THE ROYAL SOCIETY

ANNIVERSARY ADDRESS*

By SIR CYRIL HINSHELWOOD, P.R.S.

AWARD OF MEDALS, 1959

Copley Medal: Sir Macfarlane Burnet, O.M.,
F.R.S.

BURNET is among the most outstanding workers in the field of the viruses. Since 1925 he has made a long series of contributions to knowledge of the bacteriophages and he has elucidated the phenomenon of lysogenesis. He has shown how study of the range of activity of phages against various bacteria can be used to classify not only the phages but also the bacteria themselves.

He has studied many viruses pathogenic for vertebrates. He has shown how psittacosis is endemic in wild Australian parrots, and has thrown light on the epidemiology of herpes and poliomyelitis. He is well known for his development of several techniques for cultivating viruses in living chick embryos and their application in immunological studies of viruses. He has also made studies on the agglutination of mammalian and avian red blood cells by a number of viruses and virus-products, thereby throwing fresh light on the reactions taking place between viruses and the surfaces of susceptible cells. He found that an enzyme produced by cholera vibrios has an action on blood cells similar to that of influenza viruses.

From 1947 until 1951 Burnet worked on the reaction between influenza viruses and the muco-proteins on cell surfaces, and considered the mechanism whereby a virus can infect a cell. Between 1949 and 1958 he and his collaborators occupied themselves with the theme of genetic recombination between influenza virus particles carrying different, recognizable, marker characters. The possibility of a sort of hybridization between two virus strains was established. Burnet has applied these ideas in an attempt to understand how changes in virulence are brought about.

During the past few years he has turned to the study of fundamental aspects of immunity and has offered in a recent book on the 'clonal selection theory' a novel explanation of antibody production based on the idea of somatic mutation. His ideas about the body's ability to recognize 'self' and 'non-self' to a large extent predicted later findings on immunological tolerance. He applies the new ideas to tentative explanations of auto-immune diseases, of cancer and of ageing.

While so prolific of work and ideas, he has been of outstanding value in the councils of Australian science.

Royal Medal (A): Prof. R. E. Peierls, C.B.E., F.R.S.

Peierls's earliest work was on the theory of the solid state, a field in which he remains a leading authority. He has played an outstanding part in the development of 'fundamental theory', that is, in the

formulation of what are believed to be the most basic laws of physics from which all other laws of Nature should ultimately be derivable. The subject-matter of fundamental theory changes over the years. In the late 'twenties and early 'thirties the term was practically synonymous with the relativistic theory of electrons and photons, and even as a very young man Peierls, with Landau, made an important contribution to one of the deepest problems in this subject, that of the limits of observability of physical quantities. When in the mid-thirties Yukawa initiated meson theory and so brought nuclear physics into relation with fundamental theory, Peierls's predominant interest was also in this field. His work with Bethe on the deuteron and that with Kapur on the theory of the compound nucleus are important landmarks of the period.

More recently, Peierls has directed his main, though not exclusive, attention to the general theory of quantal fields and of elementary particles. His best-known single contribution to this rapidly developing topic is a paper on the general derivation of commutation relations for arbitrary field theory, the idea of which has since been built into a great deal of modern work.

For many years Peierls has been a leading exponent of fundamental theory in Great Britain and an outstanding leader in theoretical physics as a whole. In Birmingham he has created a large and extremely active school, and if to-day young British and British-trained theoretical physicists enjoy a great reputation and occupy leading positions, this is largely due to Peierls's work.

Royal Medal (B): Prof. P. B. Medawar, C.B.E., F.R.S.

Medawar's research has been on the biology of senescence, the problems of tissue grafting and the effects of cells upon each other. To these difficult and fundamental subjects he has brought order and clarity, and experimental approaches of great originality.

In some of his earliest work he measured for the first time a property that can be called the growth energy of the chicken's heart, by determining the amount of an inhibitor needed to stop growth. He showed how the rate of decline of growth energy can be interpreted to provide a measure of senescence, and in this and subsequent work he explored with great penetration and caution the various concepts of ageing.

Study of problems of differentiation led him to the hypothesis (with R. E. Billingham) that cells of the adult skin may actively transfer hereditarily transmissible characteristics to their neighbours. In spotted guinea pigs the dark areas may gradually encroach on the light areas, which contain pigment cells lacking the enzymes necessary for melanin formation. The encroachment was shown to be due to

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the 'infection' of the light cells by the genes of their neighbours.

Still more fundamental analysis of the problems of tissue inheritance and differentiation followed in Medawar's main work on tissue grafting. A graft from one individual to another will not in general survive (except with identical twins). He showed that this was due to the fact that the graft induces the formation of an immune reaction by the host. The power to react against homografts was, however, found to be prevented from developing if the host animal was injected very young with cells from the donor strain. A mouse, 'tolerant' in this sense, could be made sensitive again if injected with cells from a live mouse of its own strain.

Very recently Medawar and his colleagues have discovered ways of disintegrating cells ultrasonically without destroying their antigenic power. By fractionation it was then shown that this power resides in the nucleus and not the cytoplasm and may be associated with compounds of deoxyribonucleic acid and proteins.

These discoveries have thrown new light on the nature of the differences between individuals and open up important possibilities for their chemical analysis.

Davy Medal : Prof. R. B. Woodward, For.Mem.R.S.

Woodward is by general consent among the leading organic chemists of the world to-day. His most important work has been in the field of natural products, and he has made major contributions to the elucidation of the structures of cantharidine (1941), penicillin (1945), strychnine (1947), sempervirine (1949), santonic acid (1949), patulin (1949), terramycin and aureomycin (1952), cevine (1954), magnamycin (1956), rauvomitine (1956) and gliotoxin (1958).

In the course of these studies he has contributed significantly to our understanding of biogenetic pathways, especially for strychnine and in steroid-triterpene relationships. Characteristic features of his structural work have been the clarity and penetration of his reasoning and the extensive application of modern physical methods. It was by his correlation of ultra-violet spectra with substitution patterns in unsaturated compounds (1941-42) that he made his first important contribution to chemistry. The resultant 'Woodward Rules' have been invaluable, and his own subsequent use of ultra-violet and infra-red methods has been a model to organic chemists.

Woodward's achievements in the field of synthesis are among the most spectacular features of organic chemistry in recent years. His synthetic studies have included work on morphine (1951), and have resulted in the first syntheses of many other important natural products including quinine (1944), sempervirine (1949), patulin (1950), cholesterol and cortisone (1951), strychnine (1954), lysergic acid (1954), lanosterol (1954) and reserpine (1956). Not only are these syntheses notable for their elegance in conception and execution but also they have done much to bring stereospecific reactions into general use in the synthesis of complex molecules and have greatly influenced all recent work in this field.

The scope of his work is further indicated by his demonstration of the aromaticity of ferrocene (1952), his work on reaction mechanisms, especially of the Diels-Alder additions, and most recently his con-

tributions to our understanding of the theory of optical rotatory dispersion.

Hughes Medal: Dr. A. B. Pippard, F.R.S.

Pippard has made outstanding contributions to low-temperature physics, and he must be considered one of the leading experimenters in this field. He has combined first-rate experimental work with a mastery of theory.

Starting with superconductivity, Pippard introduced an important modification to the London theory, a phenomenological description of the electromagnetic properties of a superconductor, which for many years has been an important guiding light in the subject. He was led to this modification by his own experiments on the depths of penetration of currents in superconductors. These were explained by the postulate of long-range wave-functions and thus non-localized effects, the current density at a point depending on the integral of the vector potential over a region (of about 10^{-4} cm.). Later developments in the fundamental theory have tended to confirm the correctness of Pippard's conception.

He also studied the anomalous skin effect in non-superconductors and gave a simple but complete picture of what happens when the mean free path of the conducting electrons is large compared with the skin-depth of penetration of high-frequency currents.

More recently, Pippard has carried out detailed measurements, again at high frequencies, on the surface resistivity of single metal-crystals, analysing the variations which occur in different directions related to the crystal axes. In his work on copper, he has shown how such measurements can lead to a plot of the 'Fermi surface' of the metal. By this is meant that a contour can be plotted of the way in which the positions of the valence electrons of highest energy are woven into the crystal-lattice structure. This adds to our knowledge from X-ray crystallography of the lattice structure of the nuclei in a crystal, fundamental information about the geometrical pattern of the electrons.

Pippard's work is characterized by deep originality, coupled with experimental ingenuity and a profound theoretical insight into his subject.

THE INTERNAL AND THE EXTERNAL WORLDS

There has been no slackening in the flow of significant discoveries from the world of science. The most spectacular event of the recent past has been the transmission from the Russian *Lunik* of photographs showing the remote face of the Moon, an achievement acclaimed equally by the layman and the man of science. In a more recondite way interest has been aroused by an electrostatic theory of cosmological expansion, and in contrast with these escapes, in action or thought, beyond the bounds of the Earth, plans have been made for unprecedentedly deep drilling into its interior. Syntheses such as that of coenzyme A and of 6-amino penicillanic acid have further strengthened the alliance of organic chemistry and biology, and the production of specific forms of deoxyribonucleic acid outside a living cell but primed by the presence of existing deoxyribonucleic acid has been another step towards the understanding of the material basis of life.

Any of these things, and indeed many others, might well form themes for a presidential discourse, but with a special end in view I shall single out for mention one or two isolated and indeed rather specialized samples. These are chosen because they not only involve fascinating discoveries but also because they lead us to ponder once again on deep questions which should not be ignored by the contemporary man of science. They relate, in fact, to the concomitance of the inner world of conscious experience and the outer world of Nature. This extraordinary problem is always with us: but the unexpectedness of the new observations, though it does not really disclose new kinds of mystery, does reawaken us to awareness of something, the strangeness of which familiarity tends to dull.

The social life of insects cannot but fill the onlooker with wonder, and arouse speculation about the conscious elements which may lie behind the behaviour manifest to an observer. Nobody intimately acquainted with individuals among the higher animals can seriously doubt that they possess some inner life, perhaps not entirely unlike our own. But that of the insects is by our standards likely to be very peculiar indeed: yet there is in all probability an intelligible pattern to it. The Rothamsted work on the 'queen substance', transmitted from the queen bee to the other members of the hive, shows how this chemical compound regulates the whole reproductive process of the bee community and dominates the organization of their lives.

The inward concomitants of the observed behaviour we can scarcely imagine, and indeed the control of highly complex individual and communal actions by a chemical substance could easily suggest a purely behaviourist view of living creatures, and lead to the denial of the internal world altogether. This I believe to be philosophically wrong.

Another recent research provokes us to think about the matter, as it were in the reverse order. We are familiar enough with human colour vision and can scarcely doubt the existence of this as a personal experience. The external conditioning of it has recently been stated by Land to differ very surprisingly from what had been supposed, and to be of a quite extraordinary character. The essential experiment is made in the following way. A coloured scene is photographed by means of a split-image camera simultaneously through two filters, one of which cuts off the upper half of the visible spectrum and the other the lower half. Two black-and-white positive transparencies are thus prepared. These are projected separately each with a different monochromatic light, for example, two yellows differing in wavelength by a few hundred angströms, and the images are recombined. The resultant produces in the observer the whole gamut of colour sensations. Thus information can be supplied to the brain so that, as Land puts it, "the eye functions to see full colour in a universe involving only a narrow wavelength band".

The question of the relation of the internal to the external world is again brought into sharp relief by these remarkable findings.

The topics I have mentioned can, of course, be treated without specific reference to these problems, but they lose a great deal of their interest if the implications about consciousness are ignored or denied. There is indeed one group of researches, carried further during the past year, in which these implications cannot possibly be evaded, namely,

those in which physiological stimulation of the conscious brain is correlated not only with the behaviour of animals but also with the psychological experiences of a human subject.

The central problem of mind and matter is not always thought worthy of their attention by men of science, yet it was given profound consideration several decades ago by Sir Charles Sherrington, and we are vividly reminded of it in the most recent book of one of our senior Fellows, Lord Russell. At a moment, too, when Darwin is again very much in our minds, there are certain aspects of the whole matter about which it is highly important to think clearly. The question raises a still more general issue which I should first like to consider. There are few worse condemnations of a theory than to label it metaphysical, a term suggesting the attempt to arrive at truth by speculation divorced from experiment or to interpret reality by statements empty of scientific sense. Little enough enlightenment is afforded by such an assertion as that the orbit of a heavenly body has a given geometric form because this constitutes the perfect figure. Scientific theories are properly expected to account for many things in terms of few, to predict new phenomena or to yield verifiable, quantitative results. Yet too austere an application of this principle can segregate the world of science from the general world of intelligent appreciation, an unfortunate event at a moment when there is growing realization of the interest of science to the community at large.

Most men of science would disclaim any great concern with philosophy and especially with metaphysics. But what is metaphysics? In the last resort it is the search for a statement subsuming the ultimate nature of all reality. Science has more modest hopes, and modern physics led the way to a considerable renunciation in this respect which has had a profound influence on philosophy itself.

Yet in science the total neglect of philosophical aspects may be unfortunate. It can lead, on one hand, to statements which are sensational but unsound, and, on the other, to an unhealthy indifference to the relationship of science to existence in general; and in any event, even though science may seem to decline metaphysical statements, it not only throws out challenges to philosophy but also is frequently itself confronted with problems inescapably philosophical in nature.

Scientific theories, though less ambitious than the systems of the older philosophers, and though claiming neither universality nor finality, do aim to be comprehensive and do hope to stand the test of time as long as possible. Moreover, we do judge them by a criterion in which it would be hard to disclaim every metaphysical tinge, namely, by the degree of mental and aesthetic satisfaction they afford. However much we may protest, utility is not enough. There is, undeniably, in the law of gravitation some quality distinguishing it from a set of empirical formulae, however convenient. Men of science do, unconsciously at least, place hypotheses about Nature in a sort of hierarchy of esteem, where the conservation of energy and the second law of thermodynamics rank high and mere working rules rank low.

The difficulty of complete aloofness from philosophy is illustrated by parts of physics. The theory of relativity dominates cosmology and defines the relationship between matter and energy. The quantum laws and the Pauli principle provide the foundations of chemistry. Yet these powerful and

productive generalizations involve distinctly metaphysical elements. Although it seems to have been relatively late in the development of thought that a clear distinction between subject and object, between the external world and the observer was recognized at all, for most men of science there was not much question about it at the beginning of the present century. Einstein, however, asserted the meaningless character of space and time abstracted from operations with measuring instruments and clocks and thus established the observer as an indispensable participant, whose status was increased by the 'uncertainty principle'.

According to the Pauli principle, observability becomes identifiable with the very possibility of existence. Thus the foundations of inanimate Nature can scarcely be discussed without recognition of the inadequacy of earlier spatio-temporal descriptions of reality, and without admission that subject and object had been in some respects too crudely separated.

The fundamental laws of quantum physics can be summarized in the wave equation and in a set of rules for its operation. Some people, it is true, say that they are content to accept these without deeper inquiry. But in fact every one, whether he admits it or not, seeks something which he calls understanding. The professed empiricism about wave mechanics is half-hearted, and more often than not the abstract mathematical formulation is given a metaphorical translation in which symbol and reality become very much confused. 'Waves of probability' are created, electrons become 'clouds', potential barriers are 'tunnelled through'.

When sound metaphysics goes, the seven devils of bad metaphysics soon enter to fill the gap and give an illusion of clarity. Metaphors which may be helpful in illustration easily take control when the abstractness of the mathematical formulation becomes too austere, a fact which bears witness to the insistent demand of the mind for satisfaction by something beyond utility.

Incidentally it may be remarked that if the more serious and responsible men of science remain aloof from the task of relating their subject to its philosophical background, the less serious and responsible will do it for them, and will startle the uninitiated with fantastic paradoxes which may impress the layman, but do science real harm. The discovered facts of Nature are mysterious and impressive enough in their own right. That light seems to recede from relatively moving observers at the same rate: that the universe may look much the same from anywhere: that measured mass may vanish into energy of radiation: that states of energy form a discontinuous series: that indistinguishable particles cannot co-exist: that in the world of small enough dimensions particles and waves lose the significance suggested by macroscopic analogies: none of these needs dressing in sensational form to make its impact on the thoughtful mind.

Nor, on the other hand, are they merely to be made the basis of formulae for the sole purpose of computations. In the last resort what men of science search for is the vision of Nature, and this must be expressed and communicated in those terms which provide the nearest approach to real understanding.

If this is true of the physical sciences, it is equally so of biology. One of the transitions from physics to biology is illuminated by a remark of Heisenberg:

"The mathematical formulae indeed no longer portray nature but rather our knowledge of nature".

The question, then, of the relation of the internal and the external worlds cannot and should not be ignored by men of science.

It is surprising that biological discussions often under-estimate human consciousness as a fundamental experimental datum. In science we attach no value to unverifiable deductions, or to empty qualitative statements, but nobody defends the neglect of experimental data. Among these we cannot validly disregard those of our own consciousness except by a deliberate abstraction for which we must assume responsibility, and which we should not forget having made.

It is tempting to ignore observational facts when they seem intractable, since we rightly abstain from the attempt to arrive at the truth by speculation. But in this we are not always consistent, and indeed very important philosophical conclusions are sometimes propounded by men of science. Moral and aesthetic qualities in man, for example, are not infrequently said to be explained by the operation of natural selection. Again, it is sometimes asserted that suitable combinations of machines could, in principle, produce results indistinguishable by any operational test from animal or even human behaviour.

The mind-matter relation is quite often dismissed as non-existent or meaningless. But moral qualities are not explained by natural selection, human behaviour is not machine-like and the mind-matter relation cannot be ignored in an intelligent consideration of existence.

The approach to the problem of consciousness must admittedly be egocentric. I have to begin logically with the, to me, indisputable fact that I have a wide range of conscious experiences (which are indeed more important to me than anything else). The significance of this fact can be questioned in two ways: first, by the objection that so far as any operational test goes other people may well be behaving simply as machines, and secondly, by the assertion that my consciousness is a more or less irrelevant concomitant of behaviouristic reactions.

I am, it is true, not certain that other people have consciousness. Neither indeed am I certain that the atomic nucleus exists. But I regard its existence as in the highest degree probable. I regard consciousness in other people as equally probable and for similar reasons. The atomic nucleus is not directly observed. It is inferred by elaborate reasoning from many complex experiments, any one of which could probably be given alternative interpretations. What carries conviction is the fact that a coherent body of doctrine emerges from large numbers of varied tests.

We are all the time trying experiments on our relations with other people, informing, asking, ordering, obeying, resisting, with varying emotions which are correlated with our actions. Human evolution has developed an elaborate and sensitive communication system, brought into play in innumerable ways. The hypothesis that other people have an interior life not unlike my own enables me to register correspondences at point after point in so intricate a way that I accept the hypothesis, if not as absolute truth, then as something nearly as good. And with most of the basic conclusions of science I am in no position to demand more.

Thus the content of consciousness must rank as something directly experienced by everyone, and

therefore as providing observational data. This conclusion is not changed in the least by the consideration that the development of communication between individuals confers a biological advantage and is favoured by natural selection in so far as mutual assistance and the transmission of acquired knowledge can assist survival. The communication mechanisms exist and one of their uses is to enable us elaborately to test the coherence of predictions from the hypothesis that conscious life is on the whole much the same for different people. People like poets and novelists describe this inner life: their writings serve little enough biological purpose, but they are (sometimes at least) intelligible to the rest of us, and evoke memories of our own experiences, which check as significantly as those coincidences of calculations and dial readings on which we base our views about the physical world.

Nor can the observational data of consciousness be relegated on the ground that they are on the whole qualitative rather than quantitative. Science has to come to terms with qualities, and indeed Weisskopf has pointed out that the quantum theory itself introduced fresh qualitative distinctions into a region where classical physics expected only quantitative differences.

The conscious experience is sometimes set aside as supernumerary and irrelevant, on the ground that a machine can perform actions indistinguishable from those of a man (or with greater technical perfection could do so). The answer that machines like the so-called electronic brains work only to a 'programme' brings the rejoinder that a set of machines could itself be programmed by another machine. But the master machine would itself need a programme. This would have to be provided by another machine, and so on in an infinite regress, there being no way in which the sequence could be closed to a self-contained cycle.

The contention that a human being is a system of self-programming mechanisms seems to depend upon the error of neglecting relevant observational facts, those of consciousness belonging to precisely this category. In its higher functions the human brain is programmed, not by other mechanisms, but by aesthetic and moral elements which somehow have their seat in the consciousness, by elements, that is to say, which belong to the half of reality concerned with the observer rather than the observed. Of the concomitance of consciousness with brain processes there is no doubt, but concomitance does not mean identity. Changes in the electron-levels of an atom are associated with the emission of light quanta, but a photon is not a difference of quantum states. Nor in a concomitance of *A* and *B* is it justifiable to assert that *A* is the cause of *B* without admitting the possibility of a reciprocal relation. In particular, if we assert that physical happenings in the brain can affect consciousness, we must admit in principle that physical happenings in the brain may be consciously caused.

But it is an abstraction to speak of either category in isolation. For many purposes the two may be separated as a legitimate approximation, but this does not mean that they can be regarded as independent.

In parts of biology questions of consciousness are not of direct importance but cannot in general be set aside. Behaviourism might give a good approximation in describing the actions of intercommunicating individuals in a group, but it ignores the experimental

datum, known to each individual about himself, and, by the coherence argument, about others, that in their conscious minds what men individually think or feel is of far more importance to them than any mechanical part which they may play in the biological community.

There is, of course, a clear enough meaning in the statement that consciousness and moral and aesthetic feelings are developed by evolution and natural selection. The power of conscious reasoning increases the chance of individual survival: social instincts favour the survival of the community, and are related to moral feelings. Aesthetics enter deeply into intellectual activity. There need be no difficulty in agreeing that these things have selective advantage. But the recognition that something present will be selected gives no clue whatsoever to its actual nature or genesis. For the purposes of natural selection a purely unconscious reaction of the brain and nervous system would have sufficed. Beneficial reactions indeed need have no conscious counterpart, as is widely evident in human physiology. But behaviouristic descriptions in general are models and abstractions ignoring data which, so far from being trivial and irrelevant, are the only things which make us *inter alia* concern ourselves with science at all. In any event, if free will, moral feelings and other conscious elements are illusions superposed on a behaviouristic background, wherein can lie their selective advantage?

There is at present no obvious answer to the question of what kind of advance can possibly be hoped for in the problem of psycho-physical concomitance. This, however, is no reason for giving up thought which at least helps to avoid the kind of errors so easily made both about physics and about biology when the problem is ignored.

It would, moreover, be a mistaken policy for men of science to withdraw from the inquiry. Lucretius might well have been asked how any real knowledge of his primordial particles could ever be obtained and would have been unable to answer. Before Galileo and Newton there were no appropriate concepts in terms of which to understand the flight of a projectile. At one time the rusting of iron must have seemed a process *sui generis*. The discoveries of science and the evolution of its grammar go hand in hand. Negative predictions are discredited by the famous pronouncements of Comte: "Toute recherche qui n'est point finalement réductible à de simples observations visuelles nous est donc nécessairement interdite au sujet des astres. . . . Nous concevons la possibilité de déterminer leurs formes, leur distances, leurs grandeurs, et leurs mouvements; tandis que nous ne saurions jamais étudier par aucun moyen leur composition chimique".

In the earliest times the description in rational terms of physical Nature was not so much an unsolved problem as one which people did not even conceive.

Human knowledge will not be in a satisfactory state until the dichotomy of the internal and the external is somehow removed.

In one way the man of science, because he starts by demanding least of an explanation, is the most likely to succeed in finding it. The question might be asked: What happens when an atom emits light? The more naïvely this is considered the less is an answer possible. But the laws governing various correlations, change of atomic state with quantum emission, or quantum with field have been formulated in terms of concepts appropriate to the problem, and

they yield satisfaction not only by making possible quantitative predictions but also by an inherent elegance. Eddington once discussed the way in which the terms of physics link together in endless cycles and pointed out that in one way Newtonian mechanics constitutes a vast tautology. This is often true in so far as physical theories create, as it were from nothing, a series of definitions and concepts by the aid of which things previously intractable are brought together into order and intelligibility.

In the light of this analogy, the further exploration of the concomitance of the internal and external worlds appears less permanently hopeless. The right grammar and language need to be evolved. In the process the present bounds of science may expand, but they have never been established by a firm decree. Chemistry and physics have united with biology and penetrated regions once thought inaccessible. Physiology is already allied with psychology and together they may search in strange and hidden places. There will no doubt be difficulties of which

Freud's struggle for acceptance provides a warning example, but it may be recalled that chemistry and physics themselves arose from a welter of charlatanism, magic and surmise as the correct language in which to describe their phenomena grew up. There are so-called para-scientific aspects of biology and psychology, which to-day show all too often the discouraging characteristics of the worst days of alchemy. Yet the history of chemistry warns against a final condemnation.

In the meantime those numerous studies are to be welcomed which, without solving the central problem, keep it constantly alive: observations on individual and communal behaviour in animals, on perception and illusion, investigation of the processes of learning and memory, construction of machines which imitate the mental functions, search into the phenomena of sleep. Above all, there lies hope that sooner or later to the eye of genius some quite ordinary phenomena will reveal, like the fall of Newton's apple, an undreamt of but thenceforth obvious significance.

THE SHAPE OF PROTEIN MOLECULES SUGGESTED BY ELECTRON MICROSCOPY

By DR. R. C. VALENTINE

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THE weights of most of the important protein molecules are now known with a fair degree of certainty. Apart, however, from some of the fibrous proteins such as collagen, speculation about their shapes and sizes is less surely based. The weight of a protein molecule when multiplied by the readily determined value for its partial specific volume gives the volume of the anhydrous molecule. Therefore, if protein molecules were compact spheres, their diameters would be known, and values calculated in this way from available data¹ are listed in Table 1 for various proteins. But a diameter can also be calculated¹, again on the assumption of a spherical molecule, from the hydrodynamic behaviour of the protein, in particular from its rate of diffusion and sedimentation in the centrifuge and the viscosity of its solution. In almost every case this diameter comes out to be significantly larger than that indicated by the molecular weight, the ratio of the two values giving the frictional ratio for the molecule. There are three possible explanations for the discrepancy, that is, for frictional ratios greater than unity: (1) the molecules may carry water either internally or as a surface layer, and thus behave in solution as larger objects than the calculated compact anhydrous size; (2) the molecules may be elongated rather than spherical; (3) the hydrodynamic formulae involved in the calculations may not be strictly applicable to protein molecules.

The third explanation is not always considered, but in fact there is no compelling evidence that molecules behave like smooth, rigid bodies, as theoretically required; nor indeed any direct evidence that the formulae used are valid for objects as small as a molecule. The two other possible explanations are usually both taken into account and lead in the following way to a picture of the molecular shape. The

extent to which proteins are hydrated is not easily measured, but 0.3 gm. water bound per gm. protein is thought in most cases to be a good estimate. Assuming some such figure, one can next calculate from theory² the ratio of the length to the width of the molecule that would then account for its behaviour. Table 1 shows the results of these calculations. The molecules are assumed to be ellipsoids—either prolate (cigar-shaped) or oblate (disk-shaped)—but provided the structure is rigid, the length-to-width ratios are not critically dependent on the exact model. Except for ferritin, all the proteins listed come out to be distinctly elongated, and it is as long prolate ellipsoids that these protein molecules are usually visualized.

The electron microscope, with its limit at a resolution of 15 Å., ought now to be capable of confirming these theoretical deductions by showing the shape of the anhydrous molecules directly on a photographic plate. That it does not do so is due to the low electron-scattering power of proteins, and in practice no untreated molecule with a molecular weight less than about 2 million can be detected at all. However, the contrast is greatly increased by metal shadowing and in this way Hall has obtained some fine pictures, for example, of catalase³ and fibrinogen⁴. But such pictures require exceptional technical skill, and as usually employed the metal coating is too grainy to give a reliable picture. In addition, the structure of the supporting film is inevitably brought out and can cause confusion. But even allowing for these difficulties, it is curious that in every attempt so far published the electron microscope has failed to show the expected elongated forms of the protein molecules.

A method that shows very fine detail on the surface of virus particles has recently been developed by Brenner and Horne^{5,6} and which they have termed