on this very simple picture, nothing else can happen. Surprisingly, as early as 1967, Katz and del Castillo[27] had demonstrated not merely that $Ca^{2+}$ influx is habitual at synaptic junctions but that $Ca^{2+}$ influx is essential for the release of acetylcholine at neuromuscular junctions — still the only easily accessible model of a specific synapse.

### A possible function

Kandel and his associates have been able to endow the movement of $Ca^{2+}$ across the presynaptic membrane with more subtle significance: briefly, there seems to be a connection between the fluxes of $Ca^{2+}$ ions under various circumstances and long-term modifications of cell behaviour, linked possibly with the phenomenon of learning and of memory.

As things are, however, nothing is known of the function of $Ca^{2+}$ ions in presynaptic neurones except, phenomenologically, that they are necessary and perhaps even sufficient for transmitter release. Plainly there is a task ahead for the biochemists to work out what happens. Fortunately they are now equipped with the necessary tools: calcium chelating agents and also ligands that, when bound to calcium, will fluoresce. □

## Benefits of tissue slices

THE technique which depends on the use of tissue slices, introduced in the past five years by Professor P.O. Andersen of the University of Oslo, appears to have its origins in the work of Professor H.C. McIlwain in the early 1960s. Although principally interested in the biochemistry of nervous tissue, McIlwain made electrophysiological recordings from nerve cells in the samples he prepared, only to find that physiologists complained that the recordings could not be physiologically significant. McIlwain's use of brain slices was, however, developed by C.D. Richards at the National Institute of Medical Research of the Medical Research Council.

Andersen's development of the technique depended on the recognition that the cells of the hippocampus form an exquisite sequence of lamellae, so that the process of cutting slices through the hippocampus need not sever too many neuronal processes. Now the technique is being applied to other parts of the central nervous system where regular structures are expected, the olfactory lobe for example, but also the columnar structures in the visual cortex.

Properly incubated slices of tissue will remain physiologically active for several hours. For practical purposes, the technique offers the only effective way of studying the effect of the excitation of one neurone on others lying downstream.

# Towards understanding the acetylcholine receptor

THE acetylcholine receptor, the workhorse of classical physiology, is likely to be the first of the neuronal receptors to be subjected to the full treatment of molecular biology. The explanation is straightforward. Species of the electric eel *Torpedo* use arrays of the receptors as means of generating the electric fields with which they can surround themselves, and are thus potentially rich sources of messenger RNA specifying the protein content of the receptor.

Several groups are occupied with two applications of modern techniques to this RNA. First, systems are being developed for the translation of the messenger RNA in cell-free systems, so as more fully to characterize the protein constituents of the receptor. Second, by using the mRNA as a template for generating the corresponding stretches of DNA and cloning the product, several groups hope to accumulate enough material to work out the nucleotide sequence corresponding to the mRNA. It is still not clear whether those concerned will be ready to announce their results at the meeting of the Society of Neurosciences in Los Angeles next week.

Meanwhile, a great deal of interest has been stimulated by the report[28] of a high degree of amino acid sequence is constructed. Approximately, the four distinct units have molecular weights of 40,000, 60,000 and 65,000, and the intact receptor includes two of the lightest units.

The sequence of amino acid residues at the amino terminal end of each of these units, spanning some 56 residues altogether, contains enough common elements arranged in the same order as to suggest that they evolved from a common gene. Was the primitive receptor an aggregate of five identical subunits, and does that suggest a way ot tackling the problem of the function of the modern receptor? No doubt it is only a matter of time before putative primitive structures are synthesized.

The importance of this development is not easily underplayed. There is every

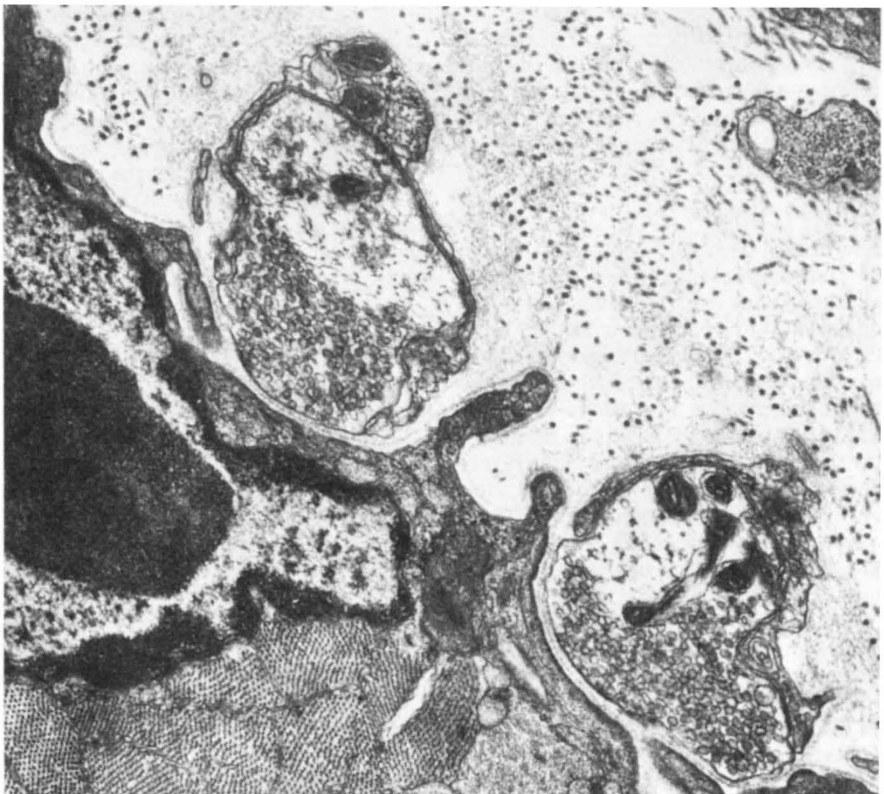

**Fig. 8** Electron micrograph showing two frog neuromuscular junctions. Two nerve terminals can be seen, lying close to the muscle membrane. They contain vesicles of the neurotransmitter acetylcholine. Muscle fibres can be seen in the bottom left-hand part of the figure, running out of the plane of the paper. (Photo: Dr P. Gordon-Weeks.)