XXII. NEUROPHYSIOLOGY*

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RESEARCH OBJECTIVES

The aims of this group can be stated best under six main headings:

1. Computation

Our purpose is to develop the necessary logical and mathematical theory for an understanding of parallel computation such as occurs in our brains, and thus lay foundations for an attack on the problem of decision making in the presence of a redundancy of potential command like that encountered in the reticular formation.

M. Blum, W. S. McCulloch

2. Structural Properties of Cells

Our purpose is to gain basic knowledge about the structural properties of water inside cells by any suitable experimental method, including nuclear magnetic resonance, and to investigate critically the consequences of these properties for nerve action, including membrane function and proton conduction.

H. J. C. Berendsen, W. S. McCulloch

3. Olfaction

Our study of the mechanism of olfaction and the rational classification of odors has progressed considerably, through the discovery of a convenient preparation and with the use of the tiger salamander (Ambystoma tigrinum), in which the primary olfactory fibers and the mucosa are both accessible. Besides recording responses from the fibers, we expect to measure the local variations of the receptor potentials in the presence of various concentrations of different odors, and perhaps the variations in the membrane impedance of the receptors.

With respect to the synthetic aspects of the problem, guided by the fragmentary literature on the variation of the impedance of electrodes in the presence of monomolecular layers of adsorbed substances (for example, the familiar displacement of the electrocapillary maximum of mercury), we are beginning to explore the selective "poisoning" (as measured by ac impedance changes at defined dc potentials) of electrodes, particularly those more closely allied to the natural olfactory detectors, such as suitable selective ion-exchange membranes. Our purpose here is to converge upon a model electrode that imitates the olfactory receptors (or some of them) as nearly as possible in its selective response to traces of various substances.

R. C. Gesteland, W. H. Pitts

4. Impedance Determination

I am making measurements for the determination of the mechanical impedance presented by the human postural reflex to the environment. Apparatus for the measurement of applied Gaussian random torque and the resultant angular deflection of the hand about the wrist (flexion force) has been completed, and the records obtained are being processed by the TX-0 computer for computing autocorrelation and crosscorrelation functions and their Fourier integrals in a straightforward approach to impedance determination.

A. R. Johnson

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5. Vision

Our aims in this project are defined as: The operational analysis of animal vision and human vision; the synthesis of these operations with analog devices, the analysis of synaptic transmission, and the synthesis of models thereof. The first objective is illustrated by a paper to appear in Proceedings of the Institute of Radio Engineers (J. Y. Lettvin, H. R. Maturana, W. S. McCulloch, and W. H. Pitts, "What the Frog's Eye Tells the Frog's Brain"); the second by a paper to be published in Proceedings of the International Symposium on Principles of Sensory Communication, M.I.T., July 19 - Aug. 1, 1959, edited by W. A. Rosenblith; the third is an approach to electrical transmission, in which inhibition and facilitation are both accomplished by the same process. In the first case the process causes a shunt, and in the second, it transmits a current. There is some physiological evidence for this now. The demonstration, yes or no, will occupy our coming year.

J. Y. Lettvin

6. Sensory Systems

This group will work on the function of relay nuclei in sensory systems. We have already analyzed the properties of the central nervous system cells that receive fibers from the body skin. We are now proceeding to study the nuclei by dealing with the face skin. The filtering and selective properties of these neurons have already been studied, and the basis for various skin sensations has been shown. The first, second, and third neurons in a skin-sensory system will be studied in normal and various abnormal states. The abnormal states, to be studied in cooperation with Dr. Paul Weiss of the Rockefeller Institute, New York, will include animals with an additional limb or with an additional cornea. It may also be possible, in cooperation with Dr. R. Melzack, of the Department of Economics, M.I.T., to examine animals reared under conditions of relative isolation. By examining normal, overloaded, and underexercised sensory systems, we intend to explore the basis of sensation and the mechanism by which connections are established in the central nervous system.

P. D. Wall

A. ON PARALLEL COMPUTATION

We now have methods of constructing nets of nondegenerate neurons that are logically stable for functions of 1 or 2 jots, and 1 or 2 blanks, for all steps of threshold between tautology and contradictions of the output neuron, and for all δ, where δ is the number of independent axons afferent to a cell. We know how to find and can enumerate all such nets. For those of more than 2 blanks or 2 jots, some form of degeneracy is necessary and we know that it is sufficient to let neurons run beyond tautology or contradiction.

In this work we have noted that the output neuron always requires interaction of afferents, as well as inhibition and excitation on the neuron. We have shown that these are necessary and sufficient for the construction of all neuronal diagrams for all δ. Among the output neurons generating logically stable functions, we noted that many passed through a series of steps, at each step defining functions that, given the arguments, suffice, like Sheffer's stroke functions or like Charles Peirce's amphecks, to construct all 2^{2^δ} functions. We have found that the number of such functions is

$$2^{2^\delta}\left[\frac{1}{4} - \frac{1}{2 \cdot 2^{2^{\delta-1}}}\right]$$

which rapidly approaches 1/4 of all functions as δ increases. We call all such functions "polyphecks."

In terms of complements and duals, we are able to describe polyphecks thus: (a) because they have a jot in the NONE space and a blank in the ALL, they are able to complement; and (b) because they are not their own complementary dual, they can produce the disjunct, or logical sum. By a complement we mean the negation of the function described by a Venn diagram. The dual of a single jot is the product of the complements of the component propositions of the jot. The dual of a Venn is the disjunct of the duals of the individual jots.

When we do not limit ourselves to the arguments and inquire what classes of functions will serve in lieu of the arguments, we find that each function must have $2^{\delta-1}$ jots, and that there are $2^{\delta}!$ such classes, each of which is characterized by being a set of permutations of the Venn spaces of the arguments. To our surprise, we note that every $2^{\delta-1}$ jot function that can be computed by nondegenerate nets without interaction of afferents becomes an appropriate set by permutation of the arguments. Constructions and proofs are reserved for a technical report.

M. B., W. S. McC.

B. STRUCTURE OF WATER IN BIOLOGICAL TISSUE

As a result of observations made by a number of investigators the question arose as to what extent the water molecules inside living cells are organized as in a solid or liquid-crystalline state, and what the consequences of such an organization would be in the function of nerve cells. In short, the main support for the suspicion that water in cells does not behave as a liquid is expected to come from the following observations:

(a) DC potentials measured inside cells appear to be very nearly the same, whether the electrode material is antimony, saturated KCl solution or Ag-AgCl.

(b) When a piece of tissue that has been kept under an inert gas pressure of 60 atm is brought suddenly into a vacuum, the individual cells do not explode, as would be expected if the gases were dissolved in the cells, but the cells are torn apart with their individual structure undisturbed.

(c) The specific conductivity for an alternating current of the axoplasm is not homogeneous inside the axon, but is low near the membrane and higher in the central cylinder of the axon.

These observations, although they do not prove that the intercellular water is not in a liquid state, certainly justify a deeper investigation, whose results may be significant to neurophysiology with respect to ion mobility, role of proton conductance and membrane properties. It is likely that theoretical problems here enter the realm of solid-state physics.

One of the nondestructive tools for the attack on this problem is the nuclear magnetic

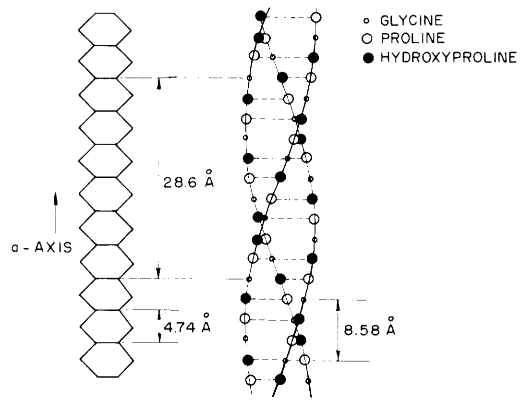

Fig. XXII-1. Scheme of the collagen molecule (after A. Rich) with a column of organized water molecules. This column, in which joints represent oxygen atoms, has been turned 90° to show the structure.

resonance of the proton. This, however, has the disadvantage of requiring a volume of approximately 1 cc, which excludes working with one cell. In order to investigate the possibilities of this tool we worked on tendon. Collagen has a fairly well-known structure which permits interpretation of the measurements. It also has a parallel arrangement of fibers in a sample of suitable size.

The measurements, which are still in progress, show a very marked effect of the angle between the fiber and the direction of the magnetic field on the absorption curve. Quantitative inspection of the second moment of the absorption curve as a function of this angle indicates that the main interaction between protons arises from pairs of protons lined up in the direction of the fiber. The spin-lattice relaxation time is intermediate between that of water and that of glycerol, which indicates that the individual water molecules are not part of a rigid crystal lattice, but are subject to fairly rapid translation and/or rotation.

Observations of spinal cord and of muscle yield the same result, but no strong relation between the direction of the fiber and the absorption curve has been found.

It may prove important that the structure of collagen and the structure of water have certain similarities. The distances between structurally similar points along the threefold spiral of the helical polypeptide chains, notably the C=O of glycine with its ability to form H-bonds with water in collagen II, appear (1) to be 28.6 A. If side chains permitted an uncoiling of the threefold spiral, the distance would become 8.58 A. (See Fig. XXII-1.) Now any coiling that relates similar groups on the three polypeptide chains by a translation parallel to the axis of the spiral makes the translation distances multiples of $\left(n \pm \frac{1}{3}\right)$ 8.58 A, where n is an integer permitted by side chains. The short-range structure of water is thought to be that of ice I, extrapolated to higher temperatures. The repeat (2) along its a-axis at 25°C is 4.74 A, and at 37°, 4.85 A. Its a-axis, not its c-axis, is important because H-bonds may be formed perpendicular to it at each repeat. It turns out that the actual existing right-handed threefold spiral n = 3 fits the water lattice, for a sixfold repeat along the a-axis, and yields $6 \times 4.74 = 28.4$ A for 25°C.

Structures that so fit the water lattice tend to stabilize the order of "bound" water in one or more directions, and thus to regiment adjacent layers of water. This order does not mean that individual H-bonds are not broken and reformed rapidly, but that the "ice-cluster" at any time around the stabilizing macromolecules have the same structural relation to the macromolecules, enabling them to build long-range order. [This is not the main factor in the case of collagen, for there is just not enough water. Once the molecule has been formed, bonds between polar side chains stabilize the long-range order.]

A similar study of the relation of structured water to various natural macromolecules is required to discover general properties.

A consequence of a stable water lattice is that it considerably accelerates the diffusion-controlled transfer of protons along the macromolecule: this is also a subject of our study.

We may even have to consider ice VI, which can exist at temperatures as high as 80°C, but only at high pressures, for local forces may be sufficiently strong to form ice VI locally, extended in only one or two dimensions, thus perhaps being constructive in cholesteric states. The reported optical activity of ice VI is interesting in this connection (3).

H. J. C. B., W. S. McC.

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