normal epithelium of the human gall bladder and bile ducts there is high aminopeptidase activity in the luminal borders of the cells. Hitherto none of the other tumours has shown aminopeptidase activity.

On the basis of these observations we think that it is worth while to apply this histochemical method for aminopeptidase activity in fresh surgical specimens: (1) in lymph node biopsies with metastatic tumour cells, to investigate the possibility of gastric or bile duct origin; (2) during operations for gastric and bile duct carcinoma, to detect tumour cells in regional lymph nodes and surgical margins.

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Recording Inhibition and Excitation in the Cat's Retinal Ganglion Cells with Intracellular Electrodes

In the light-adapted state, the receptive fields of retinal ganglion cells in the cat consist of excitatory and inhibitory areas. Thus predominantly excitatory and inhibitory pathways converging on a ganglion cell can be stimulated selectively[1] and thereby the mechanism of excitation and inhibition can be studied. It has recently become possible to record from retinal ganglion cells with intracellular leads for short periods[2]. In the present study, penetrations into cells were fairly frequent; but most cells gave injury discharges and their membrane potentials declined within several minutes. However, intracellular records from some ganglion cells were recorded with stable membrane potentials of 50–70 mV. for as long as 20 min. Discharge patterns were similar to those obtained during extracellular recordings.

The following typical changes were seen in the membrane potential and in the discharge patterns of ganglion cells in the light-adapted state. If in an 'on'-centre receptive field a light spot was shone in the centre of the field, a maintained graded depolarization was set up, accompanied by an increase in frequency of impulses (Fig. 1*A*). The magnitude of the maintained depolarization as well as the discharge-rate were graded according to the strength of illumination. When the light was turned off the membrane potential and discharge frequency gradually returned to original levels. If an annular-type stimulus was used, throwing light only on the outer portion of the same receptive field, the maintained background activity was suppressed. At the same time the membrane potential of the cell was increased (Fig. 1*B*). As the light was turned off, there was a further increase of the membrane potential, followed by depolarization and an off discharge. In Fig. 1*C* the entire receptive field was illuminated, resulting in an interaction between the excitatory and inhibitory portions. The excitatory component predominated, but was much less effective than if the centre alone (as in Fig. 1*A*) was illuminated. Thus stimulation of the entire receptive field caused less impulse activity and less membrane depolarization than illumination of the central portion alone. A marked increase in membrane potential and inhibition of impulse activity occurred as the light stimulus was turned off.

Quite frequently an impaled ganglion cell stopped firing impulses a few minutes after penetration, presumably due to injury by the electrode. But the maintained decrease or increase in the membrane potential could still be observed with appropriate illumination, indicating that these slow potential changes were not dependent on the propagated impulse mechanism.

A few intracellular recordings were obtained from the retinal, presumably unmyelinated, portion of axons of ganglion cells. Membrane potentials were near 50 mV., and the axons were identified by the following criteria. The centre of the receptive field

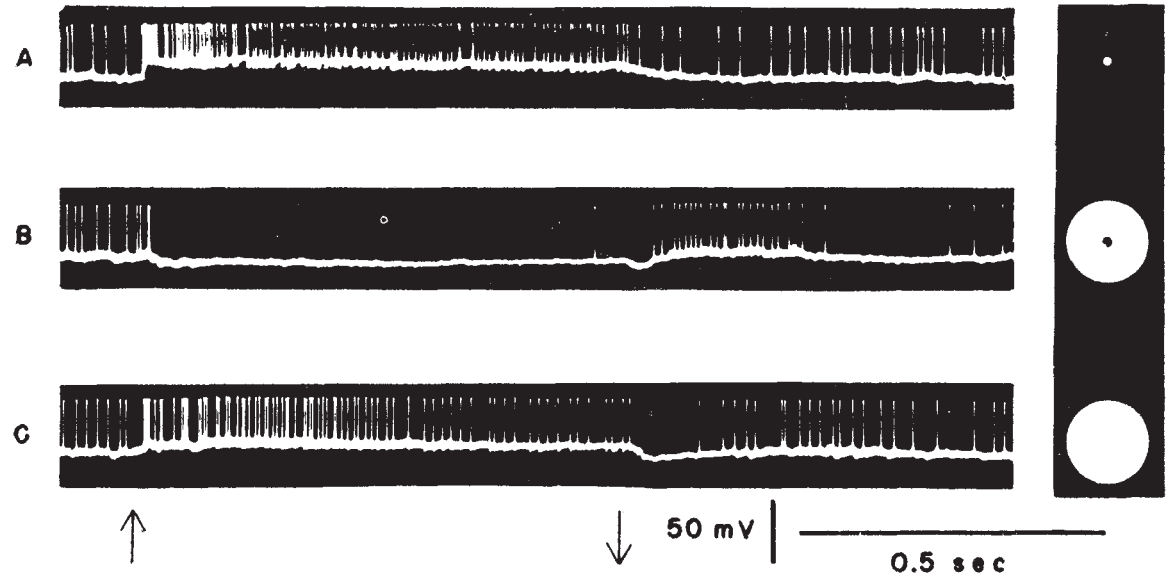

Fig. 1. Intracellular recording from retinal ganglion cell. Membrane potential about 65 mV. Period of illumination marked by arrows. Right, illuminated area marked white. *A*, small light spot of 1° (0·25 mm.) diameter; *B*, annular stimulus, outer diameter 12° (3 mm.) (central area of 1° is not illuminated); *C*, entire receptive field illuminated. Background illumination 0·34 log m.c. Stimulus intensity about 1·85 log m.c.

of such a fibre was some distance from the electrode tip toward the periphery of the retina. The typical slow changes of ganglion cells were absent, the potentials rose sharply and were all or none. Further, there was no sign of synaptic noise which was always present in ganglion cells.

The present observations may be compared with those in a variety of nerve cells. Thus, Eyzaguirre and Kuffler[3], recording from the cell body of the stretch receptor of crayfish, showed corresponding excitatory and inhibitory changes which determined the discharge frequency. Further, Hartline, MacNichol and Wagner[4] and Fuortes[5], leading from the eccentric cell in the *Limulus* eye, described a similar graded depolarization during illumination which was directly related to the discharge frequency. Corresponding slow potentials, both with excitation and inhibition, have been reported by Kolmodin and Skoglund[6] in the motoneurons and interneurons of the cat's spinal cord. The cortical cells studied by Phillips[7] also had similar slow potentials.

The retinal ganglion cells are the final points of convergence from the neuronal network of the receptive fields, which can extend over an area up to several mm. in diameter. The cells can integrate the excitatory and inhibitory synaptic influences in terms of slow changes in their membrane potential. Presumably, these in turn control the discharge frequencies of the optic nerve fibres.

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Bacterial and Testicular Hyaluronidase

IN papers from this laboratory, the actions on dermal connective tissue[1,2] and on ocular structures[3,4] of different kinds of hyaluronidase have been studied. In these experiments, 'Hyason', manufactured by Organon, Oss, Holland, was used as a source of staphylococcal hyaluronidase. This is also preparation *D* of Chauncey *et al.*[5].

We have recently been informed that batches of 'Hyason' released after January 29, 1958, contain testicular instead of bacterial hyaluronidase and we write this communication in order to prevent confusion arising from the change in composition. The manufacturer keeps a stock of the old preparation, and samples are available for research purposes.

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Excitation of the Squid Axon Membrane in Isosmotic Potassium Chloride

THE interesting recent findings in the frog node of Ranvier of an 'action potential' in isosmotic potassium chloride by Müeller[1], and of two stable states in 20–40 m*M* potassium chloride by Stämpfli[2], raise the question as to whether or not similar phenomena are to be found in the squid axon membrane.

I have made a preliminary study of the approximate steady-stage voltage-current relationship for the squid (*Loligo pealii*) giant axon membrane in 0·5 *M* potassium chloride. When the potential was controlled ('*E*-LOC') and varied, a continuous variation of the current is found, including a negative resistance region. The characteristic shape seen in Fig. 1 is typical, although there are some minor variations in the *E–I* curves depending upon the previous potential history and the rate and direction of sweeping. When the current was controlled ('*I*-LOC') and varied the voltage showed the hysteresis loop to be expected about the unstable negative resistance region. This is in complete agreement with Segal's[3] recent finding of two stable potentials for the squid axon membrane in high potassium under current control.

Franck[4] has compiled examples of dynode type characteristics with a negative resistance region which give excitation phenomena. The squid axon membrane in sea water with normal sodium concentration exhibits such a characteristic[5] and gives a normal action potential. Thus, it would also be expected that the squid axon in 0·5 *M* potassium chloride with a similar but displaced characteristic should exhibit excitation under the proper conditions. If the membrane is subjected to a constant hyperpolarizing current, an 'excitation' threshold for superimposed depolarizing current pulses should be found when the net current is less than about 0·15 m.amp./cm.^{2}. Fig. 2 demonstrates the threshold and also shows a recovery so that the process may well be called an 'action potential'.

At present, the description of the processes involved in the 'action potential' in 0·5 *M* potassium chloride seems to be as follows: If the squid axon

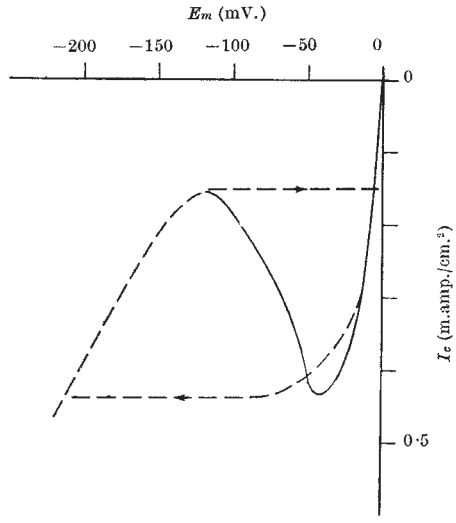

Fig. 1. Voltage-current characteristics of the squid axon membrane in 0·5 *M* potassium chloride. The continuous line was obtained with potential control; the dashed sections with current control. Arrow heads indicate abrupt changes