

XX. NEUROPHYSIOLOGY*

W. S. McCulloch
R. C. Gesteland

A. R. Johnson
J. Y. Lettvin

W. H. Pitts
P. D. Wall

RESEARCH OBJECTIVES

The neurophysiology laboratory is mainly concerned with synaptic transmission; that is, the way neural relays operate. One of its major findings in the past two years is that an impulse does not necessarily invade all of the terminal processes of an axon. The probability of impulse passage at certain axon bifurcations is significantly lower than unity, and is easily altered by activity in neighboring fibers. Such interaction occurring before the synapse (the relay point) may account in part for some of the lability of spinal reflexes – their facilitation and inhibition. At present, we are engaged both in explaining this decremental conduction on the basis of the geometry at a bifurcation and in demonstrating its occurrence in known reflex arcs.

Since that explanation suggested and subsequent experiment proved that no similar block occurred in the reverse direction, and we were able by backfiring to map any system afferent to the grey matter of the spinal cord, we are now able to analyze synaptic transmission by measuring the changes in thresholds of axonal terminations of afferents produced by their own antecedent activity. We are able to measure, as well, threshold changes of motor neurons and so to analyze other types of facilitation or inhibition than those attempted heretofore.

A second project is the investigation of more prolonged sources and sinks produced by barrages of impulses. A third project is the recording from within simple cells to determine small changes in resting potential in response to any variety of facilitating or inhibiting volleys. Appropriate microelectrodes are being produced and the design of suitable amplifiers is underway for both of these new studies.

A. SYNAPTIC TRANSMISSION AND PRIMARY AFFERENT FIBERS

Having shown the interaction between neighboring group II fibers of the dorsal roots in the dorsal parts of the cord we proceeded to search for similar processes that might occur in the group I fibers more ventrally. Our results are presently quite unambiguous in disposing of some older hypotheses but we propose no public interpretation of the data yet.

During post-tetanic potentiation we found that the tetanized afferent sensorimotor collaterals all the way to their terminations exhibit a marked rise in threshold of the same order of duration as the reflex potentiation and that this change in threshold is not reflected in the excitability either of recipient motoneurons or neighboring group I fibers not previously excited. This gives very strong indication that if humors are involved in such a phenomenon they do not seem to be disseminated locally to affect other fibers.

We found by following single shocks to group I fibers in a peripheral nerve that there is a consistent decrease in threshold in the sensorimotor collaterals extending, again,

*This work was supported in part by Bell Telephone Laboratories, Incorporated; in part by Teagle Foundation; in part by National Science Foundation; and in part by Offner Electronics, Incorporated.

all the way to the terminations and lasting for about 40 msec. This change in threshold is of the same order of duration as that of the synaptic potential recorded on the ventral root or intracellularly in a motoneuron. It is not reflected by a corresponding change of threshold in either direction in neighboring unexcited group I fibers, even when they end on the same cells. Neither do antidromic impulses in the motoneurons affect visibly the threshold of the fibers ending on them.

Thus, despite the extreme close packing of neuropile in the grey matter, and despite our strong emphasis on presynaptic interaction through the currents flowing during excitement, it appears that the monosynaptic excitatory systems show a marked dromic independence of afferent fibers up to the motoneuron, as well as antidromic independence from the motoneuron. Within the next six months, we expect to be able to hazard a guess about the mechanisms involved.

In neuropharmacology, we published our work on strychnine ("Effects of strychnine with special reference to spinal afferent fibers") in *Epilepsia* (1955). In this paper we demonstrate that strychnine appears to exert its action in the spinal cord by affecting the size of the afferent signal (as with potentiation) rather than the threshold of the postsynaptic cell. We also have taken some pains to justify strychnine neuronography.

Our anatomical work on antidromic stimulation as a means of tracing nervous pathways to their terminations has appeared in the *Yale Journal of Biology and Medicine* (January 1956), wherein we discuss at length the results on pyramidal tract and peripheral nerves epitomized in earlier progress reports.

B. TREMOR

We have embarked on setting up nembutal tremor and shivering as a paradigm of Parkinsonian tremor in animals. Some drugs that affect Parkinsonism affect such tremors. We are also concerned with the action of some of the long cranio-spinal tracts of these tremors.

C. DC AMPLIFIER

Our new dc amplifier renders the controls of balance and common mode rejection markedly independent. We find this feature necessary for our work, since we do not repeatedly balance the amplifier to a fixed level in the course of an experiment.

D. SENSORY PROCESSES

In our collaboration with Tufts University in sensory processes of insects we published one paper in *Science* (E. S. Hodgson, J. Y. Lettvin, and K. D. Roeder, Physiology of a primary chemoreceptor unit, *Science*, 2 Sept. 1955). We successfully

(XX. NEUROPHYSIOLOGY)

isolated and measured single units responsive to salt, sugar, and so forth. In further work with Dr. Royce at Tufts we have now apparently succeeded in measuring, without dissection, the activity of receptors sensitive to smell and others to touch by a new method that does not require the masking of a sensitive hair by the encasing electrode. A preliminary report of this work will appear in Science.

E. INTRACELLULAR ELECTRODE POTENTIALS

Curious about the possibility of recording intracellular pH, we checked the behavior of antimony microelectrodes. These probes were extremely good at measuring pH even in buffers with added protein. Yet intracellularly they apparently ceased to function as a reversible H^+ electrode and recorded the same change in potential across the membrane as was exhibited by a saline bridge or by a noble metal electrode. Since this is manifestly impossible under the conditions of known ionic concentrations and activity across the membrane, we could only conclude that somehow the electrode was poisoned. This negative result would be uninteresting were it not for the facts (a) that on coming out of the cell the antimony reverted to its former usefulness, and (b) that other less esoteric reversible electrodes, such as Ag-AgCl, exhibit the same odd characteristic. We tend to regard this sort of behavior as a common trouble in all phase-boundary reversible electrodes thrust into an unusual medium (perhaps a liquid crystal) rich in extremely surface-active compounds and dissolved gases, rather than as an indication (as Grundfest would have it) of an entirely different mechanism of membrane operation than has hitherto been constructed. We are now engaged in examining such electrodes more closely in a resumption of our studies on metal tips in electrolytes.

F. PULSE-INTERVAL METER

At the Boston Psychopathic Hospital we designed a cardiac pulse-interval meter which tested extremely well. It turned out that practically nothing but the EKG signals have a significant component in the 10-18 cps band. Sharp filtering for this band allowed us to record the heart rate and only that in subjects exercising or convulsing.