

XVI. NEUROPHYSIOLOGY*

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A. AN ELECTRONIC ELECTROMETER

By suitable feedback a conventional triode electrometer tube, in this case a Victoreen 5803, can be improved by a factor of 100 in its specified grid current and input impedance. (See Fig. XVI-1.) A gain-of-one cathode follower of good high-frequency response is given by tubes V_1 and V_2 , since all the gain required at the plate of V_2 is the difference between unity and the product of the gains at the cathodes of V_1 and V_3 . The output of this cathode follower is fed back to the plate of the electrometer tube, whose cathode looks into an infinite variational impedance obtained by the feedback to the cathode of V_6 . Thus, over a very wide range, the electrometer can be thought of as having an arbitrarily high impedance to ground, and the grid current can then be balanced out without the input impedance being changed by the injection of current from the cathode of the electrometer into the grid through the 10^{11} -ohm resistor. The high-frequency impedance (at least up to 30 kc) can be kept very high by the additional feedback through the capacitance between the hot shield and the electrometer grid lead — this loop using tubes V_4 and V_5 .

It was possible to have such a circuit sit quite stably with about 10^{-16} grid current and an input impedance so high that the voltage drop across a 1-inch length of silicon-coated glass rod, 3 mm in diameter, was negligibly small from 0.01 cps to 10 kc, while the drift of the base line stayed less than 1 volt over a period of 10 minutes.

A report on the long-term performance of this circuit will appear later.

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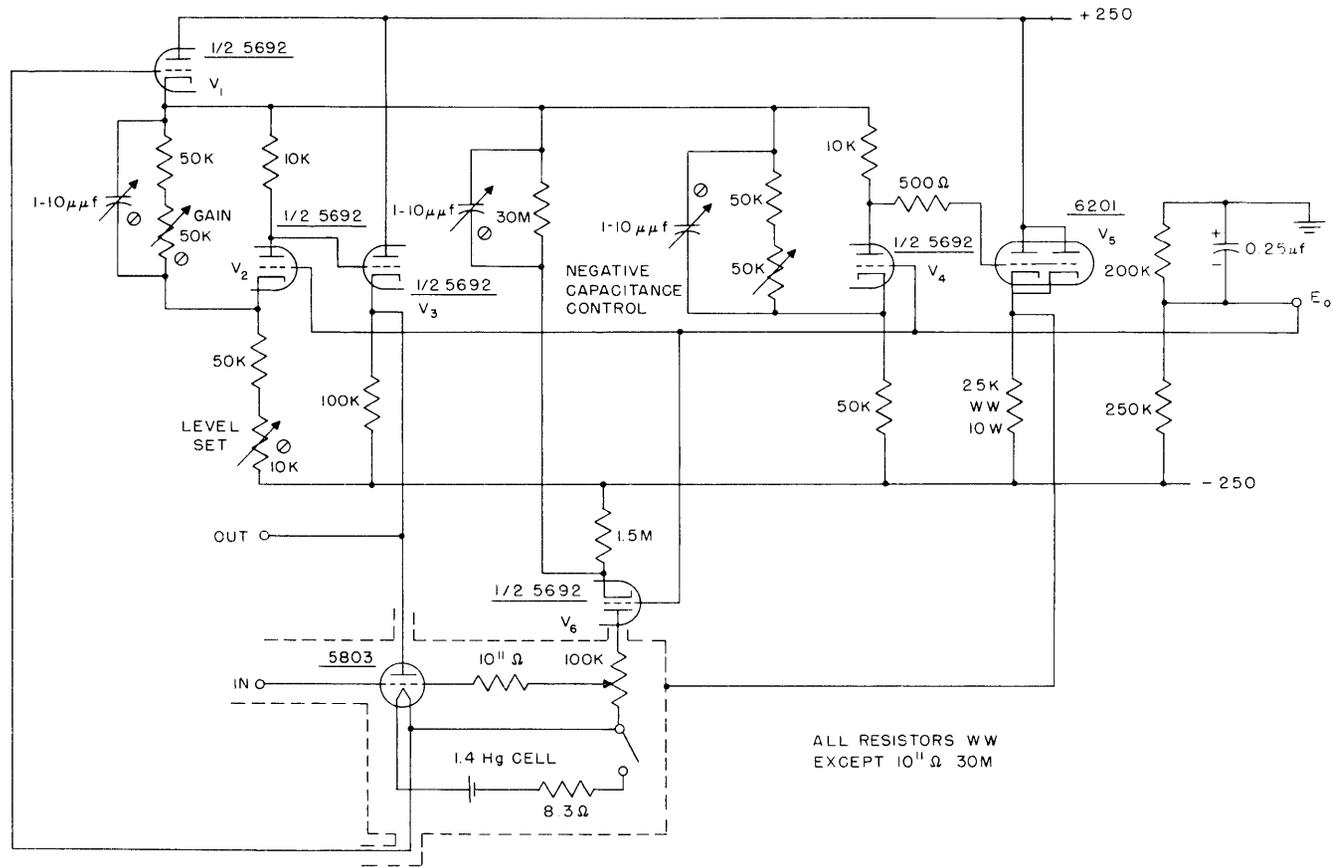


Fig. XVI-1. Electronic electrometer circuit.

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B. PROPERTIES OF INTRAMEDULLAR FIBERS

Studying the invasion of the spinal cord by small numbers of nerve impulses in specific tracts and comparing the behavior of large proprioceptive fibers with smaller skin sensory fibers has advanced this work considerably. When a peripheral nerve fiber is fired, it depolarizes and almost completely repolarizes within 1 msec but the repolarization has a slow tail that lasts 12-20 msec, the negative after-potential. After this, the membrane potential swings slightly higher than its resting level so that a positive after-potential exists for some 40-60 msec. While these swings of the membrane potential are going on, there is a coincident variation of excitability. First, during the impulse itself there is an absolute refractory period, 0.4-1 msec, followed by a partial refractory period, followed during the negative after-potential by a slight increase in excitability. Finally, during the positive after-potential, there is a small decrease of excitability. Thus by testing the changes in excitability of a group of nerve fibers that have fired off, one gets some indication of the state of recovery of the membrane potential. This we have done by placing a stimulating monopolar microelectrode in the middle of a population and recording the number of nerve fibers fired by a fixed, small stimulus at intervals after every member of the population has carried a single impulse. The records show that if we examine the large proprioceptive fibers from the gastrocnemius muscle, we find at three parts of their axons — the root entrance zone, the lumbar dorsal columns, and their terminations on motor horn cells — that they go through somewhat similar excitability changes. There is a collision period, an absolute refractory period, a partial refractory period, a rather large hyperexcitability lasting 20-30 msec, and no period of decreased excitability. If we look at intermingled fibers of the same type and origin that are passive (have not carried an impulse), we find that they are quite unaffected after the passage of an impulse in their neighbors. Furthermore, the excitability of the fiber terminations is unaffected by massive antidromic firing of the motor horn cells on which they end. Thus we find that these fibers are like peripheral nerve fibers except that they show a rather large increase of excitability and therefore, perhaps, a larger negative after-potential to a single volley. With these two exceptions, these fibers act as honest peripheral axons which do not interfere with their neighbors.

When we examine the skin sensory nerves from the sural nerve, we find an extreme contrast. The root entrance zone shows a small but very prolonged period of hyperexcitability. The terminations of these fibers show an extremely prolonged and very large increase of excitability. The dorsal-column sural fibers, however, show a series of changes similar to those seen in the gastrocnemius fibers in the same region. As one might expect when finding grossly differing states of excitability along the course of the same axon, current will flow toward the area of depolarization and we might expect to see an effect of this current on neighboring fibers. In Fig. 2 of our paper in the Journal

of Neurophysiology, January 1955, we demonstrate long-lasting currents like this, although the circumstances are slightly different. The excitability of neighboring fibers, in fact, is affected by these volleys from skin nerves, unlike the muscle nerves. Stimulating the cord interneurons, on which these fibers end, fails to produce a significant change in their excitability.

Thus we can conclude that there is a probable long-lasting depolarization of the endings of the smaller fibers after they have carried a nerve impulse. This depolarization is inherent in the fiber and is not produced by other structures. However, it does affect the excitability of neighboring structures, since the depolarization is unequally distributed along the length of the axon and therefore produces external current flows. We believe that we shall be able to make a very strong case for this prolonged terminal depolarization being the cause of the main negative dorsal-root potential that has been so widely studied and previously attributed by most authors to the activity of interneurons. Furthermore, it now seems likely that the blocks that we have previously reported occur in these smaller fibers and are cathodal blocks attributable to the enhancement of a conduction hazard by the terminal depolarization.

This finding brings up two important questions. The first is whether or not this terminal prolonged depolarization plays any rôle in exciting subsequent cells. We cannot answer this question now, but there are indications that it does. One fact is that it strongly affects the excitability of neighboring inactive fibers, so that it seems certain that it will do the same for subsequent cells. Whether it will fire them off remains to be seen. The other question is why nerve fibers that enter the grey matter of the spinal cord change their properties so radically. We know of three anatomical findings that together might produce this change: The axons decrease in diameter; they lose their myelin sheath first for long stretches, and then lose it completely; finally, electron-microscope pictures all show these terminal fibers very closely packed with only minute amounts of intercellular fluid. It is possible that this last finding may restrict the ability of ions to move freely and thus hamper the processes of depolarization and repolarization.

All of this makes it certain that the nature of the nerve impulse that excites a cell can no longer be thought of as a discrete 1-msec event that is over and done with before the arrival of the next impulse. Digital analysis has been most successful on peripheral axons but evidently breaks down centrally.

Mention should be made of other work in progress. We discussed above the absence in central axons of a positive after-potential following a single impulse. In a peripheral nerve, a high-frequency volley of nerve impulses can be produced so that the positive after-potential from one impulse overrides the subsequent positive after-potentials and produces a mounting level of hyperpolarization. The effect of this is to make the nerve more difficult to stimulate but at the same time to increase the size of the action

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potential. This increase affects the size of a reflex evoked by an afferent volley after a tetanus. This phenomenon, post-tetanic potentiation, is now being studied so that we can determine the actual change of threshold of the terminations of the muscle nerve fibers which evoke the monosynaptic reflex. This work will contribute to knowledge of the input-output relations of the monosynaptic reflex and to the nature of central positive after-potentials.

Three other projects are making good progress. Fluid-filled ultramicroelectrodes are being used for intracellular studies within nerve cells. The electrical properties of various types of microelectrode are being studied. Finally, the standing potentials within nerve tissue are being mapped with several types of electrode in order to determine their nature, location, and changes with stimulation.