

XXVIII. NEUROPHYSIOLOGY*

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RESEARCH OBJECTIVES AND SUMMARY OF RESEARCH

1. Basic Theory

Research on the functional organization of the reticular core of the central nervous system continues, in collaboration with Dr. William L. Kilmer of Michigan State University.

Our problem is to construct a theory for the reticular system which is compatible with known neuroanatomy and neurophysiology, and which will lead to testable hypotheses concerning its operation.^{1, 2}

Our first and second approaches to this problem³ were outlined in Quarterly Progress Report No. 76 (page 313).

We can report, at present, that we are embarked on a kind of iterative net statistical decision theory⁴ that is comprehensive, versatile, and penetrating enough to stand a reasonable chance of success.⁵

The computer modeling is being done at the Instrumentation Laboratory, M. I. T., by members of Louis L. Sutro's group.

W. S. McCulloch

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2. W. S. McCulloch, "What's in the Brain That Ink May Character?," Proceedings of the 1964 International Congress for Logic, Methodology and Philosophy of Science, Held in Jerusalem, August 26-September 2, 1964 (North-Holland Publishing Company, Amsterdam, 1965).
3. W. L. Kilmer, "On Dynamic Switching in One-Dimensional Logic Networks" (Information and Control, in press).

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4. W. L. Kilmer, "Topics in the Theory of One-Dimensional Iterative Networks" (to be published in Information and Control).
5. W. S. McCulloch, "Embodiments of Mind," in The Mind: Physical and Biological Approaches to Its Function (to be published by Michigan State University Press, East Lansing, Michigan).

2. Project Plans

a. Sensory Processes

Smell. Five years have been spent on the olfactory system (with Dr. R. C. Gesteland, now at Northwestern University) and the results of this study are soon to appear.^{1, 2} It has been shown that the coding of smell is holistic, that every fiber in the olfactory nerve has a broad range of sensitivity rather than a particular sensitivity to a smell and is a two-process system. These results have posed one of the most serious problems in the concept of a smell system. We now feel quite certain that the transduction is due to an allosteric action in a surface protein, but that the allostery is much broader than is usually conceived, and may be difficult to describe in terms of present theories of chemical action. It is a question that will underlie a great deal of research for several years.

Vision. It is possible to show that the firing pattern of a dimming detector (off-fiber) in the optic nerve of a frog reflects primary transductive processes in the rods and cones sufficiently well to be used to measure those processes. It appears, by this mode of analysis, that there are at least three kinds of transduction involved in the frog, and one has been tentatively identified as measuring the amount of isorhodopsin. It will be about a year before this method is utterly disabused or confidence may be placed in it. If it is valid, a new and significant tool in visual physiology has been found. The operations once reported by this group on the frog's eye can now be specified in much greater detail. These are not as assumed, either in terms of origin or exact description. This work, too, will take some time to complete.

b. Membrane Processes

During the past year and a half a number of predictions have been borne out quite accurately by experiment. It was supposed that $\text{La}^{(3+)}$ and $\text{Pr}^{(3+)}$ would act as super- $\text{Ca}^{(2+)}$ with respect to nerve membrane. This is, in fact, the case. It was also predicted that $\text{Cs}^{(+)}$ ought not to substitute either for $\text{K}^{(+)}$ or $\text{Na}^{(+)}$, and ought not to pass nerve membrane. This is also the case. Finally, nerve membrane was expected to be asymmetrical in structure, and this has been demonstrated (by Dr. S. Frenk of this laboratory) using $\text{La}(\text{MnO}_4)_3$ as a stain in electron microscopy. The present work is with artificial membranes, phospholipid paucimolecular layers, which exhibit a surprisingly low impedance and very large streaming potentials and streaming currents. The aim is to make such membranes with nonlinear properties of interesting sorts.

c. Instrumentation

A new device has been developed that is very helpful in looking at neural signals. It is a CLOOGE (acronym for Continuous Log Of On-Going Events). It presents sequential pulse intervals on linear, logarithmic or reciprocal scale extending over four decades, and includes certain additional processing that makes the output extremely easy to follow.

New low-cost high-gain amplifiers and special headstages for general use have also been designed. In fact, several low-cost, but accurate, data-processing devices are

being planned. These will permit on-line data reduction in analog; thus, the fairly expensive and still inefficient methods for use with digital computers will be bypassed.

J. Y. Lettvin

References

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2. J. Y. Lettvin and R. C. Gesteland, "Speculations on Smell" (Cold Spring Harbor Symposia on Quantitative Biology, in press).

3. Present and Proposed Research

During the past year we have pushed forward on the investigation of the properties of dorsal horn cells and have begun to exploit a number of the consequences of this research.¹⁻⁷ There are three horizontal laminae in the dorsal horn of the spinal cord. These laminae can be identified both by anatomical and physiological properties. They are laminae 4, 5, and 6 of Rexed. In lamina 4, the most dorsal, there are cells that receive only cutaneous afferents. We have shown, now, that most of them receive from the full spectrum of peripheral fibres. There is a gate control that influences the passage of arriving impulses from the periphery as they pass onto these cells. The gate is closed by activity in large-diameter peripheral fibres and by descending impulses from brain stem. The gate is opened by activity in small-diameter peripheral fibres. We have also given evidence that impulses can be generated in the dendrites of these cells. This suggests a much greater potentiality for analysis by nerve cells than previous models in which it was believed that only a single trigger point of origin of nerve impulses existed.

In lamina 5, we find cells with a special anatomy which receive cutaneous information collected by the cells of lamina 4. They are under the control of impulses descending both from the brain stem and from the peripheral tract. These cells show a new property that we have named "novelty detection." They fail to respond to the later stimuli in a train of repeated stimuli. We have been able to locate the place where this blocking of repeated input volleys occurs.

In lamina 6, the most ventral lamina in the dorsal horn, cells receive both from skin and from muscle. This convergence of inputs of different modalities is under control. In the decerebrate animal, the cells are dominated by the input from muscle and joints. In the spinal animal, where descending impulses from the brain stem have been eliminated, these cells are dominated by their cutaneous input. This process of switching is a new property of nerve cells which has not previously been described.

In the past year we have made very rapid advances in the discovery of a control mechanism that influences the effect on the central nervous system of entering nerve impulses. We had discovered some time ago that it was possible to decrease the effectiveness of entering nerve impulses by decreasing their size before they reached the first central cells. It was shown that a slow potential could be detected which measured the intensity of this "presynaptic inhibition." Next, we were able to assign the generation of this presynaptic inhibition to the activity of some very small cells whose function had not previously been known. These are the cells in substantia gelatinosa.

The next stage was the discovery that the set of the presynaptic control mechanism was in continuous action and was influenced by the position of the limbs, pressure on the skin, and by descending impulses from the head. If this system was in steady action, we wondered if the very fine slowly conducting peripheral fibres were playing a part in this tonic long-acting mechanism. We developed a technique for isolating the impulses

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in small fibres from those in large. We found that the small and large fibres were acting in opposition, the large fibres tending to close the gate, and the small to open it. The position of the control mechanism therefore depends, among other things, on the relative activity in large and small fibres. Thus far, this is the only function discovered for small fibres. This control mechanism, which can be moved either to exaggerate or diminish the effect of arriving sensory nerve impulses, has many implications for understanding sensory discrimination, and in particular the mechanism for generating pain. Anesthetics, for example, close the gate. Furthermore, a number of pathological states of the skin sensory system may be correlated with different settings of this control system. New concepts are appearing of the analysis of sensory events in context with simultaneous and preceding events.

In other work in this laboratory, we have proceeded with the analysis of skin sensation by examining third-order neurons along the pathway. We have also developed some testable theories about the method used by the nervous system in signalling the location of a stimulus. This work has involved work on normal amphibia and those with various transplanted eyes, legs, and skin.

A new theory of pain mechanisms has been developed.⁸ The activity of second-, third-, and fourth-order nerve cells in the cutaneous and proprioceptive pathways is being studied in animals in many different states of control.

Several aspects of the research reported above will be developed.

(a) Studies of pain control in man. We have already begun to test a prediction from our pain theory which suggests that continuous activity in large fibres should raise the threshold for induced pain. We shall use normal men and cases of trigeminal neuralgia, causalgia, and other types of intractable pain. Initial results are extremely promising.

(b) Spinal-cord organization in rat. We have shown that it is extremely profitable to study the activity of dorsal cells in cat cord with the animal in several different states. We intend to repeat these studies in rat with the intention of examining single cells during unrestricted movement.

(c) Descending control of spinal cord dorsal horn cells. We shall study in detail the effect of descending pyramidal volleys on the effects of arriving afferent volleys and on the firing of cells in laminae 4, 5, and 6.

(d) Effect of repeated stimulation. It is known that there are novelty detection cells in dorsal horn, and that motoneurons fail to respond to the later members of a long train of slowly repeated stimuli. We shall define the properties of this adaptation of a ventral-root reflex and probe within the cord to determine which cells adapt out in the chain from input to output.

(e) Behavior of cells in ventral horn. We have described the lamination of dorsal horn and will advance to a study of lamina 7, which contains cells of a very high degree of complexity.

(f) Origin of the way in which muscles in a reflex response direct the response to the location of the stimulus. We shall study by a series of new methods the linkage between skin stimulation and motor neuron response in the frog skin wiping reflex.

(g) Limulus eye. Studies of the coupling between light received in the eye and the generation of a local response and the coupling between cells in the ommatidium will continue.

P. D. Wall

References

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A. NUMBER OF MODES OF OSCILLATION OF A NET OF N NEURONS

Given a set of N neurons. The state of the net at time t is determined by the state of all neurons at time t. There are two possible states for each neuron at time t (firing or nonfiring). The total number of possible states of the net is 2^N .

When the net oscillates it runs through a number of states in a repetitive way. A mode of oscillation of the net is determined by the states into which the net gets during one period, and the order of these states but one. If we select k states out of 2^N , there are $(k-1)!$ ways of ordering $(k-1)$ of these states.

Selecting k states is possible in $\binom{2^N}{k}$ ways. So the number of modes of oscillation of the net, in getting into k different states is

$$(k-1)! \binom{2^N}{k}.$$

Summing this expression for all possible k gives the total number of modes of the net:

$$\sum_{k=2}^{2^N} (k-1)! \binom{2^N}{k} = \sum_{k=1}^{2^N} (k-1)! \binom{2^N}{k}.$$

If we want to be able to generate any of these modes by putting a constant binary input on a number of input lines, then this number ought to be at least the least whole number that is larger than or equal to

$$\log_2 \sum_{k=1}^{2^N} (k-1)! \binom{2^N}{k}.$$

C. P. G. Schnabel

