, in bare outline, was his career.

Hopkins made many fundamental contributions to biochemistry. Throughout his life and amid all his duties, he always managed to find time to keep his research going, though sometimes only with difficulty. He never wrote a book, but his scientific papers form a series extending over seventy years, from his first, published in 1878, to his last, sent in only a month before his death, and now in the press. He had considerable literary gifts, and many of these papers make delightful reading; it is fascinating to read them in chronological order and to follow the gradual development of his work and thought.

As a young man Hopkins was an enthusiastic collector of butterflies, moths and beetles. In 1878 there appeared large numbers of the little bombardier beetle, which ejects a cloud of violet vapour into the air when attacked. Hopkins was curious to know what this stuff could be; he showed that the vapour could be condensed in a test-tube, but at that time lacked the chemical knowledge to determine its nature. Fifty-seven years later, commenting on this, he said, "I think, however, that from that time my fate was sealed. Though the designation was not yet invented, I became there and then a biochemist at heart."

His first real chemical research, carried out between 1881 and 1895, was on the pigments of the wings of butterflies, and resulted in the discovery of the class of compounds now known as pterins, which recent work suggests may have important functions in the animal body also. Hopkins showed that they are closely related in chemical structure to uric acid, though their exact constitution remained undetermined for fifty years more. He returned to this subject near the end of his life, making further interesting observations.

This early work interested him in uric acid, to which much importance was then attached in medical circles, and he introduced in 1893 a method for its

estimation in urine, which remained the standard method for many years. He studied its excretion in various diseases, and published papers on the effect of various diets on its metabolic production. This was before the stages of nucleic acid breakdown had been made clear. Much later, in 1922, he made a further contribution to this topic by his discovery that milk contained large amounts of the enzyme which forms uric acid, namely, xanthine oxidase, upon which much work was later done in his laboratory.

In 1896 Hopkins became interested in proteins, apparently as a result of a chance observation that bromine quantitatively precipitated albumin from pathological urine. He prepared a number of halogenated proteins and gave reasons for believing that the halogen atoms were in the tyrosine rings. During this work he made a fundamental advance by devising a procedure for the easy and rapid preparation of crystalline proteins in reasonable amounts. Hofmeister's earlier method (by evaporating alkaline solutions containing ammonium sulphate) only yielded crystals with difficulty, and these were mixed with much amorphous protein. By adjusting the pH without evaporation, Hopkins obtained at once wholly crystalline material and showed that the product after recrystallization had the constant optical and other properties characteristic of a pure substance. This began a new era in protein investigation, and the method is now extensively used for the preparation of pure enzymes and other proteins.

Continuing his work on proteins in three classical papers with his pupil, S. W. Cole, Hopkins next investigated the Adamkiewicz protein colour-reaction (a purple colour on addition of acetic acid and sulphuric acid), which was believed to be a furfural reaction due to a carbohydrate group. They first showed that the test was due to glyoxylic acid present in the acetic acid and not to the acetic acid itself. Following up the substance responsible for the test, they succeeded in 1903 in isolating it by an elegant method from tryptic digests of protein as a beautifully crystalline product, which proved to be a new amino-acid and to be identical with "the much-sought tryptophane". "Tryptophane" had been the name given to the hypothetical substance in protein hydrolysates which gave the red colour on addition of bromine-water, but previously it had been nothing more than a name.

The year 1905 and those immediately following were especially fruitful. The occurrence of the indole ring in tryptophane had raised the question in his mind whether the animal body could synthesize the amounts it required or whether the ring must be supplied preformed in the diet. To decide this he made use of zein, a protein which does not contain tryptophane, and in a celebrated pioneer paper in 1906 reported that a diet containing zein as the only protein was unable to maintain growth in young mice, but that the addition of tryptophane greatly prolonged their survival period. Addition of tyrosine (already present in zein) had no such effect. It was suggested that the tryptophane was utilized as the normal precursor of some specific 'hormone' or other substance essential to the processes of the body. From this arose the subject of 'essential amino-acids', which is so important to-day.

It was but a step from this to his work on vitamins, for which Hopkins became most widely known, though it was only a fraction of his whole research output. In 1905, in order to see whether there were other

previously unrecognized essential dietary factors, he fed synthetic diets, containing all the known essential foodstuffs, but carefully purified. To them he added small quantities of meat extracts or extracts from yeast to give flavour to the tasteless food. He was thinking then of the animal's 'appetite'. He quickly found, however, that rats ate synthetic diets very well without such additions. But the extracts powerfully affected nutrition: on the flavoured purified diet the animals grew well; without the flavouring there was continuous loss of weight, although they ate the same amount of food. He reported some of these epoch-making results in an address to the Society of Public Analysts in 1906, beginning modestly with the words:

"Seldom, I imagine, has this learned society welcomed a visitor less obviously entitled to occupy its time." But already at this early date the essential conception of vitamins was clear in his mind. "No animal can live upon a mixture of pure protein, fat and carbohydrate, and even when the necessary inorganic material is carefully supplied the animal still cannot flourish. The animal body is adjusted to live either upon plant tissues or the tissues of other animals, and these contain countless substances other than the proteins, carbohydrates and fats. Physiological evolution, I believe, has made some of these well-nigh as essential as are the basal constituents of diet. . . . The field is almost unexplored; only is it certain that there are many minor factors in all diets of which the body takes account. In diseases such as rickets, and particularly in scurvy, we have had for long years knowledge of a dietetic factor; but though we know how to benefit these conditions empirically, the real errors in the diet are to this day quite obscure. They are, however, certainly of the kind which comprises these minimal qualitative factors that I am considering."

Publication of the results in full was, however, delayed until 1912 by prolonged but unsuccessful efforts to isolate the active substances. Hopkins never claimed to be the 'discoverer' of vitamins, though he might have done so with good reason; but it was certainly the 1912 paper which first awakened a general belief in the physiological significance of these substances. The battle was not won without a fight, and even so late as 1920 there was considerable opposition and scepticism towards the 'vitamin theory', especially on the part of a section of the medical profession. During the First World War, however, Hopkins had a great influence for good as chairman of official committees on war-time nutrition and famine relief, which did much important work. He frequently emphasized the inadequacy of a mere calorie figure as an index of nutritional standard—a lesson which seems in danger of being forgotten in some quarters at the present time.

In 1907 Hopkins also made, in collaboration with Fletcher, a most fundamental contribution to muscle biochemistry by showing that the production of lactic acid was intimately connected with the contraction of the muscle, and that it was removed once more by oxidation in presence of oxygen. This opened up a very large and fruitful field of work on tissue metabolism, on the glycolytic and oxidizing enzyme systems, and on the contraction process itself.

His next outstanding achievement was the discovery in 1921 of glutathione, the sulphur-containing peptide which is responsible for the nitroprusside

reaction given by animal tissues. The isolation was long and difficult and the product non-crystalline, but Hopkins was able to show that it functioned as a catalyst in biological oxidation processes, becoming alternately oxidized and reduced and so acting as an intermediate 'hydrogen carrier'. This first directed attention to the importance of such carriers, which occupy a prominent place in tissue respiration systems to-day, and stimulated much research which made Cambridge thereafter one of the main centres of the study of biological oxidations.

At that time Hopkins believed glutathione to be a dipeptide of cysteine and glutamic acid, but in 1927 two American workers suggested the presence of a third component, possibly serine, though not in the form of a tripeptide. Hopkins immediately re-investigated the matter, and in a very short time had devised an unusual but wonderfully elegant method by which in a single step glutathione was precipitated from crude extracts as a pure salt, which immediately yielded the beautifully crystalline peptide. This at once made it readily accessible for research, and Hopkins showed conclusively that it was a tripeptide of cysteine, glutamic acid and glycine. Later, he published two papers on the part played by ascorbic acid in catalysing the oxidation of glutathione.

In 1930 he studied the production of thiol groups during the denaturation of proteins by strong solutions of urea. In 1938 he discovered that the enzyme which oxidizes succinate depends for its activity upon thiol groups within its molecule; this stimulated much further work, and many '—SH enzymes' have now been found.

Meanwhile, Lohmann had shown that glutathione is the specific coenzyme of the enzyme glyoxalase, and Hopkins later took up the study of this enzyme. His last paper, now in the press, reports the discovery that the glyoxalase system contains a hitherto unsuspected protein activator, apparently of a new type.

Throughout his life Hopkins retained a remarkably sure instinct for selecting problems which would yield important results. All his papers, from first to last, contain results of much interest, and many opened up new fields of research.

Hopkins' influence on the growth of biochemistry, however, was by no means confined to the results of his own personal research, important though they were. He had a great gift of inspiring others to do fruitful work, and from the Cambridge school which he created has come a great body of research which has played a fundamental part in the development of modern biochemistry. From it, too, has come a steady stream of research workers who have played a considerable part in the development of biochemistry in other centres in many parts of the world. It is interesting to look through a list of those whose names are well known in the biochemical world to-day, and to note how many have worked in Hopkins' laboratory at one time or another.

He also exerted a considerable influence through many important presidential and other addresses, which he delivered from time to time, on the nature and potentialities of biochemistry in its various aspects. Some thirty of these were published in various journals; they are all interesting and many are accepted as classics. In several he laid great stress on the importance of the dynamic side of biochemistry—the study of processes and reactions in living matter, and not merely of chemical structure. He was never

satisfied with knowing what a substance *was*, but always wanted to know what it *did*. It was natural, therefore, that he attached great importance to the specific enzyme catalysts within the living cell which bring these reactions about, and encouraged research on them in his department.

"I will ask you to consider," he said in 1931, "whether catalysis on highly specific lines is not among the most fundamental and significant phenomena in Nature"; and later, "I myself would like to claim that the control of events by intracellular enzymes, exerted in the specialized colloidal apparatus of the cell, by itself secures the status of the cell as a system which can maintain itself in dynamic equilibrium with its environment. I am not denying for a moment that the cell has esoteric qualities which may call for organising influence of a greatly different kind, exerted maybe at some higher level. It is at any rate sure that the inter-related activity of highly specific catalysts represents a notable device of Nature which has supported during the course of evolution those dynamic manifestations which characterize living things."

Hopkins was the kindest and most lovable of men. I still have a vivid recollection, after twenty-seven years, of the kindness of his first welcome to me when I joined his Department, and it was the same with all his pupils and colleagues, by all of whom he was greatly beloved. He never made an unkind or irritable remark; though he could be critical on occasion, it was always with a courtesy that left no sting. He had great charm of manner and was invariably courteous, even to the least important of us. He was always ready to talk over our work and ideas, and somehow contrived to make us feel by the way he listened to us that our ideas were extremely interesting and our results important. A great many of the papers published from his Department carry a note bearing witness to his "inspiration and encouragement". It has been said by critics that he suffered fools gladly and all his geese were swans; but the fact is that many of them did actually turn out to be swans, and it was impossible to remain a fool for long in his company.

Under Hopkins' leadership an unprecedentedly wide range of topics was covered, both in research and teaching, and a one-year whole-time course of instruction in advanced biochemistry was developed in Cambridge which still remains unique in the world. His whole Department was permeated with a wonderful vitality and awareness of what was going on. To work there was to feel the thrill and sense of adventure in penetrating into the secrets of living matter, and life was never dull. We used to look forward to the daily tea in the laboratory, at which Hopkins, sitting at the head of the table, would make interesting and illuminating comments on the latest discoveries. He also presided at the weekly gatherings at which it was (and still is) the custom for one of the members of the Department to present the results of his research—a tradition which has now continued unbroken for more than thirty years. Hopkins' speeches at the annual 'Dunn dinners', at which for an hour or more he used to review the affairs of the Department and poke gentle fun at its members, were always a delight.

Later, when the multiplicity of committee meetings and similar duties made increasing demands on his time, we saw him less often; but the flame which his inspiration had lighted continued to burn, not only in his own Department but also in other centres to

which it was carried by many who had worked in his laboratory and come under his influence.

In build, Hopkins appeared slight and even frail, but until his last years he scarcely had a day's illness in the whole of his very active life. He was one of those fortunate people who are practically immune from colds and influenza. Perhaps this freedom from illness made it all the harder to bear when poor health did come upon him a few years before his death. In particular, the loss of his sight while he was still intellectually active was a heavy blow; but he faced it with great courage, and until the year of his death he continued to come to the laboratory almost daily and to carry out interesting research with the aid of E. J. Morgan, his assistant for forty-two years.

Lady Hopkins, whose companionship and care during nearly fifty years of married life contributed greatly to his happiness, survives him. Their son, Dr. Frederick Hopkins, is a physician; their elder daughter, Mrs. Barbara Holmes, is well known as a biochemist, and their younger daughter, Mrs. Jacquetta Hawkes, as an archaeologist.

MALCOLM DIXON

No better indication of the deep affection in which Sir Frederick Gowland Hopkins was held by biochemists in general—whether or not fortunate enough to have been his pupils—could be afforded than by the almost universal use among them of his nickname 'Hoppy'. To them he was a dear and lovable character and a great biochemist.

During his long life he saw biochemistry develop from the unfashionable interest of a few distinguished chemists to the stature of the modern science, and in this development he played a major and often decisive part at nearly every stage.

Convinced that an understanding of the processes of life must rest upon a sure knowledge of the structural chemistry of biological materials, his early work was devoted mainly to isolation and characterization. His success with Cole in the isolation from proteins of tryptophane, the indole derivative also being sought by Emil Fischer, gave him particular satisfaction; but in his work on the pterins, those pigments in the wings of white butterflies and which have recently come into such prominence, he was continually hampered by lack of material. As he sadly remarked to me not long ago, he could only make use of what he and friends could collect, whereas Wieland, prosecuting a similar study, could rely upon the proceeds of an organised, nation-wide collection of butterflies by the school-children of Germany.

An investigation of structure alone was to Hopkins a sterile pursuit. The life of the cell is change, "a dynamic equilibrium in a polyphasic system", and it was the duty of biochemistry, he felt, to study and explain the events of metabolism. His isolation of glutathione in 1921 indicated his growing preoccupation with the problem of intra-cellular oxidation, a field which he was so greatly to enrich and to cultivate to the very last. Closely linked with this was the question of the energetics of the cell, the means by which energy set free in the various steps of oxidation was utilized for the performance of vital functions. Hopkins was to see this fundamental problem attacked and developed by his pupils both in Britain and overseas.

The contributions which Hopkins made to nutrition, his careful experiments and the concept of vital accessory factors to which they led, were not divorced