XXVI. NEUROPHYSIOLOGY*

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RESEARCH OBJECTIVES

1. Basic Theory

The general problem of reliable computation in vertebrate central nervous systems has been solved in principle.[1] Also, neurophysiologists are making rapid progress on the functional organization of specialized regions in such systems. But no one has yet reported a way for thinking effectively about how the brain stem reticular system performs its task of committing an entire organism to either one mode of behavior or another.

Our problem is to construct a theory for the reticular system[2-4] which is compatible with known neuroanatomy and neurophysiology, and which will lead to testable hypotheses concerning its operation.

Our first approach was through the theory of ordinary one-dimensional iterative logic nets.[5-7] But all of the crucial questions in this theory turned out to be recursively unsolvable when considered generally, and combinatorially intractable when particularized with the required degrees of dependency among the variables.

Our second approach was through the theory of coupled nonlinear oscillators, but we soon found that there is not nearly enough of the right kind of mathematics to be of much help in our problem.

All that we can report at the moment is that we are embarked on a kind of iterative net statistical decision theory that is comprehensive, versatile, and penetrating enough to stand a reasonable chance of success.[8,9]

W. S. McCulloch

References

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2. A General Theory of Observation and Control*

It is our purpose to establish a logic of observation and control comprising (a) representations; (b) measures of relevance; and (c) policies for search. These aspects are to be considered with special reference to organization of nerve nets and epigenetic systems.

M. C. Goodall

3. Project Plans

(a) The Nature of Biological Membranes. We expect to develop our work on the effects on nerve membrane from trivalent cations and the heavier monovalent cations, such as Cs^+ or Fr^+, as well as organic ones such as choline or the cocaine substitutes. Our results in electron microscopy have suggested an essential asymmetry in nerve membrane, in that the inner surface of the unit membrane does not stain with lanthanum, whereas the outer surface does. We have taken this to mean that the inner surface may be composed of phasphatidyl choline (which repels cations). We have been led to begin study of artifical membranes of phospholipids two molecules thick. We shall also try to make more quantitative our notions on the morphe of ions and channels. Our finding that Cs^+ not only does not carry current across the membrane but also does not compete either with Na^+ or K^+, leads us to suppose that no useful modification can be made of ion-exchanger theory, which is the most prevalent theory in membrane physiology now. Partly as a tour de force, partly for the new information that it will give us, we expect to do voltage-clamp studies on the mammalian node of Ranvier.

W. F. Pickard, S. Frenk, J. Lettvin

(b) The Nature of Retinal Information. Our present view is that the information transmitted from some receptors in the frog's eye is a comparison between the restoration and the bleaching rates of the pigment, or between the total bleached pigment and the amount of bleaching. In either case, it is the former, a measure of the light adaptation, that has the excitatory sign. With respect to at least two of the ganglion cell types in frog, it seems as if we are measuring the disparity between the level to which the eye

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has become light-adapted and the level at which light is actually occurring. We now have sufficient evidence on this point; however, we are holding off in order to establish a more subtle point. It appears that, using this measure, we have been able to devise certain successful "quality definers," optical illusions for single ganglion cells, which make hash of the criticisms of Gaze and the Grüssers, and establish the importance of local order of connection in the dendrites. When our work is sufficiently advanced in the collation of data, we expect to have established the interpretability of form-function relations in dendritic trees.

S. Frenk, J. Y. Lettvin

(c) Causes of Tropistic Movements in Plants. We are studying the problem of whether geotropism is due to statoliths or to a more distributed compression-extension mechanism. We continue to work on the effect of trivalent cations on growing oat coleoptiles. We are also engaged in research on the mechanisms whereby stomata open and close.

Barbara G. Pickard

(d) Development of Some Bases for a Theory of Perception. There is enough material now on eyes of various sorts that one might consider the application of some general group theoretical methods as an approach to a theory of visual function.

W. H. Pitts

(e) Instrumentation. New devices will be built as they are needed. We shall issue a manual of useful laboratory methods and devices.

J. Y. Lettvin

(f) Physical Optics. We expect to continue our exploration of optical methods for use in physiological optics, hydrodynamics, and various other disciplines.

B. Howland

4. Proposed Research

Our group will work on spinal-cord mechanisms related to the handling of sensory information and on the nature of cell-cell interaction. Several specific subjects will be investigated: the role of fine afferent fibers in the control of sensitivity of the first central synapse; the convergence of large and small fibers on central cells; the way in which the modality of the stimulus is encoded; the way in which the location of the stimulus is encoded; the location of initiation of nerve impulses, and the influence of structures in the head on spinal mechanisms.

We shall carry out the following investigations during the coming year.

(a) A lamina of cells that receive cutaneous afferents lies across the dorsal part of the dorsal horn. Some of these cells are excited by A fibers alone, and we wish to discover if unmyelinated fibers affect the effectiveness of arriving A fibers, although the unmyelinated fibers have no direct effect. We believe that other cells are excited by all components of the peripheral nerves and we wish to establish the input-output characteristics of this system with various steady and suddenly changing states of the input. Furthermore, we suspect that descending volleys from the head also play a role in setting the characteristics of this initial stage of the skin sensory pathway. We shall also examine the effect of various analgesic agents that may play a role in modulating the over-all sensitivity of the system, and may affect the time pattern of the output impulses. This work will be done on acute decerebrate or spinal cats with microelectrodes.

(b) We now suspect that small action potentials that can be recorded intracellularly in the region of dendrites may be impulses actually initiated in dendrites. The previously accepted model of a nerve cell suggested that impulses were only initiated in the cell body region and did not propagate into the dendrites. The dorsal spinal interneurons have a particularly suitable anatomy for studying activity in the cell body and in the dendrites. We shall compare the distribution of impulses within the cell during spontaneous activity, orthodromic responses with natural and electrical stimulation and with antidramic stimulation of the axons leading from the cells. This work will be done on acute spinal cats with low impedance microelectrodes.

(c) In the frog, the fields set up in the spinal cord by volleys of arriving cutaneous impulses will be recorded. The location of single units responding to afferent volleys will also be recorded. The field maps will be reduced by calculation to source-sink maps so that the location of entering impulses can be specified. When the distribution of endings and excited cells has been established in the normal, we shall turn to the spinal cords of frogs that have been operated on as tadpoles. In this operation we have removed a strip of skin and replaced it with a reversed position on the body so that dorsal skin lies ventral, and vice versa. When these animals metamorphose and develop wifing reflexes, some of them wife as though the skin was still in its original position. There is no peripheral meandering of nerves; therefore, it is apparent that the skin is able to inform the nervous system of what type of skin has been stimulated. By comparing the central nervous system fields in normal and reversed skin animals we hope to determine the signal that is used to inform the CNS of the location of the stimulus. Similar work is in progress on animals with transplanted eyes that produce a blink reflex in the normal eye when the transplanted eye is stimulated. This work involves an analysis of the skin and corneal endings in the medulla.

(d) A survey will be carried out of interneurons deep in the spinal cord. This will take advantage of the very detailed knowledge that we now have of the functioning of the first central neurons. We have some preliminary indication of highly unusual input-output relations in these neurons, including rapidly adapting cells that respond only to novel stimuli, cells that are shifted to a new steady rate of firing by a single stimulus, and cells with very wide receptive fields that can shift their receptive field. This work will be done on cats.

(e) Previous workers have shown that in a decerebrate cat the reflexes of the two sides can be made unequal by removing half of the cerebellum. It has been suggested by other workers that this asymmetry remains even after the spinal cord has been cut across, provided that a period of 20 minutes is left between the cerebellar lesion and the cord section. We intend to try to repeat this phenomenon and investigate the details of the reflex pathway to see if we can locate this suspected long-lasting change.

(f) On the direct question of cell-cell interactions we intend to investigate some electrical interactions that have been found in the Limulus eye by Smith and Fourtes. Neighboring cells in the ommatidia have low resistance pathways between them which can be closed down by an increase of the membrane potential. The location and dynamics of this phenomenon will be investigated.

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A. AMYLOPLAST STATOLITHS AND GEOTROPISM

The belief that plants sense gravity by means of starch grains, or amyloplasts, which sink to the lower sides of the cells has been widely held ever since the idea was proposed more than half a century ago. The evidence has consisted of correlations of geotropic sensitivity with the presence of mobile starch grains of density greater than that of cytoplasm. We have recently been able, however, to obtain coleoptiles almost free of starch which respond to gravity at the same rate as do starch-filled controls.

Depletion has been accomplished by incubating young wheat coleoptiles in gibberellic acid, kinetin, and penicillin under carefully chosen conditions. All operations are performed under phototropically inactive dim red light. Controls are incubated either in penicillin and water alone or with millimolar sucrose; starch is much more abundant after incubation in sucrose than in water.

Plants are exposed to gravity by setting them horizontally on filter paper moistened with gibberellic acid and kinetin to inhibit starch regeneration and a very low concentration of glucose to support growth. Coleoptile length and curvature are measured at the beginning and end of gravitational stimulation. In four separate experiments we found that plants, judged almost starch-free by examination of squashed preparations at 400X magnification, bend geotropically at a rate comparable with that of controls. For example, on the average, depleted plants curved 40° per millimeter growth, while starch-enhanced plants curved 41° per millimeter.

More refined estimation of residual starch is under way. It would be very surprising if the amyloplasts had disappeared completely, and we expect to find minute amyloplasts abundant when we examine carefully fixed and stained sections that are cut 5 microns thick. Such tiny particles would, however, almost surely undergo vigorous Brownian movements, and should not sink to the lower side of a cell. Similar arguments lead us to doubt that any other cell organelle is acting as a statolith, but our study of 5-μ sections must be completed before any conclusions can be drawn.

Since geotropic curvature is mediated by hormone redistribution, it is desirable to show that the hormone responses of controls and depleted coleoptiles are similar. Our preliminary studies suggest such a similarity, but more work must precede a definitive answer. Time courses of response will also be necessary.

In summary, it appears that since wheat coleoptiles with almost no starch bend geotropically as effectively as do plants with abundant, large amyloplasts, the presence of starch-grain statoliths is probably not critical for the perception of gravity by these coleoptiles.

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