Progressive Biology.*

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IT is not going too far to claim that recent progress in experimental biology, though to a superficial view less impressive, has been not less significant, and indeed not less revolutionary than the progress of modern physics. I might support this claim in many ways. It is, I think, justified in that region of knowledge where cytology and genetical studies meet. The progress and the significance have become the greater since it was recognised that the material units of characters—the chromosomes and subdivisions of chromosomes—are ‘determinants’ rather than ‘carriers’ of genetic factors.

This domain of disinterested science is making many practical contacts. To mention but a single recent instance: Prof. R. C. Punnett, one of the original discoverers of the phenomenon of sex-linkage in inheritance, by applying his expert knowledge of that phenomenon, has produced what may be called a synthetic fowl, of which the qualities are such as to make it of extreme value to the now highly important industry of poultry breeding and egg production. The bearing of the same body of knowledge upon human affairs has been recently very ably discussed by Prof. L. T. Hogben.

The phenomena of heredity were long the stronghold of those who cling to the obscurantism of vitalistic doctrines. Infinitely complex as of course they are, we have now abundant proof that they are susceptible to analysis and that to-day they are yielding their secrets to well-controlled experimental studies. The results of these are becoming quantitative and are even yielding material for mathematical treatment, as the interesting writings of Dr. R. A. Fisher and Prof. J. B. S. Haldane have shown.

Another region in which accurate experimentation has removed, and is continuing to remove, inhibitions due to obscurantist assumptions is the physiology of the nervous system of vertebrates. It is, perhaps, too late in the day to refer to the work of Pavlov upon conditioned reflexes, though it is justifiable to emphasise its still growing influence upon thought. The work is a supreme proof of the success of the experimental method in analysing even such apparently transcendental phenomena as those which underlie the higher functions of the brain.

The nature of the transmission of events in the nervous system is receiving much illumination from the work of the Royal Society's Foulerton professors. Prof. E. D. Adrian, having developed a most admirable experimental technique for the purpose, is studying the nerve impulse and its origin with highly profitable results. He and his colleagues are now able, with great gain, to work with single nerve fibres and single isolated end organs.

A striking circumstance, brought to light by Adrian's work and that of his colleagues, is that the nervous structures so far examined exhibit

such physical regularity in their behaviour that results can often be predicted within about one per cent. His experiments on animals have shown how the phenomenon of a grading in the contraction of muscles is controlled by the frequency of impulses sent out from the central nervous system, and by the number of nerve and muscle fibres involved. Moreover, he has been able to observe the activity of a single nerve cell in his own spinal cord by needle electrodes placed in his muscles, and finds human voluntary contractions are regulated in exactly the same way.

Further, Adrian has found that slow potential changes occur in nerve cells and that these are connected with their discharge of impulses; so far this work only extends to isolated nerve ganglia from insects and to nerve cells in the brain stems of fish, but the phenomena he has found are extremely significant, and it seems possible that changes of potential may be of fundamental importance in the activity of nerve cells.

Adrian has found that damaged nerve fibres set up impulses at very high frequencies, and these perhaps play an important part in sensations of pain, though his more recent work has made it clear that impulses in the smaller slowly conducting nerve fibres must also be concerned in the physical mechanism responsible for pain. A most striking feature of all this work is the general similarity of behaviour of nervous structures from whatever animal they may be taken.

Prof. A. V. Hill is studying the nerve impulse from the point of view of the thermal phenomena which accompany it. So small, of course, is the heat production in the nerve that its measurement, like that of the potential changes, calls for great refinements. It is becoming clear, though we do not yet know the details of its nature, that the nerve impulse consists of a transmitted physico-chemical event, probably involving changes of ionic concentrations at membranes with consequential changes of electric potential; the whole cycle of events, comprising activity and recovery in the nerve, being supported by the energy derived from metabolic oxidative processes which, very small in scale, are associated with the cycle.

When we hope for an increase in our knowledge of the nervous system we are always accustomed to look to researches from the laboratory of Sir Charles Sherrington. An extended study of reflexes has shown that the centripetal impulses do not pass straight through the spinal cord, but at central stations in the cord they are transformed into an enduring excitatory state, which may in turn set up fresh nerve impulses yielding the reflex discharges. The nature of this central excitatory state is being studied and will link up, I think, with some of Adrian's observations upon cell potentials.

It has long been suspected that when a sympathetic nerve is stimulated, adrenalin is liberated at the nerve ending, and that the observed

* Excerpts from the presidential address at the anniversary meeting of the Royal Society on Nov. 30.

effects are immediately due to the action of that substance. Now Dr. H. H. Dale, in conjunction with a member of his staff, Dr. Gaddum, has investigated the case of the para-sympathetic nerves, the influence of which in general opposes that of the sympathetic group, and has obtained good evidence that when one of these is stimulated, the substance acetyl-choline, previously existing in some inactive form, is liberated at the nerve ending. The action of acetyl-choline when injected into the circulation resembles in general the effect of stimulating para-sympathetic nerves, and there is every reason to believe that the physiological activity of the substance, rather than the transmitted physical impulse itself, is immediately responsible for the observed effects of stimulation. I may say that Otto Loewi, of Graz, has shown that when the heart beat is inhibited by vagus stimulation, acetyl-choline is actually formed in the organ, and the same substance, when artificially injected, is known to produce effects like those of the vagus.

In rather unexpected circumstances we have thus brought before us an example of specific physiological effects due to the influence of the specific structure of an organic molecule. Such effects and such relations are being demonstrated in increasing diversity as fundamental factors of organisation in the animal body. This is illustrated most strikingly, of course, in the domain of the control of its activities by a group of hormones. We find in the cases of adrenalin and thyroxin, the constitution of each of which is accurately known, widely different influences depending on differences of molecular structure.

I may logically pass from hormones to devote a few words to vitamins. We now possess proof that vitamin A is closely related to the carotenes, and this knowledge may well lead, without long delay, to the artificial synthesis of the vitamin itself. With respect to vitamin D, it seems probable, if not yet quite certain, that its artificial production is already accomplished. Some four years ago the constituent of animal and vegetable substances, which is converted into the antirachitic vitamin D by ultra-violet radiation, was identified as ergosterol by Rosenheim and Webster at the National Institute for Medical Research, and concurrently by Windaus in Göttingen. A team of workers at the National Institute, led by Dr. R. B. Bourdillon, appear now to have arrived at the next stage, of isolating the vitamin itself, in crystalline form, from the mixed products of irradiation; and Prof. Windaus, following with his co-workers a different route, has again arrived simultaneously at the same goal.

There is no doubt that the substance which the British group now term 'calciferol', and which they have isolated as a dinitrobenzoate from the mixed product, is identical with the 'vitamin D₂' which Windaus and Linsert obtained by a different method; and there is little doubt that this substance, as obtained in either laboratory, is the essential vitamin D in a state of practical purity. One milligramme of calciferol has an antirachitic activity corresponding to 40,000 of the newly accepted international units.

Before I close I would like to refer to a certain aspect of the chemical dynamics of living cells, concerning which progressive studies have been made during the last few years. The cell is, of course, a seat of catalysed chemical reactions and would seem to possess a multitude of catalysts each highly specific in the influence it exerts. In the case of reductions and oxidations, however, there are other agencies of less specific activity which promote the final stages of oxidation. Of great interest among these are certain combinations of metallic iron with pyrrol groupings. One such compound is concerned, possibly with the intervention of yet another, in bringing molecular oxygen into the field of activity. What, however, is specially interesting about these associations of pyrrol groupings with a metal is the wide extent of their biological functions.

We have long known, of course, of the presence of one such association in the chlorophyll molecule, where it functions as part of the trap for solar energy, and we have been long familiar with the presence of another in haemoglobin, where its function is to hold oxygen during its transference from the lungs of vertebrates to their tissues. Further, we now know that, within the tissues, two others promote oxidation, and yet a third prevents by its presence any deleterious accumulations of hydrogen peroxide. For adjustment to each separate function there is some slight modification of a fundamental structure. Compounds of the type in question are found in many of the lower organisms. Just as Nature seems to have hit upon sound principles for nerve structure early in evolution, so she seems to have satisfactorily chosen, very early, the chemical materials for life. This same suggestion is carried by all the more important constituents of living stuff; fundamentally the same throughout, yet always with minor differences underlying specific morphological differences.

To return to cell dynamics. Knowledge of enzymic catalysts which, with highly specific relations, activate in a certain sense the molecules which are to suffer oxidation, is almost daily accumulating. It is because this specific activation must precede oxidation that the indiscriminate action of oxygen on the living cell is prevented. Although an understanding of the complex organisation of chemical events in the living unit is far beyond our present powers, we are, I think, beginning to see what kind of organisation it may be.

One last word, however. We have assumed that the living cells we have best known are the ultimate units in biology. But of late years the viruses have forced themselves into our thoughts. What are viruses? Do they merely simulate some of the properties of the living? Can we conceive of them as something between the non-living and the living? Are they alive? We do not yet know. Research upon them is at any rate intensely active at the moment. Its results may make it necessary to modify some fundamental biological concepts, and indeed be as revolutionary in their effects as the breaking up of the atom.