responsiveness to the background stimuli. This increase has been seen to last as long as 50 milliseconds.)

The extra stimulus can be applied in either of two ways: (*a*) electrically in the same direction as the background stimulation or (*b*) in the opposite direction. Under both conditions a response can be produced. In the first case the response varies in height as the extra stimulus varies in its time relations with respect to the stimuli of the high frequency background. This indicates that the response is dependent upon the summation of stimuli and accords with the observations of Bugnard and Hill.[6] When the two sets of stimuli are opposed in direction a full-sized response is produced with great regularity. Obviously summation of stimuli plays no part here, and the probable factors concerned will be discussed below.

Discussion

We can, therefore, present the following potential picture which describes the decreased effectiveness of stimuli applied at rates on the order of 2,500 per second: (1) The response to these high rates of stimulation is largely but not completely abolished. (2) This decreased response is partly due to a decreased excitability at the stimulating electrodes, since the response can be increased by raising the strength of the high frequency stimuli or by summating an extra shock with the background excitation. (3) The decreased excitability which obtains at the high frequency electrodes is not present elsewhere on the nerve, since extra stimuli of normal strength applied through other electrodes can produce practically full-sized responses. Furthermore, the decreased excitability at the high frequency electrodes is localized in the region of the cathode, since an extra just supermaximal shock applied at the electrodes carrying the high frequency stimulus, but reversed in electrical sense, produces almost a full response.

From the foregoing picture the decreased effectiveness of high rates of stimulation can be explained on the basis of two factors: refractoriness and cathodal depression, as suggested by Bugnard and Hill.[6] At any one time most of the fibers are refractory to successive stimuli of the series. The ineffective stimuli, therefore, produce a cathodal depression such as was described by Gildemeister[7] and by Erlanger and Blair.[8] Our observations are in accord with the conclusions of Bugnard and Hill[6] (p. 424) that "shocks which are 'ineffective' owing to falling in the refractory period, nevertheless depress the excitability and extend the refractory state,"[9] and also that extra shocks applied through the same electrodes and in the same sense electrically are effective only when they summate with background stimuli. Bugnard and Hill, however, conclude that an extra shock "in the opposite electrical sense, raises the excitability and shortens the refractory state" (p. 424) and postulate that such a shock does not itself excite but enables the next following background stimulus to become effective. Although such a condition may exist in alternating high frequency stimulation, it does not occur when an extra reversed shock is applied against a background of unidirectional stimulation as in the present experiments. Oscillograph records of the time relations show, on the contrary, that the large response following the extra stimulus is produced by the latter and not by the succeeding background stimulus. We have furthermore tested, both at the anode and at the cathode, the excitability of the nerve immediately after 30 or more seconds of high frequency stimulation. At the cathode the response to a maximal testing shock does not reach full height until after 10 to 12 seconds, while at the anode there has been almost no change in excitability and the response to the testing shock is nearly maximal immediately after the background stimulation is removed. We therefore conclude that with high rates of stimulation the local depression is confined to the region of the cathode, so that an extra reversed stimulus is effective because the anodal region is not significantly depressed.

[7] M. Gildemeister, *Pflüger's Arch.*, 124: 447, 1908.

[8] J. Erlanger and E. A. Blair, *Am. Jour. Physiol.*, 99: 108, 1931.

Summary

Observations of individual action potentials during high frequency stimulation show that the failure to excite, in so far as it is not due to refractoriness, depends upon a localized depression at the cathode which may last for a considerable period after the stimulation has been discontinued. Excitability of all other regions of the nerve, including that at the high frequency anode, is not significantly altered.

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[9] Bugnard and Hill use the term "refractory state" for a local decrease in excitability owing to a combination of the effects of refractory period and local excitatory change.

BOOKS RECEIVED

Finger, Charles J. *The Distant Prize: The Opening and Settlement of North America.* Pp. ix + 330. Appleton-Century. $2.50.

Munz, Philip A. *A Manual of Southern California Botany.* Pp. xxxviii + 542. 310 figures. J. W. Stacey, Inc., San Francisco. $5.00.

Yates, Raymond F. *The Art of Inventing.* Pp. xiii + 284. 68 figures and plates. Appleton-Century. $3.00.