Transmission of Excitation in Living Material

ON Thursday, June 3, at the Royal Society, Dr. C. F. A. Pantin opened a discussion organized by Prof. A. V. Hill on "The Transmission of Excitation in Living Material", which was largely devoted to the consideration of the rival merits of electrical and chemical theories of conduction.

The electrical theory, which has been worked out mainly in connexion with the nerves of vertebrates, is briefly as follows. We know that conducting tissues may be excited at the cathode by an applied electric current, and we also know that the propagated wave is invariably associated with an electric disturbance which is in such a sense that the current flowing between the active and the inactive regions of the tissue has the cathode on the inactive part, and is hence in the direction which tends to excite it. Thus it is clear that if the disturbance is intense enough, the inactive region in front of the wave must be raised to activity, thereby achieving propagation. Whether in fact this is the mechanism therefore rests upon the measurement of the adequacy of the electrical disturbance to excite the region in front of the wave.

This study was presented by A. L. Hodgkin (Cambridge), working on frog's nerve in which the propagation was blocked by the application of pressure or by freezing. Though the impulse is not able to traverse the block, yet the electrical current spreads out into the inactive region and produces there a considerable exciting effect, for, when the shock setting up the impulse is followed by a second shock applied this time to the inactive region just beyond the block, and so timed that it coincides with the electrical disturbance due to the blocked impulse, it is found that the second shock can be effective at only 10 per cent of the intensity necessary when applied alone. The excitability thus measured is found to follow a time course nearly identical with that of the electrical wave from the blocked impulse. It is clear that if at some distance from the disturbance the excitability is raised to 90 per cent threshold, at the active region itself the current will be fully adequate. Thus the electrical theory is established for conduction in frog's nerve.

But the adequacy thus shown for a full-grown impulse will not apply to the very small impulse arising from the area under the cathode of an external stimulating circuit. It is clear that a stimulus, to be effective, must not only excite the tissue at a point, but also must nurse the new-born impulse until it has reached a size adequate to propagate on its own.

The results of a mathematical development of this aspect were presented by W. A. H. Rushton (Cambridge), who pointed out that, in spite of shortcomings due to over-simplification, it is possible to describe quantitatively the whole range of excitability measurements both spacial and temporal, including some observations hitherto unexplained, with only two arbitrary constants.

Now in the intact organism, nerve-muscle activity is carried out by impulses following each other in rapid succession, hence the electrical generation of repetitive impulses from continuous currents is of interest. A. Monnier (Paris) has found that excised nerves and muscles in solutions of low calcium ion content respond to prolonged continuous currents with prolonged rhythmic discharges. The bearing of this upon the mode of origin of central nervous rhythms was strongly indicated by B. H. C. Matthews (Cambridge) from oscillograph records of single motoneurones. When these cells are provoked to reflex activity by sensory stimulation, in addition to the quick potential change associated with each impulse there are slowly developed changes localized somewhere in the spinal cord, apparently produced by the cumulative effect of the sensory impulses, and acting like the prolonged currents in Monnier's experiments. This similarity has been further confirmed by passing a prolonged current in at the nerve and out at the cord, which, even in the absence of sensory stimulation, produced repetitive impulses of reflex character.

Though these experiments suggest that electrical considerations are sufficient to explain the passage of an impulse from one cell to another, there is quite other evidence, primarily pharmacological, which shows that the liberation of a specific chemical substance in relation to the cell junction may be of great importance.

Adrenalin has long been known to produce, when injected, the same general effects as widespread sympathetic stimulation, and it is now recognized that sympathetic nerves act by liberating adrenalin (or something very like it) in intimate relation to the cells of the organ supplied. Later, a similar state of affairs was found in connexion with the parasympathetic nerve endings, but the specific chemical, acetyl-choline is rapidly inactivated by an enzyme normally present and hence cannot be obtained unless the enzyme is inhibited by eserine. Chemical transmission was thus established in conduction between cells in two important classes, and the question arose as to whether some chemical was invariably necessary for such conduction. In particular, the cases of nerve-voluntary muscle, sympathetic ganglion and central nervous system are receiving consideration, but the possibility of a similar chemical counterpart of transmission down the nerve fibre itself is not overlooked.

A. von Muralt (Bern), realizing that any liberation of acetyl-choline during nerve transmission must be almost instantaneously reversible, adopted the following method to 'fix' the chemical liberated by a single impulse. The stimulated nerve together with an unstimulated control were shot instantaneously into liquid air, withdrawn, and ground to powder in solid carbon dioxide and then extracted and tested pharmacologically for acetyl-choline. It was found that the stimulated nerve contained about twice as much as did the control, but as was brought out in discussion with Prof. J. H. Gaddum, this was possibly due to the effect of the applied current (as in Gaddum's own experiments) for the results were more pronounced with prolonged currents, and the 'resting' control was probably excited by contact with the liquid air.

G. L. Brown (Hampstead), continuing the work of Dale and his other colleagues, showed that when an impulse passes from nerve to muscle, not only is acetyl-choline liberated in circumstances strictly limited to the passage of the impulse, but also that the injection of it suddenly into an artery in close relation to the muscle gives rise to a twitch very similar both from mechanical and from electrical records to that produced on nerve stimulation.

F. Buchtal (Copenhagen) has made a more minute study of the structures involved in this transmission. Working with single muscle fibres from the lizard, he measured the resting and active potentials on the surface of the muscle and the nerve-muscle junction. There is a resting potential of some 50 mV. between junction and fibre, and this difference is reversibly reduced to zero by the drug curare, which simultaneously produces a reversible nerve-muscle paralysis.

Z. N. Bacq (Liège) treated from a much wider zoological aspect the question of chemical transmission, and showed that, though acetyl-choline may be regarded as transmitter over a great range, yet this substance is not present in the Protochordates, the Crustacea, or the Cœlenterates.

J. C. Eccles (Oxford) considered the application to ganglion and central nervous system. He presented evidence for two transmitters, one rapid, and apparently related to the electrical effect, the second slower and probably related to acetyl-choline.

This same duality was advocated by C. F. A. Pantin (Cambridge) in his opening communication. His own work on sea anemones and crabs shows that facilitation at the nerve-muscle junction depends upon both the number and the frequency of impulses arriving there. A chemical transmitter is suggested because the time relations of the decay of facilitation are much longer than those of electrical effects, and are not dependent upon ions as are the electrical phenomena. On the other hand, the accumulation of facilitating chemical is never sufficient to set up repetitive impulses on its own account, nor are the ionic changes which increase facilitation capable of allowing a first impulse to pass; it seems that in these systems it is necessary to have the electrical change associated with the present impulse as well as the chemical facilitation resulting from a previous impulse. He also pointed out that the study of comparative physiology is rich in examples of the same end being achieved by different means, and of the same means being employed to different ends, or to no end at all. The fact that a certain chemical has important function in one tissue and that it is also present in another tissue, cannot be used as indicating that it has any biological significance in the second case.

Prof. E. D. Adrian, starting the open discussion, was also of the opinion that both electrical and chemical conditions are involved in transmission. He pointed out, however, that the secretion of molecules so strongly polar as those of acetyl-choline may involve quite considerable potential changes, while on the other hand the diffusibility of acetyl-choline through lipoids makes this ion of importance in the passage of electricity through cell walls. It is therefore possible that some of the phenomena variously considered as electrical or chemical may in fact be merely two aspects of the same process.

W. A. H. RUSHTON.

The Individuality of Gliadin

By Prof. A. G. Kuhlmann, Research Institute of the Baking Industry, Moscow

THE principal proteins of wheat are, as is well known, glutenin and gliadin. These proteins, upon the interaction of wheat flour with water, form the so-called gluten, the quality and quantity of which is of such great significance in the baking of bread, in the manufacture of macaroni, noodles and similar products. In the numerous works devoted to the proteins of wheat, a great deal of attention is paid to the question of the individuality of glutenin and gliadin.

Considering gluten to be a natural high polymer, we must come to the conclusion that it represents a complex of proteins, forming micelles of various length. Such a conclusion has been fully confirmed by an investigation which I conducted in my laboratory, which showed as well that the longest and most stable micelles are those of glutenin. Gliadin consists of shorter micelles, which are less stably built and more flocculent than those of glutenin.

According to the literature, the gliadin of wheat is best extracted by a 70 per cent solution of ethyl alcohol. A study of the influence of the concentration of ethyl alcohol on the peptization of the proteins of gluten carried out in my laboratory gave the following picture (Fig. 1). In one series of experiments, samples of one and the same gluten were treated with alcohol-water solutions. The experiments were repeated, this time a given sample of gluten being treated with alcohol solutions of increasing concentration (alcohol of higher concentration being used only after complete extraction with alcohol of the preceding lower concentration).

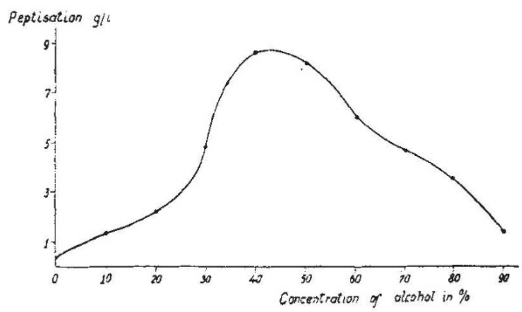

Fig. 1.

Results of these experiments are shown in Fig. 2. The data of both these series of experiments are in good agreement with each other and show that maximum peptization occurs with alcohol having a concentration of about 40 per cent. The