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Rotation of Activity and Spontaneous Rhythms in the Retina.¹

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(With 4 figures in the text.)

Several years ago (GRANIT and THERMAN, 1935) we made the first observations on rotation of activity in the eye. Later this same phenomenon turned up in some experiments with constant stimuli as an alternation between types of electroretinograms so different, that we felt compelled to speak of a "switchboard" in the retina (GRANIT and MUNSTERHJELM, 1937). With rhythmic stimuli rotation of activity has also been observed by BARTLEY (1937) and recently BARTLEY (1939) and BERGER and BUCHTHAL (1938) have emphasized the general significance of this phenomenon in the physiology of vision.

When I now return to this subject it is partly because our present micro-electrode technique (GRANIT and SVAETICHIN, 1939) brings it out with hitherto non-paralleled clarity and regularity, partly because of my conviction that rotation of activity is a very essential property of the nervous system.

From the point of view of the general physiology of the special senses one would be prepared to state that there are good reasons for accepting as a law of end-organ differentiation that the evolution of structurally more complicated sense organs takes place in such a manner as to counteract the effects of adaptation with their tendency to make the stimulus ineffective. Rotation of activity is one of the means whereby this end is attained. The retina which is forced to continuous, accurate activity within an

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enormous range of illumination has this mechanism well developed and, in addition, possesses several other means of suppressing or modifying the effects of adaptation. These, however, cannot be discussed now.

Technique and Procedure.

The experiments were carried out with the silver-micro-electrode described by GRANIT and SVAETICHIN (1939). In many cases the glass-covered platinum micro-electrodes of TAYLOR and WHITAKER (1928) were used, yet without making them non-polarizable. Experiments proved, as was to be expected, that the metal-micro-electrode has a polarization capacity which greatly deforms the slow retinal action potential without preventing the fast spikes from appearing. If the glass covered metal-micro-electrode be used with a directly coupled amplifier it is found to record a rectangular input current with the distortion characterizing a condenser-coupled instrument having somewhat larger coupling condensers than those used in my amplifier for micro-recording of spikes from the retina.

The micro-electrode is applied on to the retina with the aid of a micro-manipulator under a binocular microscope. Leads are taken to a condenser-coupled amplifier with a balanced input stage. A cathode ray and a loudspeaker are connected to the output stages in the usual manner. When the light is switched on or off discharges composed of spikes follow from elements which are more or less isolated as the case may be (see figures). These remind one of the spikes recorded with micro-electrodes, for instance, by FORBES and his collaborators RENSHAW, THERMAN ET AL. (1937, 1940, 1940) from the hippocampus area and by LORENTE DE NÓ (1939) from the nuclei of ocular nerves.

GRANIT and SVAETICHIN (1939) held these spikes to arise from the neurite not too far from the axone hillock of the retinal ganglions. The reason for this, not mentioned in their paper, was that spikes could be obtained when their micro-illuminator was pushed into the retina several millimeters away from the micro-electrode. According to HARTLINE (1939) the "receptive field" of a single fibre would have much narrower dimensions and the retina itself is only a fraction of a millimeter. On the other hand the spikes cannot arise too far away from the ganglions as they are absent or minute in the blind spot.

In the experiments to be described below the *whole retina* was illuminated with some wave-length from our monochromator. For technical details the reader is referred to the paper by GRANIT and SVAETICHIN (1939). The experimental animals were frogs and tortoises.

Results.

The Response to Intermittent Stimuli.

Rotation of activity is conspicuous and most disturbing in experiments presupposing a constant threshold. To this type belongs the colour work taken up by GRANIT and SVAETICHIN (1939) and at present continued in this laboratory with a variety of animals. Sometimes one finds the threshold to undergo sudden changes which could be ascribed to the pressure of the micro-electrode were it not for the fact that these changes may come and go without, in the long run, involving any progressive diminution of the sensitivity. In fact, I have followed dark-adaptation for two hours with a well placed micro-electrode. That pressure *can* lead to spontaneous discharges is a different matter. But this source of error can with some experience be avoided and then the sudden shifts in the level of sensitivity must be ascribed to causes in line with those leading to the spontaneous rhythms to be described in the next section. These factors cannot, as a rule, be put under experimental control, though the phenomena are interesting to record and try to modify when they occur.

But inasmuch as rotation of activity depends on stimulation, which may be supposed to activate after-potentials or other mechanisms of blocking or facilitation, then one certain way of regularly bringing these into play would be intermittent illumination. Every flash of light then leads to a state of excitation which has to force its way through a bed of receptors and neurons modified in excitability by the foregoing flashes. Records from such experiments are shown in Fig. 1.

From above downwards I have selected cases designed to illustrate the rotation of activity of a gradually increasing number of neurons. There are also variations in the frequency of the flashes and in their strength. The essential features of the phenomenon are displayed, independently of the conditions chosen. The units come and go in a rotation of activity which is irregular with respect to the rhythm of stimulation. The active unit of

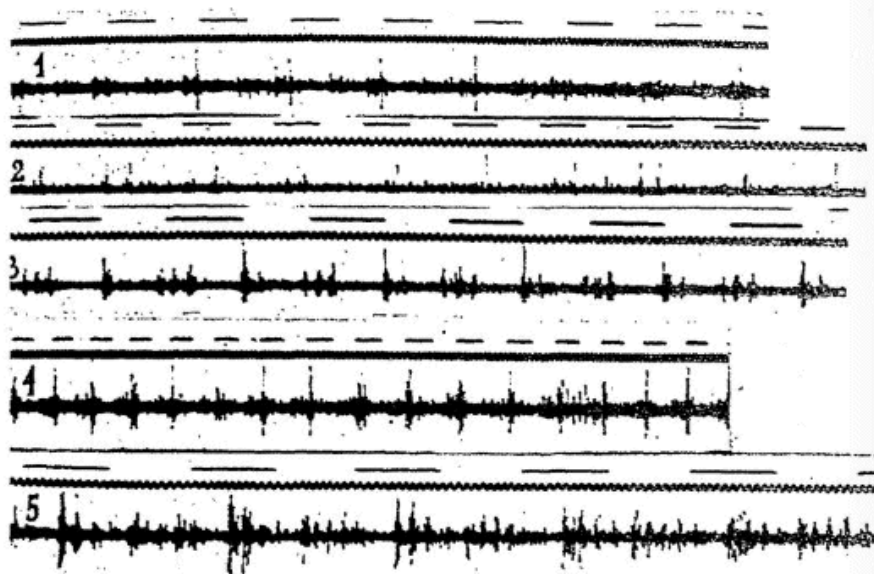


Fig. 1. The response to intermittent light at different frequencies. Light signal above time signal (50 per sec.) in this and the following records.

1. Tortoise, wave-length 0.680 μ . "Off"-spikes.
2. Frog, wave-length not noted.
3. Frog, spikes at both "on" and "off". Near threshold for wave-length 0.530 μ .
4. Tortoise, wave-length 0.620 μ .
5. Frog, wave-length 0.600 μ . Well above threshold for intermittent light.

curve 1 pauses every now and then, and again returns after a few flashes. In curve 2 there are three units fairly well placed relative to the electrode and the picture in this case as well as in curves 3—5 with a greater number of elements in activity is already very complicated. Continued stimulation with intermittent light neither seems to make the rotation of activity more regular nor does it abolish it.

Spontaneous Rhythms.

ADRIAN and MATTHEWS (1928) made the first observations on spontaneous rhythms and synchronization in the retina when recording from the whole nerve. The off-effect is quite often synchronized (GRANIT and THERMAN, 1935), particularly in the fibres that merely react to cessation of illumination (HARTLINE, 1938).

With the micro-electrode technique spontaneous discharges are quite common and very often these consist of grouped spikes

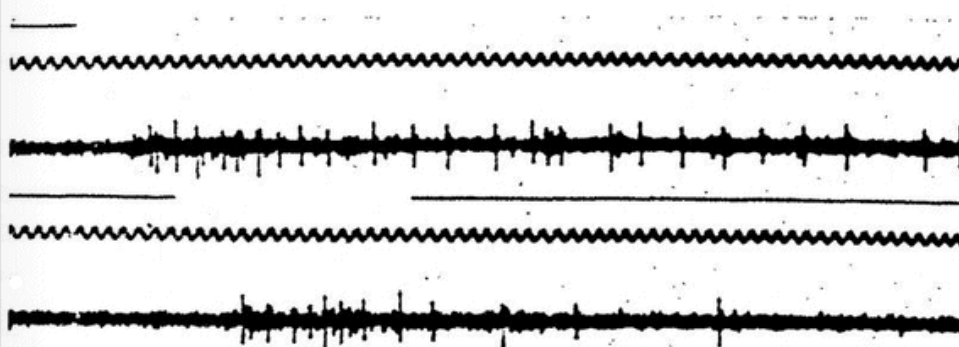


Fig. 2. Tortoise. Upper curve: off-effect control. Lower curve: inhibition caused by re-illumination. Wave-length 0.600 μ , near threshold.

which for some time may be synchronized. In connection with the problem of rotation of activity it interested me to find out to what an extent such discharges and rhythms, when they occur, can be modified by stimulation.

Very variable, though in each case repeatable, results were obtained. At one end of the series of observations could be placed the ordinary inhibitable off-effect, illustrated in Fig. 2. Somewhat similar properties has the spontaneous discharge of the dark-adapted eye, particularly when it is diffuse and not synchronized. With the frog's eye it is often a sign of dark-adaptation that the retina begins to discharge spontaneously. This discharge, as a rule, is very effectively inhibited by illumination. "Dark" rhythms of the eye of the water-beetle (*Dytiscus marginalis*) behave similarly, according to ADRIAN (1937).

An interesting case is curve 1 of Fig. 3. There was a spontaneous discharge having the fairly regular rhythm illustrated. A light flashed into this discharge (see the curve) led to a temporary inhibition probably caused by the on-discharge elicited in the neighbourhood. Signs of this on-effect are seen under the micro-electrode. Cessation of stimulation was followed by a brief off-discharge and another temporary silent period after which the receptor again picked up its original rhythm. The rhythmic discharge lasted for some time so that the experiment was several times repeated. The results show that cessation of illumination also can exert inhibitory activity. This hitherto seemed to be a prerogative of illumination falling into an off-discharge. The

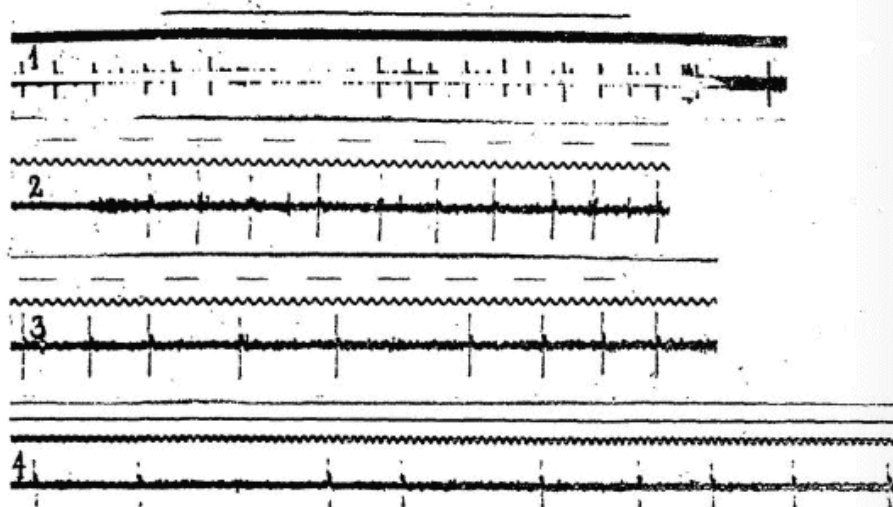


Fig. 3. 1. Tortoise. Spontaneous rhythm inhibited by onset and cessation of stimulation with wave-length 0.620μ at maximal intensity of monochromator. 2 and 3. Tortoise. Wave-length 0.620μ , well above threshold (see text). 4. Tortoise. Active unit firing spontaneously also during illumination.

Note. The single units illustrated in these experiments are the "red" receptors of the tortoise with maximal sensitivity around 0.620μ (GRANIT 1941).

inhibition at "off" is probably to be parallelized with the well-known "silent periods" of other receptors.

The counterpart to curve 1 of Fig. 3 is curve 4. This shows the spontaneous activity of a single element which seemed to be quite independent of whether the eye was illuminated or not. This is nearly always the case with a discharge caused by the pressure of the micro-electrode. But here there was no reason to suspect that mechanical stimulation had caused the activity. When slowly screwing the micro-electrode into position and looking at it all the time in the microscope one often first hears the rhythm in the loudspeaker as a faint distant noise which then gradually increases in strength as the point of the electrode approaches the active unit from above. When this is so there is no reason to ascribe the discharge to mechanical stimulation, the less so as the spontaneous activity quite often may cease as suddenly as it has begun. When light does not influence such rhythms the reason may have been that the monochromator gave too feeble stimuli. But there was always a check on this in the

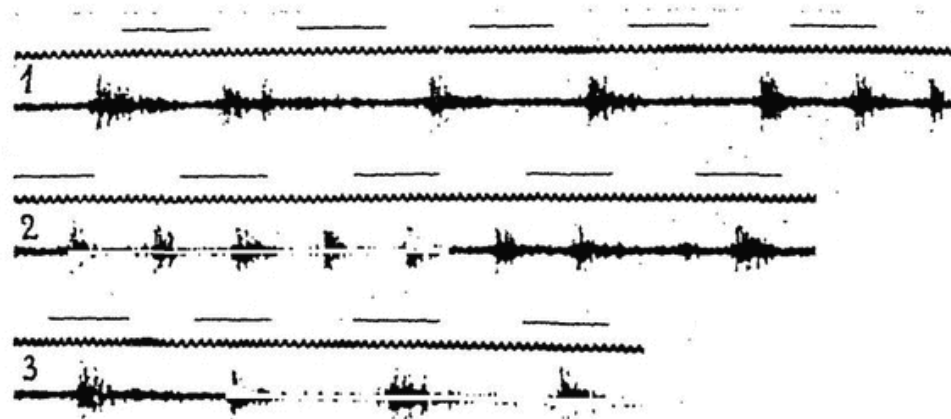


Fig. 4. Frog's eye which has been in the apparatus for 1 h. 40 min. During this time it has dark-adapted and begun to discharge spontaneously 15—18 times a minute. The active region is of the type giving a "grouped discharge", which comes above and goes below the threshold as a grouped unit when the intensity is varied. The spontaneous discharge looks like the discharge caused by stimulation. Wave-length 0.520μ . For explanation, see text.

ab. 2,400 m. c. light of the lamp of the preparation microscope illuminating the retina from above. This light could be switched on and off as a final control on the relative independence of the rhythm.

There are undoubtedly, particularly in the eye of the tortoise, spontaneous rhythms which behave as if they had succeeded in blocking every path around the discharging units.

Curves 2—3 of Fig. 3 show the beginning and end of intermittent stimulation with the micro-electrode in a place which at the moment of recording was silent, but some minutes later began to discharge spontaneously. At the moment of recording the tendency to spontaneous activity probably was *in statu nascendi* and its appearance was facilitated by the flashes from which the rhythm of the discharge rapidly disconnected itself.

In such cases the result may become very complex. Fig. 4 illustrates an eye tending to give a grouped, spontaneous discharge very much like the ensuing response to flicker. The active spot is silent when the recording begins and, upon illumination, follows the slow rhythm of the intermittent stimulus. Spontaneous activity begins soon (end of curve 1) but immediately is pressed into the rhythm of the stimulus where (curve 2) the extra

discharge takes up a definite place. In curve 3 it has disappeared and the eye now again reacts as in the beginning (curve 1).

These experiments, chosen to illustrate some properties of spontaneous rhythms in the retina, could easily be multiplied and would then provide samples of most of the phenomena of a similar nature observed in the central nervous system. But as they seem to have relatively little analytical value in their present form I have merely used them as a complement to the observations on the rotation of activity. From this point of view their significance is that they illustrate how inhibition can block a discharge of spikes and how rhythms imposed by a stimulus can play upon rhythmic tendencies in a given group of neurones.

Discussion.

It is clear that excitation, spontaneous or caused by stimulation, is surrounded by inhibitory and excitatory influences spreading over the retina in complicated patterns. These may well be of the nature of after-potentials. The net result of the waxing and waning of such effects must lead to rotation of activity among the active elements. There is also at the threshold a fluctuation of excitability which may or may not be of different origin, but whether it is of any significance with "flicker" is open to doubt. In order to make a group of spikes follow an intermittent stimulus the illumination must be well above the threshold for a constant light.

For the physiology of vision the rotation of activity, apart from what it may do to counteract the effects of adaptation, is of great interest and emphasizes points of view advocated by BARTLEY (1939), BERGER and BUCHTHAL (1938) and WRIGHT and GRANIT (1938).

Summary.

"Spikes", recorded from the retina with micro-electrodes and a condenser-coupled amplifier, are elicited by stimulation with intermittent light.

Single units of activity as well as a greater number of active elements responding to intermittent light, show a very marked

rotation of activity, the individual elements pausing and re-entering into activity at irregular intervals.

Spontaneous activity in the retina can with respect to an interposed stimulus be divided into two categories, (i) discharges which can be temporarily or completely inhibited by illumination or even temporarily inhibited by cessation of illumination, and (ii) discharges which continue independently of whether the eye is illuminated or not.

Spontaneous rhythms can be activated and facilitated by rhythmic stimulation.

The experiments thus give further support to the view that waves of excitation passing through the retina are surrounded by spreading patterns of inhibitory and excitatory influences. With stimuli well above the threshold, these probably are the main causes of the rotation of activity.

From the sensory point of view rotation of activity may be regarded as one of the means whereby the effects of adaptation are counteracted, and it also emphasizes the fundamental truth behind "pattern" theories of visual processes.

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