

XXVII. NEUROPHYSIOLOGY*

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RESEARCH OBJECTIVES

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

1. Basic Theory

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

J. A. Aldrich, M. Blum, J. D. Cowan, N. Onesto, W. S. McCulloch

(a) Computation in the Presence of Noise. An information theoretic model for probabilistic logical computation has been devised, and using this, we have shown that, in principle, there exists a nonzero rate for arbitrarily reliable computation in the presence of noise. Many-valued logical schemes have been used in an attempt to realize such rates, with negative results. The conclusions drawn are not that nonzero rates are unrealizable, but that more sophisticated structures are necessary.^{1, 2}

J. D. Cowan

References

1. J. D. Cowan, Many-valued logics and reliable automata, Symposium on Principles of Self-Organization, edited by H. von Foerster and G. Zopf, Jr. (University of Chicago Press, Urbana, Illinois, 1961).

2. J. D. Cowan, Toward a proper logic for parallel computation in the presence of noise, Proc. Bionics Symposium, edited by J. E. Steele (Dayton, Ohio, 1961).

(b) Multiple Error-Correcting Codes. Codes that correct many errors but do not correct few errors have been investigated. In these codes only received words that are a distance x from a transmitted word are decoded as the transmitted word ($np - n\epsilon \leq x \leq np + n\epsilon$, where n is the block length, p is the probability of error, ϵ is any positive number).

An example of $n = 60$, $p = 1/3$, $k = 5$ has been worked out in detail. The circuits for encoding and decoding this code can be realized by logically stable nets.

J. D. Cowan

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(XXVII. NEUROPHYSIOLOGY)

2. Project Plans

(a) Olfaction Physiology. We plan further study of patterns of activity in primary receptors of olfactory mucosa, extending the work of R. C. Gesteland and W. H. Pitts.

R. C. Gesteland, J. A. Rojas, W. H. Pitts, J. Y. Lettvin

(b) Olfaction Chemistry. We plan to use reversible poisoning of carbon electrodes activated in different ways as a model for olfactory receptors.

W. H. Pitts, R. C. Gesteland, J. A. Rojas, J. Y. Lettvin

(c) Electrodes. We shall prosecute the study of specifically sensitive O₂, pH, and other sorts of electrodes, partly for oceanographic application, partly for biological application.

W. H. Pitts, R. C. Gesteland, J. Y. Lettvin

(d) Instrumentation. Various electronic devices will be built as the need arises.

J. Y. Lettvin, R. C. Gesteland

(e) Visual Processes. We shall continue studies on octopus and frog eyes.

H. R. Maturana, J. Y. Lettvin

(f) Mechanical Components of Nervous Activity. We intend to continue our study of nerve twitch, collaborating with Professor G. Sten-Knudsen.

J. Y. Lettvin

(g) Evolution of Scientific Language. We intend to continue study of the origins of scientific language.

Herta von Dechend, W. H. Pitts

(h) Chemiluminescence. Further studies are to be made on the nature and applications of this phenomenon.

B. Howland, W. H. Pitts, R. C. Gesteland

3. Problems of Sensory Projection Pathways

This group continues its work on problems of sensory projection pathways with particular emphasis on cutaneous sensation. The past year's work will result in the following publications:

(i) "Four Aspects of the Trigeminal Nucleus and a Paradox," which will appear in the Journal of Neurophysiology, deals with the organization of the nucleus that receives the sensory news from the face. It shows that the apparent complexity of the nucleus can be explained by assuming that the cells nearest the entering nerve are affected by all types of fiber, while only the largest entering fibers penetrate for long distances. The paradox is that no "pain" cells could be found even though destruction of the descending tract abolishes pain reactions.

(ii) "The Mechanisms of Cutaneous Sensation" will appear in Brain, early in 1962. In this paper we analyze the historical solutions to the problem of modality analysis and transmission and show that they are inadequate to explain our results. We propose instead that the information is transmitted as a space-time pattern of nerve impulses and specify exactly what is meant by the patterns and how they could be analyzed.

(iii) "Coding of Information in the Cutaneous System" will appear in the

December 1961 issue of Proc. IRE. It translates the paper that will be published in Brain from biological language into a problem of interest to communication scientists.

(iv) "The Relation of Morphology and Physiology of Skin Nerve Terminals." This paper will be submitted to Experimental Neurology. It goes a long way toward solving the problem of why large nerve fibers have different properties from small nerve fibers, even though the entire terminal twigs are identical. It suggests that the missing factor is the number of branches on the end of each fiber.

(v) "The Origin of Slow Potentials in the Spinal Cord" will be submitted to the Journal of Physiology. This paper presents evidence that will destroy previous theories on the function of the small-cell component of the dorsal horn and presents very strong evidence that they are the generators of the dorsal-root potential. These small cells have been completely neglected in modern physiology and this paper will introduce, essentially, a new component into the working of a transmission pathway and may explain not only the slow potential but the origin of presynaptic inhibition.

Three other studies are steadily progressing, but we are not yet ready for publication:

(i) The effect of descending pathways on a sensory transmission pathway. In this work we are studying the discharge pattern of first central cells that respond to a specific skin area while the cell is being affected by descending pathways. It is hoped that the nature of this descending influence can be discovered. This work is of importance in explaining the filtering properties of way stations in transmission pathways.

(ii) The method of transmitting information on the location of the stimulus is being studied in frogs with particular reference to the corneal reflex. The work involves transplantation experiments and is being done in collaboration with Dr. Weiss at the Rockefeller Institute.

(iii) Nerve-cell tissue culture is being developed successfully with the intention of studying those factors in the interaction between nerve cells and other cells which determine the formation of junctions.

These eight approaches all point to the problem of describing the rules of convergence of nerve cells onto other nerve cells and the mechanism by which relay stations in sensory pathways act as filters.

J. E. Brown, K. Kornacker, Diane Major, A. Taub, P. D. Wall

4. Effects of Early Sensory Isolation*

There is considerable evidence that severe restriction of the early perceptual experience of animals produces profound disturbances of their perceptual, emotional, and intellectual development. The purpose of our investigation is to carry out a series of studies on the physiological mechanisms that underlie the highly abnormal behavior observed in animals reared in isolation. The focus of individual studies will be on three salient characteristics of the behavior of animals reared in isolation: (a) a frequent failure to perceive and respond to the appropriate environmental cues, including stimuli that are painful to animals that are reared under normal conditions; (b) an extremely high level of excited activity that pervades virtually all of the animals' behavior; and (c) a low capacity for learning new responses in problem-solving situations. The method of procedure for the first problem is to observe the behavior of restricted and normally reared animals from the same litter in response to brief burns and pinpricks and simultaneously to record responses evoked at the midbrain, thalamus, and cortex.

R. Melzack

*This work is supported in part by the National Institutes of Health [Grant M-4235-(C1)].

(XXVII. NEUROPHYSIOLOGY)

A. NEAPOLITAN STUDIES

Our work in Naples this summer with Dr. H. R. Maturana, Dr. O. Sten-Knudsen, and Miss Hilary Maunsell yielded some interesting data.

1. Octopus Opticus

There is no need to repeat the background of this problem which was discussed in Quarterly Progress Report No. 61 (pp. 193-209). We did succeed in recording from single fibers (or rather, a spectrum of a few neurons that could be resolved into single units by height and shape of discharge). At any rate, some of the properties of a single reticular cell are these:

(a) It has a preferred plane of polarization of light.

(b) Adjacent units have orthogonal planes of polarization. Groups of a hundred fibers, or so, show clear-cut stimulating planes of polarized light which are orthogonal to each other.

(c) The receptive field of a single unit is a function of dark adaptation. It is very large in the totally dark adapted eye, and may be measured in degrees. It is very small under mild background illumination or after light adaptation, and is measured in minutes. The shrinkage of the receptive field in light is rapid – almost complete in approximately 60 seconds with moderate illumination, and the expansion in dark is slow – almost complete in 10 minutes. These dilatations and constrictions of the receptive field fit with what is to be expected from the pigment migration in individual cells – the equivalent of a distributed stop or collimator in the image plane of this eye. For this reason, incidentally, one must not trust electroretinographic data in this animal any more than in vertebrates.

(d) There appears to be a lateral interaction between retinal fibers. It shows itself in two ways:

(i) Any single unit has two stable states in absolute darkness – either it is firing at a slow rate or it does not fire at all. Successive turning off of a stimulating light shows that any fiber alternates irregularly between these two states. This alternation is really tentative but we saw enough such units to think that we can explain thereby the dark discharge reported in Quarterly Progress Report No. 61 (pp. 193-209).

(ii) If a unit shows discharge in the dark, that discharge can be turned off by casting a dim light on visual areas some distance away.

(e) Some of the units show the effects of efferent control, although it is difficult to say exactly how this control is manifested. The quantification of such data is still remote and we work by feel.

We should like to point out an interesting consequence of property (a). In a real

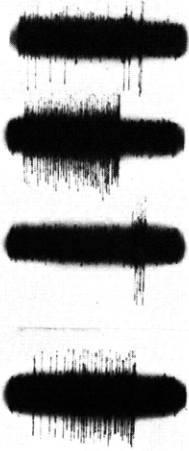
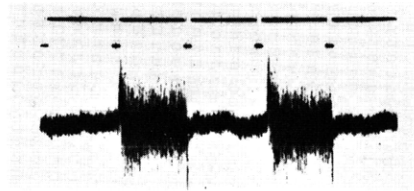
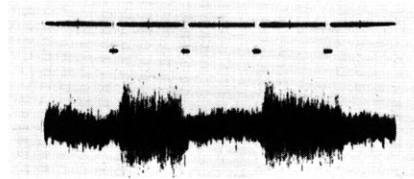


Fig. XXVII-1. Single-unit record from the optic nerve of the octopus, obtained while moving a white spot through its receptive field. The noise level is very high, and barely appearing above it are small bits of junk which is background noise from other fibers. Note how fluctuant is the height of the large unit because of the noise. Time is 20 seconds for the full sweep.



(a)



(b)

Fig. XXVII-2. (a) The record from a bundle of more than 100 units which was recorded during initial darkness, then light, then dark, then light, then dark, with 2 sec between each change. (b) The same bundle has been allowed to come to its lowest resting activity with the light on and a Polaroid filter between the eye and light. The filter was so rotated that the resting activity was minimum. The markers then show sequential 45° rotations. Two orthogonal planes of polarization produce maximum activity. Unless the population consisted of 2 groups, each sensitive to one of the two planes, such a picture could not result. This has been verified with single-fiber records that are not shown here but that prove that each fiber has a maximum sensitivity to a particular plane of polarization. The neighbors of the fiber are also sensitive in the same way, either in that plane or in the orthogonal plane, as is shown here for large groups.

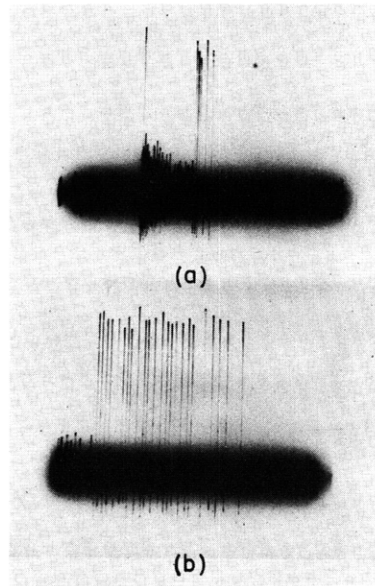


Fig. XXVII-3. The large spike is a single efferent fiber recorded with the microelectrode. The small hash above the base line is the afferent activity. (a) The light was turned on part way through the sweep; the afferent begins firing and there is a single efferent spike. The light was turned off two seconds later; the afferent activity stops and the efferent fiber shows a burst of spikes. (b) The light had been left on for 20 seconds before the sweep started and was turned off sharply during the first part of the sweep. The afferent activity stops and the efferent fires for a considerable period of time.

image a sharp boundary exhibits a narrow band of polarization of light along the boundary. Thus the sensitivity to polarized light may not reflect submarine lighting conditions as much as it gives edge detection in the primary fibers. Direct evidence for this process would be useful, but thus far we have only hints that some units do sense oriented boundaries, for the confirmation or denial of this guess requires a more stable mechanical and optical arrangement than we had.

At the same time we did studies on efferents without finding too much more than we have already reported. But our preparation now permits us to view a single efferent and a few afferent fibers, all concerned with the same minute field, simultaneously in the intact visual system, and thus permits us to adduce various interactions. We shall require much more subtlety to present an unequivocal account, however.

2. Squilla Heart Muscle

Unfortunately, we have to retract much of what we reported in Quarterly Progress Report No. 61 (pp. 209-212). A later report will discuss the problem in detail. There is some reason to suppose that the earlier observations are still

useful but the interpretation was premature

3. Mechanical Response in Nerve

We and Dr. Sten-Knudsen put a nerve from the walking leg of lobster between a clamp at one end and a sensitive crystal at the other, and showed that, on stretching the nerve slightly, stimulation of the membrane throughout the whole length of the nerve with a transverse field produced a twitch of a few hundred micrograms. The twitch is

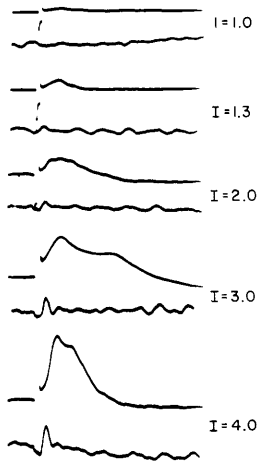


Fig. XXVII-4. Simultaneous display of the nerve spike on the top sweep and the nerve twitch on the bottom to show the relation in time as the current is increased. The artifact is 0.1 msec long, and because the nerve spike had to be recorded, the physical arrangement was much altered and the twitch is much reduced.

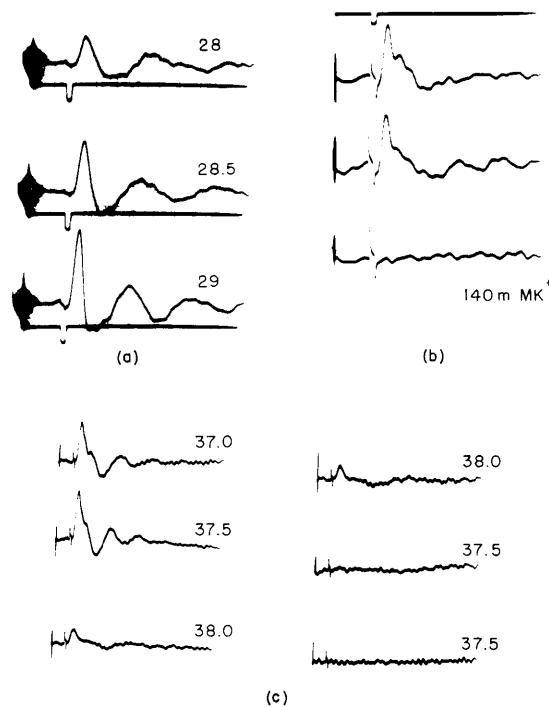


Fig. XXVII-5.

- (a) Nerve twitch in the first sweep which is under tension that is gradually increasing as indicated by the numbers. The artifact is 0.1 msec long and represents the period during which transverse current is applied to the whole nerve, in this case that from the walking leg of the lobster.
- (b) The same phenomenon on another nerve in sea water at constant tension but with the bath replaced in the lowest sweep by 140 millimolar KCl. Both the nerve spike (not shown here) and the twitch disappear.
- (c) This is the result of increasing tension until the nerve blocks. At stretch, 38 mm, the block occurred after 2 pulses, and the nerve did not return to function after slackening.

(XXVII. NEUROPHYSIOLOGY)

shorter than the nerve spike, reaching its peak and declining to zero in approximately 0.3 msec and then overshooting. We showed that the twitch occurred only if the nerve spike was present, and it was abolished by the same procedures that abolished the spikes.

J. Y. Lettvin, W. H. Pitts

B. COLOR VISION IN THE FROG

Mr. W. Muntz of Dr. S. Sutherland's group at Oxford University spent the summer in our laboratory to discover the character of color vision in the frog. He found that the information is conveyed by a distinct group of optic nerve fibers directly to the lateral geniculate nucleus in the diencephalon of the frog. None of these fibers go to the superior colliculus. Instead, part of the collicular outflow also goes to the lateral geniculate to admix there with color as input to the nucleus.

The fibers of this group are, seemingly, myelinated, have approximately 10° receptive fields, and, in all respects, resemble the "on" fibers of Hartline. We had taken, by default, our "edge detectors" to be Hartline's "on" group, but in fact were wrong, for Mr. Muntz went to him to compare data and discovered that the color sensitivities and sizes of the receptive fields of the fibers that are bound for the lateral geniculate were the same as those that Hartline found for the "on" group. (Thus, in fact, nobody had recorded the unmyelinated fraction of the optic nerve before our study. This point is made, not so much in pride, but to show that there is stronger justification for our electrode methods than we had thought.)

Each of these fibers responds to the "on" of a light throughout the receptive field, and this response is not contingent on boundary. The response to "on" is strongly affected by the hue of the light — that to blue being earliest, strongest, and longest in duration. As one varies the blue toward red or violet the response drops off and changes in pattern of firing. One of us (J. L.) who saw the earlier experiments had the impression, in fact, that hue was sufficiently encoded that one might, from watching the response, guess which color had been presented. In later discussion Muntz remarked that he felt the same way but had not enough quantitative data to prove this, so he would not publish that point. At any rate, the most efficient blue was that also given by Granit¹ for the frog but with the use of other techniques. Variation in hue seems to affect the system more than variation in saturation or brightness.

Muntz, shifting then to the behavioral aspect, found that the same blue is that color to which a frog will jump when irritated — going to it in preference to any other color. All of his work on this question is to appear as a paper.

For a complete account of the frog afferent system, a study of the fibers that go to the mesencephalic tegmentum still remains to be done.

J. Y. Lettvin

References

1. R. Granit, Sensory Mechanisms of the Retina (Oxford University Press, London, 1947).

C. DESIGN OF MICROELECTRODES

Most of the successes of our Laboratory in the past few years have been a direct consequence of our preoccupation with the design and construction of new types of microelectrodes. Perhaps three-quarters or more of the elements of the nervous system consists of fibers that are 0.5μ in diameter and very small cells. All of our experience indicates that these carry information that is quite different from that carried by the large fibers and cells that are observable by classical neurophysiological methods. Consequently, these studies may well have given us a systematically prejudiced view of the kind of information transmitted by the nervous system and how it is transformed. Certainly this was true in the frog visual system. It is therefore of the highest importance to carry on an intensive study of electrodes and associated recording systems until the signal-to-noise ratio attains its ultimate limit. (Here the definition of the "signal" will depend, of course, on the experimenter's objective.) Only then does it seem reasonable to attempt further resolution by statistical methods, which always involve restrictive hypotheses about the statistics of the signal, which can not be checked without circularity. (Statistical analysis applied afterward to clean records is a totally different matter.)

The platinized metal microelectrodes described by Maturana and Lettvin¹ have been by far the most successful in recording from unmyelinated elements, notably in the frog optic nerve and the colliculus, the octopus optic nerve, the olfactory mucosa, and even (sometimes) in the olfactory nerve. These electrodes record essentially through the capacitance constituted by the double layer at the metal-solution interface, in parallel with the Faradaic admittance of local electrode reactions. It therefore happens that quite small, accidentally discovered variations in the plating methods or solution have a large influence on the impedance by affecting the adsorbed surface layer in a way that is familiar from experience with catalysts. Thus we found, last year, that replacing the gelatin that was formerly used in the plating bath (as a binding medium for the Pt black) by agar-agar gave an immediate reduction in impedance to nearly half its former value, and the electrode persisted at a low impedance much longer than before.

An important advance during the past summer suggests that the average impedance and noise level of the electrode may be less important in recording from very small elements than that of small spots on the electrode which have special properties and are in immediate contact with these elements – and carries the lesson that it is useful

(XXVII. NEUROPHYSIOLOGY)

to know electrochemistry even when using null-current electrodes. When Pt black is plated onto a base metal it forms a very fine deposit, giving a very great surface-volume ratio and thus permits a coupling to tissue through a very low impedance. If one only monitors impedance, then there is only a small ratio, perhaps 2:1, between a tip plated at low current density and one at high current density, the latter giving the lower value. Yet with the former it is not possible to record, for example, the unmyelinated fibers of the optic nerve in the octopus, whereas with the latter it is easy. That the important factor is not impedance per se can be shown by using a set of tips that vary from $2\ \mu$ to $10\ \mu$ in diameter; one records invariably with the high-current plate but seldom with the low, although the overlap on impedances between the two sorts is now very great. Furthermore, it is hard to see how a very limited spectrum of single units (each $0.2\ \mu$ in diameter) is recorded with a $10\text{-}\mu$ tip rather than the hash of hundreds of units seen if one dissects a $10\text{-}\mu$ bundle and records from it on a hook. The most probable explanation is that with high-current plating there occur some "hot spots," that is, points at which the exchange current of the electrode is high and the energy barrier at the interface is low. These are known to be present in an electrode that is Pt-plated for use as a hydrogen electrode and are the points at which bubbles form near the hydrogen overvoltage.

Thus the microelectrode so prepared cannot be thought of as having an homogeneous surface but rather as a congeries of more or less well-spaced recording points, infiltrating the population to spy on activity at each one.

If this is true, and no reasonable alternative presents itself yet, we have an explanation for our success with both the olfactory mucosa and the octopus visual nerve.

The question now arises: Can we use recent work on the properties of electrode-solution interfaces, particularly in the presence of surface-active substances, to make further substantial advances in our recording methods? There are reasons for thinking so, and we plan to try them during the coming year.

It is well known that the differential capacitance of a polarized electrode is dependent on the dc voltage at which it is maintained, being least at the "electrocapillary maximum," and increasing away from it in both directions. This is the potential at which no ions are specifically adsorbed on the surface. If ions having a specific affinity for the metal are present, the minimum capacitance is shifted to a different voltage determined by the balance between chemical affinities and electrostatic repulsions. In any case, the change in capacity is not very great, varying perhaps by a factor of 2 or 3 over the range of dc voltage that is possible without incurring electrode reactions. (Still, it is clearly desirable to clamp the dc voltage of a recording electrode at a value at which the capacitance is high, when one is recording ac signals.) Frumkin² has shown, however, that in the presence of a pair of specifically adsorbed ions of opposite sign there exists a very precise voltage at which the double layer reverses its sign entirely, from cations outside and anions next to the metal, to the reverse position; the strong

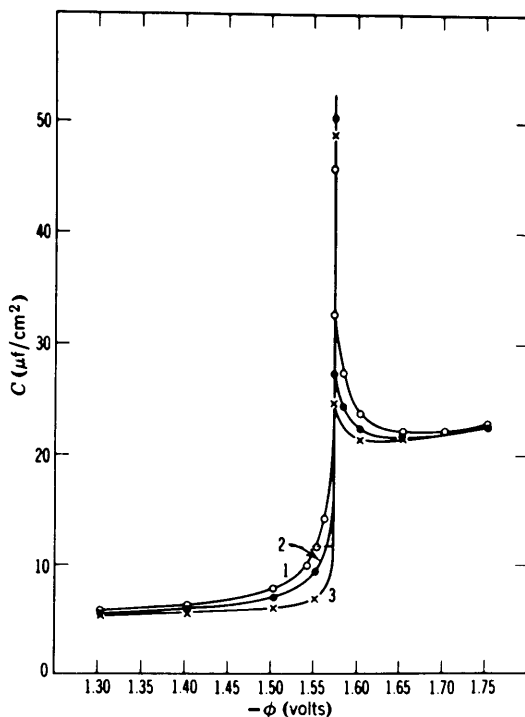


Fig. 8. Dependence of the differential capacity C on the potential in the neighborhood of the desorption potential. 1. $1N$ $KCl + 10^{-3}N [N(C_4H_9)_4]_2 SO_4$; 2. $1N$ $KBr + 10^{-3}N [N(C_4H_9)_4]_2 SO_4$; 3. $1N$ $KI + 10^{-3}N [N(C_4H_9)_4]_2 SO_4$. A-c frequency 1000 cycles/sec.

Fig. XXVII-6. Reprinted with permission from A. R. Frumkin's Fig. 8, p. 8, Trans. Symposium on Electrode Processes, edited by E. Yeager (John Wiley and Sons, Inc., New York, 1960).

interaction between the two kinds of ions causes, moreover, a kind of two-dimensional phase transformation, or condensation, on the electrode surface. The result is an extremely high and sharp peak in the capacitance at a very precisely defined dc potential, as seen in Fig. XXVII-6, which is Frumkin's figure.² This curve is for Hg, but corresponding phenomena will occur with other metals at potentials of approximately equal distance from their normal electrocapillary maxima.

Suppose that we try to use this behavior by adding a suitable pair of compounds to our plating bath. (The difference between agar and gelatin shows that our binding medium holds plenty of substance to form a monomolecular layer, at least in pores, even for long periods.) Then we bias the electrode to the desorption potential and maintain it there by feeding back, through a current generator, the current that is necessary to keep it at the point of maximum capacitance — that is, have the system hunt the voltage of minimum impedance — then our coupling is maximally efficient. Let us go still

(XXVII. NEUROPHYSIOLOGY)

further, and, viewing the steepness of the change in differential capacitance in, say, Frumkin's curves, ask whether it would not be possible to use that change to generate the signal to be amplified as in a parametric amplifier. After all, a variation in capacity of more than 10:1 for a shift of several millivolts is considerable, and, if the electrode acts as an almost true capacitor (as it does), we can perhaps reduce the noise level to that of the solution up to the electrode, the interface contributing very little. At any rate we have a few designs in progress which make use of these suggestions. In particular, the desorption potential detector is of greatest importance in handling the artificial smell receptors made of activated carbon.

We shall continue this work.

J. Y. Lettvin, W. H. Pitts

References

1. H. R. Maturana, J. Y. Lettvin, W. H. Pitts, and W. S. McCulloch, Two remarks on the visual system of the frog, Symposium on the Principles of Sensory Communications, edited by W. A. Rosenblith (The M. I. T. Press, Cambridge, Mass., and John Wiley and Sons, Inc., New York, 1961), pp. 757-776.
2. A. R. Frumkin, Adsorption of ions and electrode kinetics, Trans. Symposium on Electrode Processes, edited by E. Yeager (John Wiley and Sons, Inc., New York, 1960), pp. 1-15.

D. ELECTROCHEMILUMINESCENCE

We have previously shown that the phenomenon of electrochemiluminescence may be used advantageously to display the pattern of flow at the boundary of an anodic hydrofoil. (See Quarterly Progress Reports No. 57, pp. 171-173; No. 58, pp. 253-254; No. 59, pp. 149-155; and No. 60, pp. 227-228.) The distribution of intensities of glow at the electrode is evidently controlled by mass-transfer phenomena and is therefore analogous to heat-transfer effects, which have been well studied for the case of flow about objects of simple shape, as, for example, cylinders, spheres, and so on.

Our present knowledge of electrochemiluminescence is insufficient to enable us to predict the conditions, as, for example, pH, voltage, temperature, concentration of reactants, and so forth, for which we may expect it to be useful as an analogue for heat and mass transfer. Preliminary experiments to establish this correspondence, however, have been quite promising. In the first such test, we measured the total light outputs from cylinders of equal length, but different diameters, as a function of Reynolds number (Re) for a fixed voltage; we used our standard general-purpose flow-visualization solution. The dimensional laws governing both mass and heat transfer indicate that the total mass transfer, heat transfer, or, in our case, light output, should be independent of the diameter of the cylinder; moreover, heat-transfer measurements suggest that the light output should vary as $Re^{1/2}$. The data shown in Fig. XXVII-7 tend to support

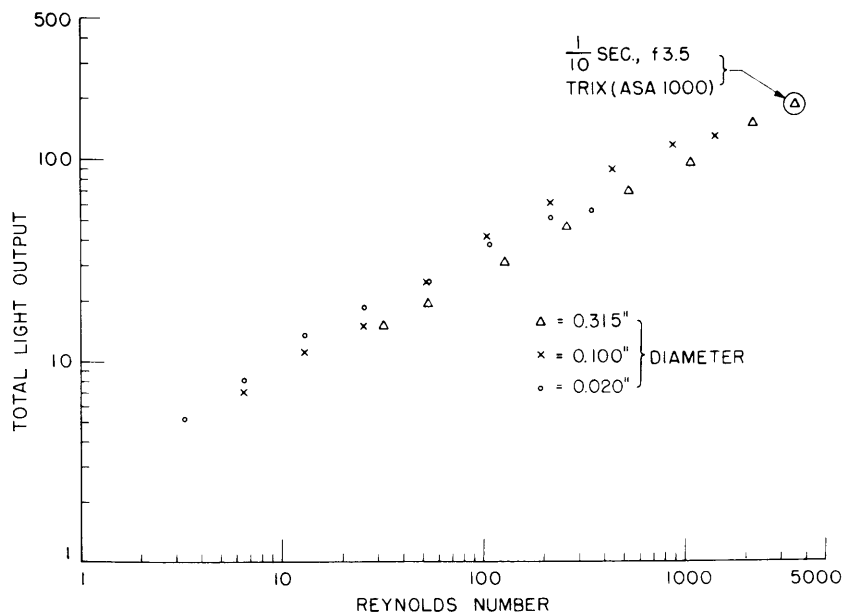


Fig. XXVII-7. Total light outputs from cylinders of the same length and different diameters as a function of Reynolds number.

both these predictions within the accuracy of the experiment. Measurements of the fluid-stream velocity, and hence those of the Reynolds number, are accurate only to ± 20 per cent.

The next important step in establishing the analogy will be an experiment that demonstrates a correspondence between the intensity of the electrochemiluminescent glow and the corresponding mass- and heat-transfer coefficients over the entire surface of a hydrofoil. We choose for such studies the cylinder, since extensive data are available for it. Figure XXVII-8 shows measurements of the heat transfer over the surface of a cylinder. These data are based on interferometric measurements in air.¹ Figure XXVII-9 shows the electrochemiluminescent flow patterns for flow past various frustra of cones for a somewhat greater range of Reynolds numbers. Note that the dark lines indicating the loci of points at which flow separation occurs correspond in angular aspect to the minima of the heat-transfer curves of Fig. XXVII-7. The line of separation evidently, in both experiments, moves continuously to the rear as the Reynolds number is reduced.

The photographs of Fig. XXVII-9, while interesting in a qualitative sense, are unsuitable if one wishes to establish an exact correspondence with the curves of Fig. XXVII-8, for two reasons: (a) the angular aspect of the camera relative to the surface is not constant, and since it is known that the brightness of the surface varies with this angle, it would be extremely difficult to obtain a measure of the actual intensity of glow, measured everywhere normal to the surface, from these pictures (this effect

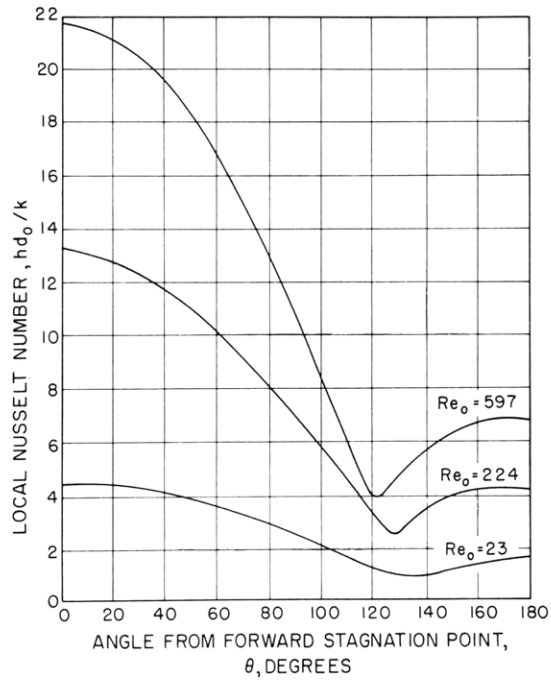


Fig. XXVII-8. Local Nusselt numbers for the flow of air past cylinders at low Reynolds numbers. (Based on a figure of E. R. G. Eckert and E. Soehngen, Trans. Am. Soc. Mech. Engrs. 74, 343 (1952).)

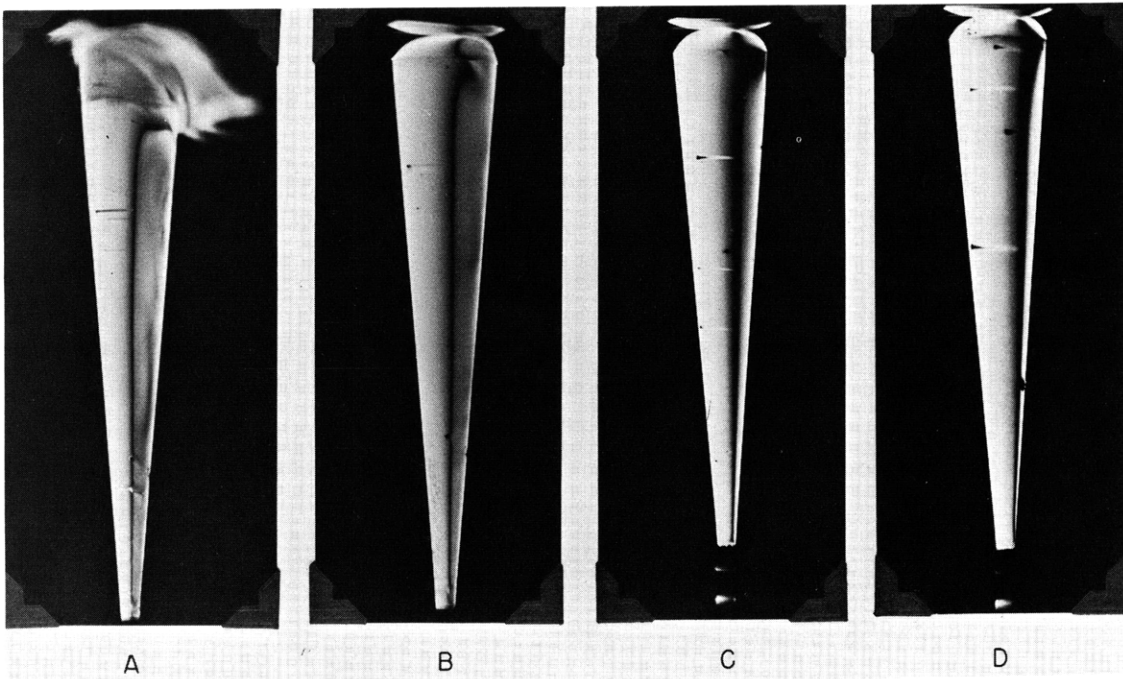


Fig. XXVII-9. Patterns of flow past frustra of cones, for various Reynolds numbers: (a) $Re = 4800-800$, (b) $Re = 1200-200$, (c) $Re = 200-33$, (d) $Re = 60-10$.

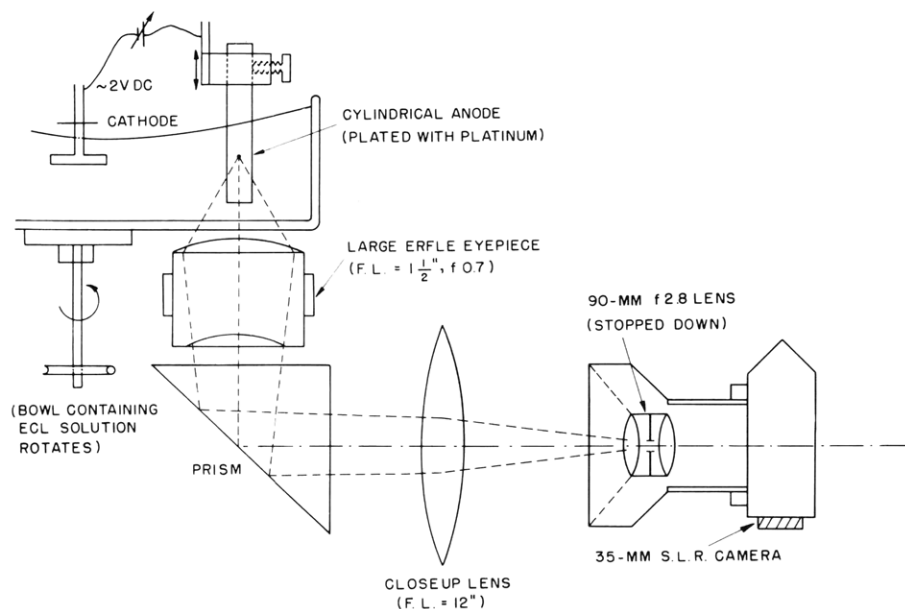


Fig. XXVII-10. Optical system for photographing the surface of a cylindrical hydrofoil with negative parallax distortion.

will be reported on later); (b) the optical distortions of this system are such as to make direct measurements of angles from the forward stagnation point very difficult. In par-

ticular, we cannot see at all the line of separation on the opposite side. Lacking this information, it is extremely difficult for us to establish a plane of symmetry relative to which measurements can be made. For this reason we have developed an alternative method, illustrated in Fig. XXVII-10. The cylinder here is photographed from below, through the flat bottom of the rotating cylinder containing the electrochemiluminescent fluid. Directly below and colinear with the anode is placed a wide aperture ($f 0.7$), highly convergent lens (focal length, 1.5 inches) having an appreciable back-focal distance (1 inch). An object viewed through such a lens, from a distance of several focal lengths, either directly or through a reflex camera, exhibits negative parallax distortion; that is, those

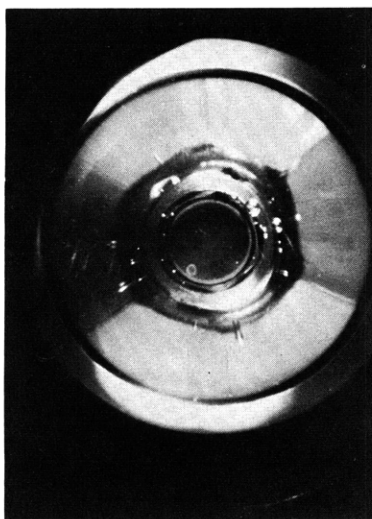


Fig. XXVII-11. View of lead pencil, showing eraser, to illustrate negative parallax distortion.

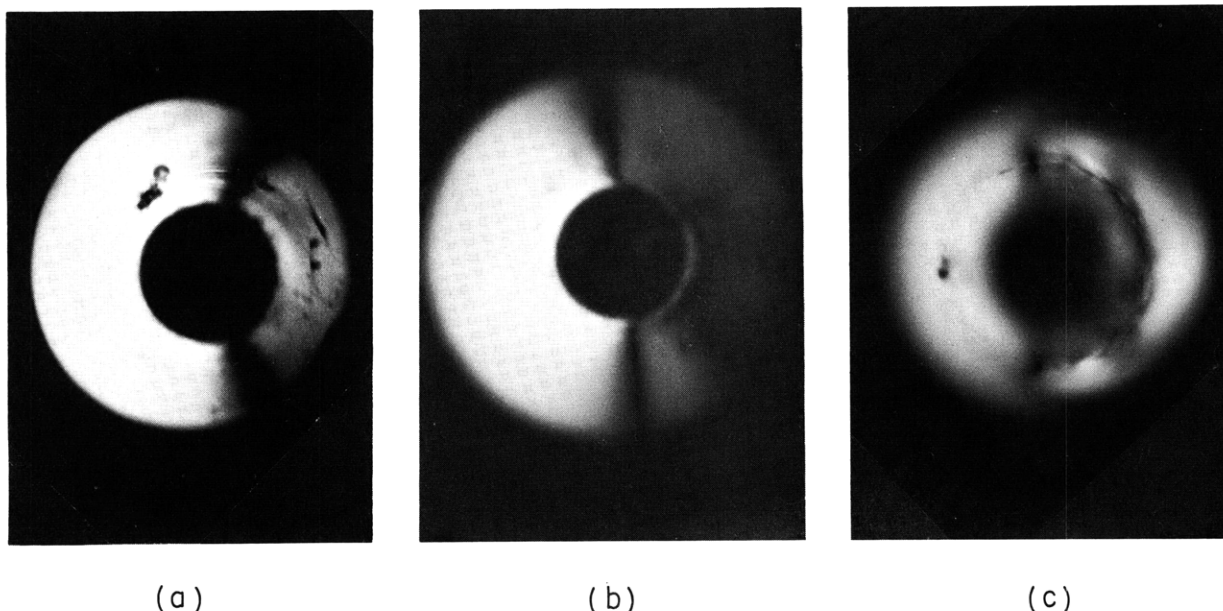


Fig. XXVII-12. Cylindrical hydrofoil viewed with similar optical system. (a) Low-speed flow; $Re \approx 50$; f 33. (b) High-speed flow; $Re \approx 5000$; f 33. (c) High-speed flow; $Re \approx 5000$; f 2.8. Flow is from left to right.

parts of the object nearest the camera appear smallest, whilst those parts farthest away are reproduced with the greatest scale of magnification. This effect is such as to transform a cube into a pyramid (with a flat top), and a cylinder into a cone. The advantage is that we can see the entire submerged surface of a cylindrical hydrofoil. By this means, photometric or sensitometric measurements may be expected to indicate accurately the angular distribution of intensities of the electrochemiluminescent glow.

The alignment of this optical system is greatly facilitated by the use of a ruled, dummy cylindrical hydrofoil. For this purpose, we use the eraser end of an ordinary lead pencil, shown in Fig. XXVII-11, to illustrate the optical distortions on which the method depends. The various concentric rings starting at the center are identified as follows: eraser, black ring, gold ring, black ring, and finally the hexagonal wood. It is seen that the radius on the photograph is a nonlinear function of distance measured along the hydrofoil.

In Fig. XXVII-12a we illustrate, by a time exposure with the same optics, the flow about a cylinder for $Re \sim 50$. This photograph clearly shows the angular aspect of the lines of flow separation, and also indicates that the intensity of glow forward of separation is considerably greater than that aft. In Fig. XXVII-12b we show the pattern of flow with a higher Reynolds number, approximately 5000. Figure XXVII-12c shows a similar flow photographed with a wider aperture; the depth of field is insufficient here

to include the entire cylinder, but the advantage is that we now use a much shorter exposure, and it is possible to observe some of the structure of the turbulent wake to the rear of the lines of separation.

The radial dependence of the glow intensity seen in Fig. XXVII-12b shows the effect of the variation of brightness with the angular aspect by which the surface is viewed. The end of the cylinder is also glowing brightly, but since it is viewed with near-normal incidence, the light is insufficient to register on the film. On each of these film strips we have also recorded a stepped grey wedge, for the purpose of making precise determinations of the angular distribution of glow intensities; these results will be reported, at a later date.

B. Howland, J. Y. Lettvin, W. H. Pitts

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E. OCEANOGRAPHIC-SURVEY ELECTRODES

During our work of the past two summers at the Stazione Zoologica in Naples we have become aware of the great need for simple devices for continuously measuring chemical and physical properties of sea water in a fashion suitable for oceanographic surveys, without having to take enormous numbers of samples and subsequently analyze them. Electrochemical methods have been used to some extent, but it appears to us that a great field exists for improvement, both in the electrode systems and in the associated apparatus. In particular, we are trying to modify the Berl activated-carbon electrode,¹ which is reversible to dissolved oxygen in strongly alkaline solution, so as to function at the pH of sea water. This modification may require a chemical modification of the surface structure of the active carbon that is used; or perhaps its replacement by some of the organic high polymers having enough through-conjugation to function as conducting electrodes (such as dehydrohalogenated polyvinyl chloride, xanthene polymers, partly pyrolysed polyacrylonitrile, certain polycyclic quinonoid vat dyes, to mention a few), and functional groups present on the surface enabling them to catalyze the Berl reaction at a reasonable rate. It is true that O_2 -tension can be measured polarographically on Pt, but the method is notoriously difficult to make reproducible, especially for routine surveys. Associated with this is a project mentioned before in these reports (Quarterly Progress Report No. 59, pp. 154-155), to use one such electrode to reduce O_2 to H_2O_2 (which carbon does with almost 100 per cent efficiency in alkali), and measure the concentration of the latter, as is possible in several ways, by means of an electrode placed behind the working electrode on the same streamline. This should provide a

(XXVI. NEUROPHYSIOLOGY)

continuous measure of current strength and velocity, with advantages in a number of important cases over the devices now employed.

Other electrode systems, known in electrochemistry, have likewise never been tested under the high and variable pressures present in the sea; for example, an unpoisonable iridium pH electrode recently described¹ (requiring a very high impedance amplifier) may prove superior to the glass electrode, which is fragile and requires complicated mechanical devices to compensate it against changes in pressure. Other recently discovered methods in ac polarography, hardly used, at present, for chemical analysis, may well make it possible to survey other chemical properties of great biological importance, particularly since the electronic instrumentation previously used seems capable of much simplification and improvement. We hope at least to be able to repay some of the great courtesy and help we have received from the marine biologists in our physiological studies. This work is being carried on by R. C. Gesteland, who is staying for some months at the Stazione Zoologica in Naples, in (remote) collaboration with J. Y. Lettvin and W. H. Pitts in this Laboratory; later in the year we expect to continue this work together.

R. C. Gesteland, J. Y. Lettvin, W. H. Pitts

References

1. For details, see D. J. G. Ives and G. J. Janz (eds.), Reference Electrodes in Theory and Practice (Academic Press, New York, 1961).

F. OLFACTORY ELECTRODES

We have mentioned twice before in these reports (Quarterly Progress Reports No. 56, p. 193, and No. 60, p. 224) our plan to use the changes produced in the capacitance – dc potential curves of an electrode by the presence of adsorbable substances as a model of the olfactory receptors, on which the presence of a monomolecular layer has a profound influence on the electrical events leading to the generation of the spike. We have planned to use various forms of carbon and chemically modified carbon, on which the adsorbability of substances, even totally nonpolar ones, has a certain very rough correlation with their odor strength, as well as other inorganic and organic electrodes, so as to use the combination of the adsorbabilities on different types of electrodes to characterize the odor as specifically as possible, and even perhaps detect it individually in mixtures. The discussion of microelectrodes given in Section XXVII-C shows how a large electrical change can result from adsorption-desorption effects. A further variation of the method to secure greater selectivity consists of prepoisoning the electrode with an un-ionized substance having less affinity for the odorant than the given one, which others of still smaller affinity cannot displace; or, more flexibly, with a specifically

adsorbed ion, whose affinity for the electrode surface can be delicately adjusted to compete with the odorant to be detected, by adjusting the dc potential of the electrode to cause an electrostatic attraction or repulsion of the desired degree. The electrode capacity should then show rather sharp peaks as in Frumkin's figure (see Fig. XXVII-6), and for similar reasons, namely, a reversible change in the structure of the Helmholtz double layer and, perhaps, an associated kind of "two-dimensional condensation." It is certain that this kind of displacement of adsorbed substances happens: there is a kind of carbon that takes up mineral acids in the presence of O_2 and varies its dc potential concomitantly, and thus acts like a reasonably good pH electrode; upon the addition of a bit of toluene, most of the acid is promptly desorbed, and the potential changes accordingly. However, the capacitance variation should be far more sensitive. Gesteland, Lettvin, and Pitts will continue work on this project.

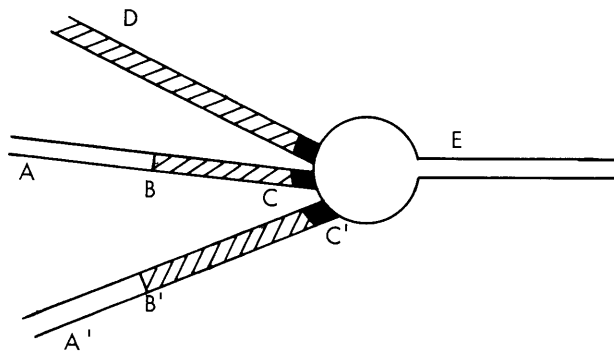
R. C. Gesteland, J. Y. Lettvin, W. H. Pitts

G. THE IRON-WIRE NEURAL NETS

Between 1930 and 1940, and even earlier, there was considerable interest in what was called the "iron-wire 'model'" of nervous conduction. When suitable iron or steel wire is immersed in rather strong HNO_3 , an extremely thin transparent layer of metal oxide forms on the surface almost at once, which prevents further attack, and the wire assumes a bright silvery appearance. It is said to be "passive." If current is now drawn from the wire at one spot, by touching it with a piece of zinc or the negative pole of an electrode, the passivating layer is destroyed, so that the iron beneath turns brown and commences to dissolve; the spot becomes negative in relation to adjacent regions, and draws current from them. This inward current soon reforms the passive layer on the original spot, but the outward current depassivates the adjacent regions, so that the active or depolarized region, formed in advance and restored behind, travels along the wire very much as the conducted impulse in an axon. The formal analogy is quite close: there is a negative, depolarized region in both cases, flanked by positive ones; the distribution of current in the external medium is quite similar; cathodic polarization from external electrodes facilitates and speeds both regions, anodic polarization has the reverse effect; both exhibit "refractoriness," or an increased difficulty in setting off an impulse immediately after a previous one, and so on. But there are substantial numerical differences: the iron wire produces more than 1.25 volts, as compared with, say, 100 mv; its depolarized region is slow enough to be visible as a moving brown or bubbly band, at least if the HNO_3 is strong enough; the velocity and, concomitantly, the length of the refractory period, can be controlled within wide limits by changing the concentration of HNO_3 , adding oxidizing agents such as HNO_2 or H_2CrO_4 , or polarizing the whole wire anodically or cathodically with an external battery.

(XXVII. NEUROPHYSIOLOGY)

With the advance in our understanding of the actual mechanism of nervous conduction, interest in this merely formal analogue nearly disappeared, and nothing has been heard of the iron-wire model for nearly 25 years. It occurred to us, however, that it can be used as the basis of an analogue computer for the behavior of large nets of neurons, with promise of substantial superiority over the use of digital computers to simulate their behavior. For this purpose, we must modify the system to represent the behavior of several impulses converging at synaptic junctions upon a subsequent cell. Fortunately, an electrical theory of synaptic facilitation and inhibition, which we developed some years ago, points out at once some reasonable ways of accomplishing this modification conveniently. Suppose that ABC and A'B'C' in the following diagram are different steel wires stuck on to the "cell" N, say, a ball bearing, with some kind of inert cement that



protects the junction C; between ABC and N there is a layer of conducting paint of suitable resistance R . The segments BC and B'C' are likewise covered with conducting paint capable of passing current but not of depolarizing. The same is true of the whole "dendrite" D that is attached to N, lies along the incoming wires, and serves as a return path for current when desirable. Another "axon" wire N is attached to N to carry away the outgoing impulse. Several extreme examples may now be distinguished:

(a) The painted segments BC and B'C' are absent; the contact resistance R is low. The network is a syncytium, any impulse along ABC or A'B'C' passes to N and E, and conversely. There is no true synaptic behavior.

(b) BC and B'C' are short or absent; R is high. The impulse goes as far as C or C', then draws a current from N (and D) which is limited by R in the return circuit. If the current is insufficient to depassivate N, it may require the coincidence of impulses in ABC and A'B'C' to fire N and E. This represents spatial and temporal summation; there will also be a "synaptic delay." When R is very high, we have merely facilitation.

(c) BC is long; R is high. The impulse in ABC dies at B, drawing current from the "blocked" segment BC. This current passes inward across the surface of N, and returns

through the inert surface of D. The resulting anodic polarization produces inhibition of N; any impulses approaching N over other wires such as A'B'C' terminating as in (b) must be greater in number than otherwise necessary to reverse the sign of this current and exceed the net outward current required to set off an impulse in N and E.

Someone may object that under conditions (a), or (b) approaching (a), an impulse in N may propagate backwards along all such afferents. This is quite true; but it also happens in the nervous system when the synaptic connections are massive enough.

A system like this is rather flexible; it is capable of quite a range of behavior when the geometrical relations and the contact resistances are properly varied, and ought to be able to represent real neurons reasonably well, and idealized ones, such as are simulated on computers, even better. Interaction between afferent impulses before they reach the synapse can also be arranged. Moreover, a large network of such "neurons" can be put together almost as easily as molecular models, by using nothing more expensive than piano wire, ball bearings, acid-resistant conductive paint, and acid-resistant cement for covering the junctions. After that, one merely immerses the whole apparatus in HNO_3 , starts it off by external stimuli from a battery, and follows its behavior either visually or with a probe electrode for as long as desired. The mean threshold of the "neurons" can be varied at will at any time by applying an external voltage from a battery.

During the coming year J. A. Aldrich plans to develop the method for a Master's Thesis.

J. A. Aldrich, W. S. McCulloch, J. Y. Lettvin, W. H. Pitts

H. APPARATUS

Several years ago, using an ac bridge with microelectrodes, we devised, with Dr. José del Castillo of the University of Puerto Rico, a microtransducer for muscle. We have recently succeeded in simplifying this device. Using an ordinary KCl-filled micropipette of long shank and small aperture, which has a resistance R of approximately 10-20 mhos, we touch a bit of connective tissue attached to the fiber whose excursion we mean to measure. Small movements of the tissue give large changes in the resistance seen at the tip. Thus, if the electrode feeds a cathode follower equipped with a positive capacitive feedback to the grid to reduce the capacitive shunt at the input, the grid current of the cathode follower usually provides enough signal to detect very small movements indeed. The device is monotonic and, if carefully positioned, almost linear in voltage-movement relation over a surprising range.

We have recently devised a circuit that measures pulse interval on a logarithmic scale and has a useful span of four decades. The principle is simply the rapid charging (to a fixed voltage) of a capacitor that is then allowed to discharge through a diode in

(XXVII. NEUROPHYSIOLOGY)

the forward direction. Some silicon diodes provide a range of 6 decades, or more, in displaying $E = \log I + K$. We use the FD 300.

During the summer of 1961, in Naples, we designed and constructed (with Miss Susan Sperling of the Department of Zoology of the University of California at Los Angeles) a heart-lung device (that is, aerated sea-water infusion at the average blood pressure of the animal) to keep the isolated head of an octopus alive for many hours. With this, Miss Sperling was able to do work on rotation of intact statocyst organ in the octopus.

J. Y. Lettvin, W. H. Pitts

I. OLFACTION IN THE FROG

During the past year, Dr. Robert C. Gesteland has perfected a method of recording from single receptors in the olfactory organ of the frog, by using a variety of the plated-inized microelectrodes that he, Howland, Lettvin, and Pitts invented.¹ His technique is now simple enough for routine use, so that the pattern of responses of a chosen receptor which results from 30 or 40 different chemical stimuli can be measured over a period of 2 or 3 hours. His work is described in detail in his doctoral thesis.² A brief summary will be given here.

The olfactory mucosa of a decapitated frog is exposed in the way described by Ottoson. The electrode is inserted into the mucosa at an angle that is acute to the surface. As it is advanced into the tissue, the impedance (measured by the noise level on an oscilloscope) increases sharply at a depth ranging from 50 to 100 microns. This is probably due to the fact that the electrode pushes up against the basement membrane. If the electrode is very gently moved around in this region, spikes appear out of the noise. The amplitude can be optimized up to approximately 1 millivolt peak-to-peak by manipulation of the electrode. The spike is initially positive, triphasic, and has a duration of from 5 msec to 7 msec. The maximum rate of action potentials from a single unit is 10 spikes per second with an appropriate odor stimulus. Some units are quiet in the absence of a stimulus; others have a very irregular rate of no more than 2 per second. A particular unit can be recorded for at least 2 hours with no apparent degeneration, if the stimulus concentration is kept small and adequate time is allowed between stimuli. Often, several units can be observed simultaneously, each having a different amplitude on the oscilloscope and responding to different odors. This seems to preclude a simple topographical arrangement of olfactory qualities according to position of the receptor on the mucosa (see Fig. XXVII-13).

The units may have any of several different responses to an appropriate stimulus. A spontaneously active unit may have its rate increased or inhibited. A quiet unit may respond. Either type of unit may respond only to the onset of the stimulus, or may fire during all of the time that the stimulus is present. The responses are chemically

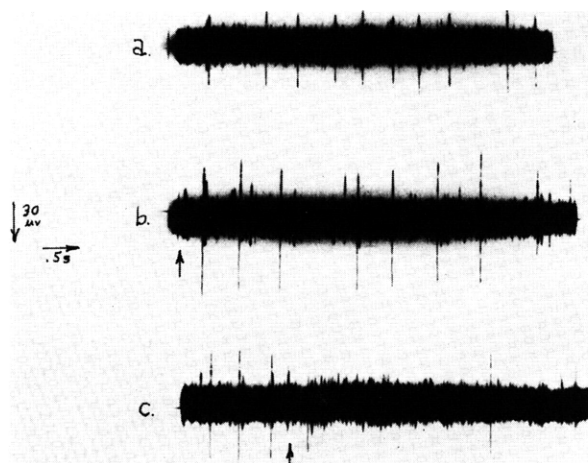


Fig. XXVII-13. (a) Resting rate, (b) response to a 1-sec puff of *m*-butanol, and (c) response to a 1-sec puff of pyridine of two units. Note the absence of the large spike in (a), and the inhibition of the smaller spike in (b). Arrows indicate stimulus onset.

specific. We have seen units that will each respond to only one among the following: pyridine, coumarin, carbon disulfide, camphor, and ethyl butyrate. Also, we have seen a unit that responds to nitrobenzene but not to benzaldehyde, substances with very similar odors.

This is the first time that a really straightforward and objective analysis of the data of smell has been possible. Past classifications of odors have been notoriously subjective, vague, and discordant; the problem seems to be nearly inaccessible to the methods of experimental psychology. Neurophysiologists before have succeeded in recording with any consistency only from large numbers of elements at once, and the resulting signal seemed to carry little of the discrimination exhibited in the sense of smell.

Lack of time compelled Gesteland to confine himself to a small number of chemical stimuli applied routinely to each receptor; he naturally chose them to be as different as possible, and arrived at results that are already quite striking for any theory of olfaction. Nevertheless, for a rational classification of the receptors into functional types, and the difficult problem of finding the relations between the odor and chemical structure of substances, we shall have to use a much wider variety of stimuli, preferably in groups differing systematically in chemical structure, such as the aliphatic esters, alcohols, acids, and aldehydes. These groups have a particular advantage in occurring in the normal habitat of frogs.

The character of the signals, consisting of slow and more or less irregularly spaced trains of spikes, whose average frequency is either increased or decreased by a

(XXVII. NEUROPHYSIOLOGY)

stimulus, poses some problems in recording the data in a convenient form for interpretation, especially in view of the number of trials which must be made with each receptor. To count variations in this average frequency, we have devised an automatic method for determining the logarithm of the interval between successive spikes, even superimposed on noise, and displaying it as a voltage; this device, described in Section XXVII-H, should find a wide range of application in neurophysiology, when similar data must be analyzed.

This project will be carried on by A. Rojas, J. Y. Lettvin, R. C. Gesteland (upon his return from the Stazione Zoologica in Naples), and W. H. Pitts.

J. Y. Lettvin, W. H. Pitts

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2. R. C. Gesteland, Action Potentials Recorded from Olfactory Receptor Neurons, Ph. D. Thesis, Department of Biology, M. I. T., August 21, 1961.