XVI. NEUROPHYSIOLOGY[*]

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A. INFALLIBLE NETS OF FALLIBLE FORMAL NEURONS

At the time of the Quarterly Progress Report of April 15, 1958, I thought that no circuit could preserve error-free action if it were composed of 3 neurons, each receiving only 2 inputs. To correct this, let me replace the jot in any Venn symbol (1) by 1 if the jot is always present, by 0 if it is always absent, and by p if it is present with a probability p due to a shift of the threshold θ of the neuron that it represents. Thus $1 \diagdown\!\!\!\diagup 1 \diagup\!\!\!\diagdown p$ represents a neuron that always fires when A alone occurs or both A and B occur, and fires with a probability p when B alone or neither A nor B occurs. For error-free operation, some spaces in the Venn symbols must have 0 or 1. I place each symbol inside the idiogram of its neuron and draw Fig. XVI-1, in which each of the neurons of the first rank receives signals from A and from B, and both play on the output neuron at the bottom.

For nets of neurons of 2 inputs, that is, with $\delta = 2$, zero error can be achieved only for tautology and contradiction with some p in every chi (χ), that is, by keeping the fixed jots or blanks in such positions that, when added, they form tautology or contradiction. But, since the complement of tautology is contradiction and the complement of contradiction is tautology, these lead only to themselves and to no significant functions of their primitive propositions.

This limitation disappears with $\delta = 3$. For instance, consider the net of Fig. XVI-2a for nondegenerate neurons, with $\delta = 3$, and their Venn symbols showing the succession of jots with decrease of θ (Fig. XVI-2b). Let $J = 2^{\delta} \mod \delta$, and let ψ be the number of jots that may be added harmlessly to the Venn symbol that can stand fewest additions of any Venn symbol in its rank; write the desired function of J or fewer jots as 1's in more than half of the V_j, write a 1 in the corresponding space of V_k, and write p in all of its other spaces for the intersections of more than half of its arguments (see Fig. XVI-3). There are $2^{\delta-1}$ of these spaces, one of which contains the 1. Therefore the number of p's in V_k, call it ψ_k, is $2^{(\delta-1)} - 1$. In Every V_j there remain $2^{\delta} - J$ empty spaces in which p's may be placed if they do not occur in the same space in more than $\frac{1}{2}(\delta-1)$ of the V_j. This permits them harmlessly in $\left[\frac{1}{2}(2^{\delta} - J)(\delta-1)^{\delta} - 1\right]$ spaces of each V_j. Now, for δ odd, J is even, and it is 2 if δ is prime. Harmless p's are
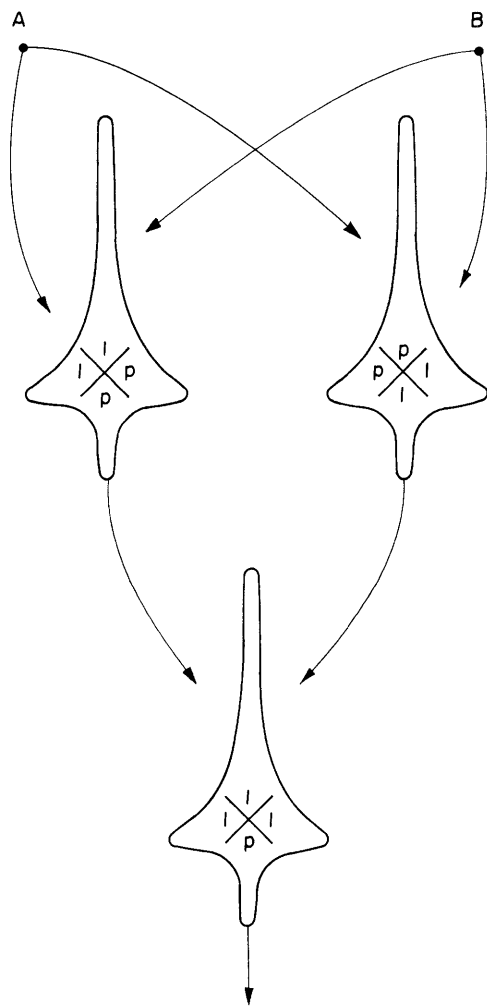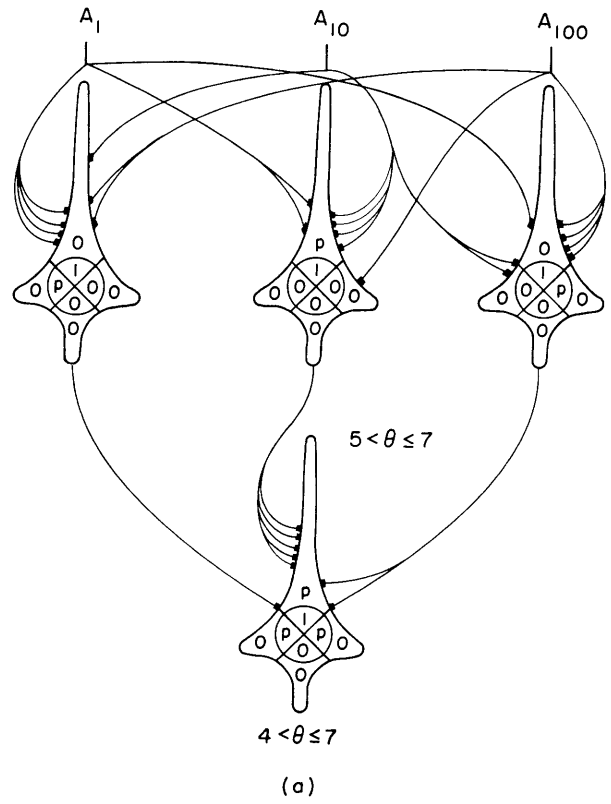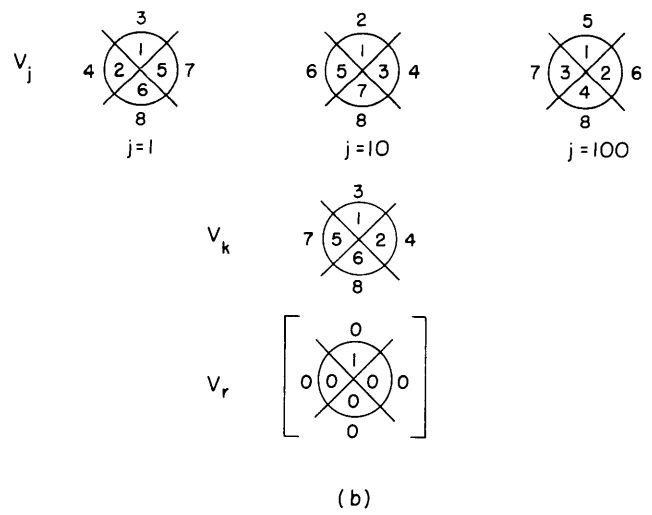
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Fig. XVI-1.

$5 < \theta \le 7$

$4 < \theta \le 7$

(a)

(b)

Fig. XVI-2.

most numerous when J is smallest. Hence the maximum

$$\psi_j = (2^\delta - 2)(\delta^{-1})\frac{1}{2}(\delta-1) = (2^{\delta-1} - 1)(\delta-1)\delta^{-1}$$

Writing ψ^* for $2^\delta\psi_{max}$, we have

$$\psi_k^* = 2^{-\delta}(2^{\delta-1} - 1) = \frac{1}{2}(1 - 2^{1-\delta})$$

and

$$\psi_j^* = 2^{-\delta}\delta^{-1}(2^{\delta-1} - 1)(\delta-1) = \frac{1}{2}(1 - 2^{1-\delta})(1 - \delta^{-1})$$

Hence,

$$\lim_{\delta\to\infty} \psi_k^* = \lim_{\delta\to\infty} \psi_j^* = \frac{1}{2}$$

The binomial coefficient for the central term when δ is even has to be allotted either to the V_j or to V_k, and its effects diminish comparatively slowly,
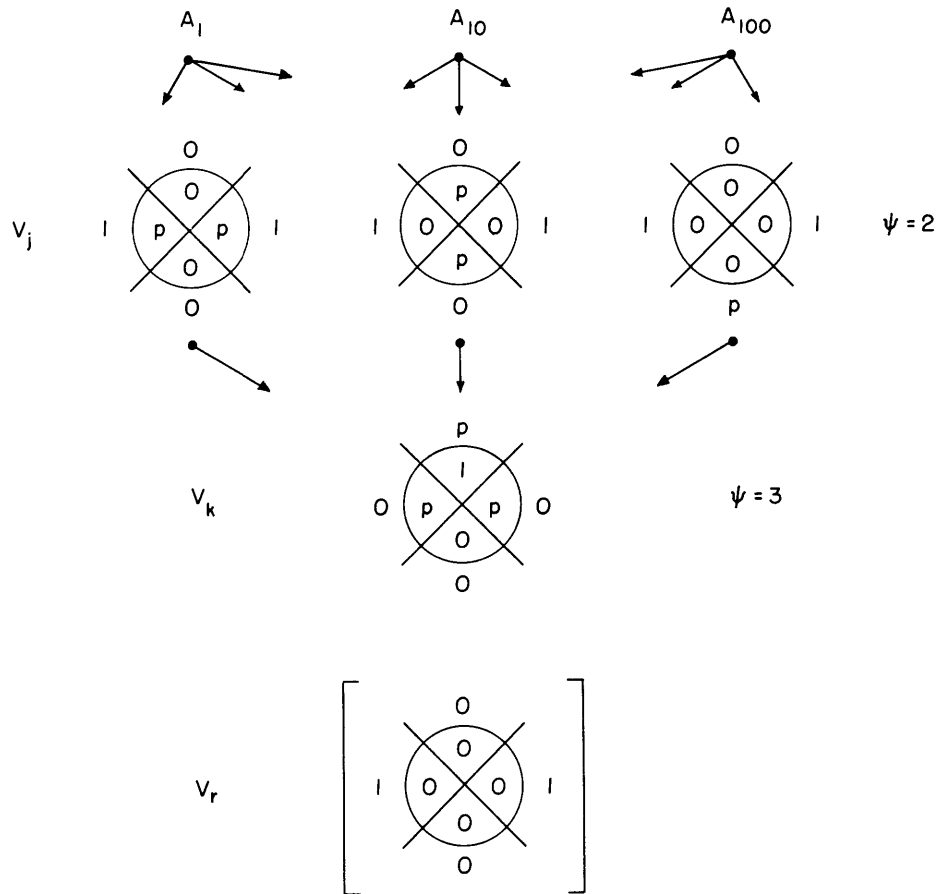

Fig. XVI-3.

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without affecting the limits.

Functions of J or fewer 0's can be constructed similarly; but any additional 1 or 0 decreases ψ_j by 1, reaching a maximum loss of $\frac{1}{2}(2^\delta - J)$ in the V_j, thus effectively halving ψ_j^*. When not all J are used for 1's or 0's, this space can be occupied by p in only some of the V_j, and so ψ_j^* is not increased.

For nets with two ranks of neurons (V_j and V_h), and one third-rank or output neuron (V_k), ψ_j and ψ_h increase to equal ψ_k for all neurons, and almost all may have one additional p harmlessly, as in Fig. XVI-4, where $\psi = 3$ in $V_{j=100}$ and in $V_{h=10}$ and in V_k.

We compute the number of nondegenerate infallible nets of two ranks thus: For each V_j there are $\psi_j! \left(\psi_j \frac{\delta+1}{\delta-1}\right)!$ which meet the requirements, and for V_k there are $\psi_k! \left(\psi_k \frac{\delta+1}{\delta-1}\right)!$ The number of nondegenerate nets is

$$\left(\psi_j! \left(\psi_j \frac{\delta+1}{\delta-1}\right)!\right) \psi_k! \left(\psi_k \frac{\delta+1}{\delta-1}\right)!$$

and, for large δ, it is nearly $(2^{\delta-1}!)^{2\delta+2}$, which is a large number but, divided by the number of all nets, is the negligible fraction

$$\frac{(2^{\delta-1}!)^{2(\delta+1)}}{(2^\delta!)^{\delta+1}}$$

If nets with more jots than J were equally numerous, and they are not, this fraction would not be multiplied by more than $\left(2^{2^\delta} - 4\right)$, which still leaves it negligible. Chance is unlikely to produce such nets or to discover them among nets supposed to be equiprobable.

No comparable measures of the number or fraction of diagrams that are degenerate, either because (a) they do not change the fraction computed with every step of θ or because (b) they change the symbol by two or more jots per step in θ, can be similarly computed. What misled me before was that I had examined only output neuronal diagrams in which $\delta \leq 3$ and in which there was no inhibition of afferents by afferents but only a direct action on the recipient neuron, and that, among these, only degenerate diagrams give ψ_k. Clearly, the degeneracy of the second kind is greatest when all afferents have equal signal strength; and the degeneracy of the first kind is greatest when the strength of the afferents goes up maximally between none and the least one, and so on. The first kind is therefore minimized by using the smallest whole numbers possible, and the second by having them as unequal as possible.

Since, in V_k the spaces for $\frac{\delta+1}{2}$ arguments must be filled before any spaces for fewer arguments are filled, inputs each equal to one would produce the desired result with no degeneracy of the first kind but with maximum degeneracy of the second kind.
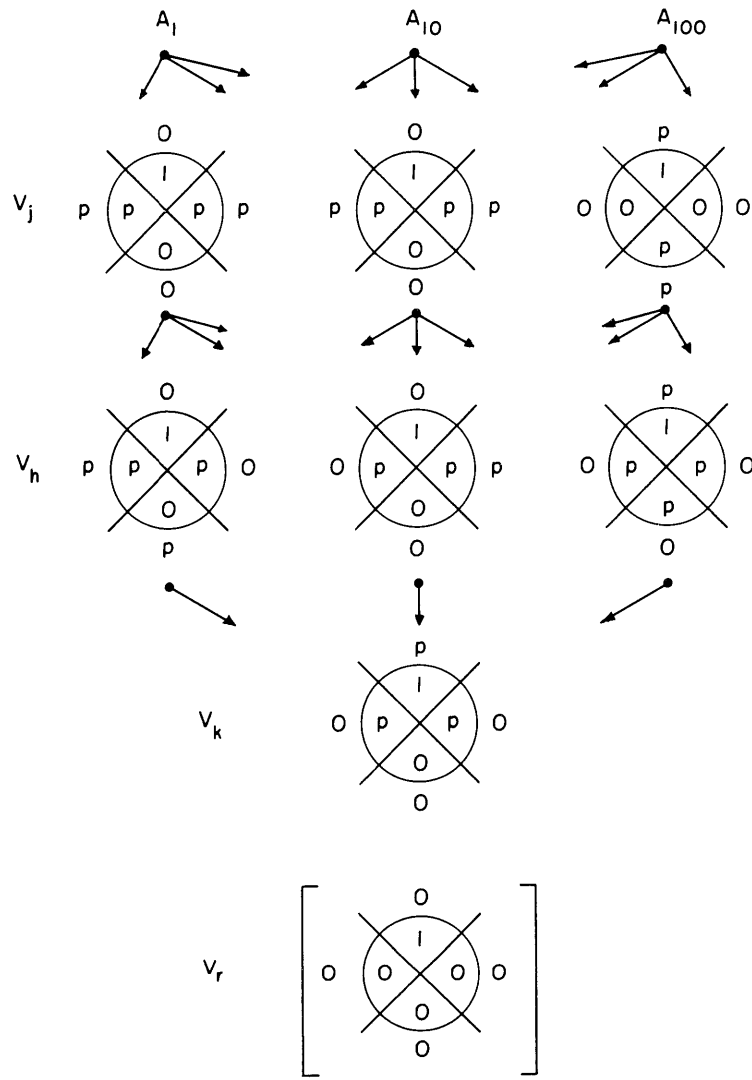
Fig. XVI-4.

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To minimize degeneracy of the second kind, we define the least as $x + 1$ and suppose that the values differ from each other by 1 step in θ. Then

$$\frac{\delta + 1}{2} x + \sum_{1}^{\frac{1}{2}(\delta+1)} \text{(integers)} > \frac{\delta - 1}{2} x + \sum_{\frac{1}{2}(\delta+1)+1}^{\delta} \text{(integers)}$$

and

$$x > \frac{\delta + 1}{2} \left[(\delta+1) - \left(\frac{\delta + 1}{2} + 1 \right) \right] - \frac{\delta + 1}{2} , \quad \text{which is} \quad \frac{\delta + 1}{2} \cdot \frac{\delta - 3}{2}$$

Hence the least term is $\left(\frac{\delta + 1}{2} \cdot \frac{\delta - 3}{2} \right) + 2 = \left(\frac{\delta - 1}{2} \right)^2 + 1$, and the greatest is $\left(\frac{\delta + 1}{2} \right)^2$; but this, which yields ψ_k^*, is as far from equal strengths as possible. The allowable change in threshold is decreased only by a factor $\frac{1}{2\delta} \left(\frac{\delta^2 - 1}{\delta^2 + 3} \right)$.

For example: if V_k has 7 inputs, each with a value of $+13$, its output is error-free for $39 < \theta < 91$, which is reduced by letting the inputs range from $+10$ to $+16$ to $45 < \theta < 91$. Thus the remaining usable range of θ, $\Delta^* \theta$, exceeds $\frac{1}{2}$, while $\psi_k^* = \left(\frac{1}{2} - \frac{1}{2^7} \right)$.

Note that if we are willing to forego the possibility of a jot appearing in the position for none in V_k, thus reducing ψ_k to $\left(\frac{1}{2} - \frac{1}{2^6} \right)$, the value of $\Delta^* \theta$ is 66.6 per cent for equal afferents and 56 per cent for afferents ranging from $+10$ to $+16$.

Since the measured variation, $\Delta\theta$, of real neurons is ± 5 per cent, we look next at the permissible independent variation of the strength of afferent signals to V_k when these strengths were intended to be equal. Clearly, any selection of $\frac{\delta - 1}{2}$ signals has a maximum sum less than the minimum sum for δ signals. Let t be the intended strength of a signal and Δt its variation. Then

$$\sum_{0}^{\frac{1}{2}(\delta-1)} (t + \Delta t) < \sum_{0}^{\delta} (t - \Delta t)$$

Hence

$$\frac{|\Delta t|}{t} < \frac{\delta + 1}{3\delta - 1} = \frac{1}{3} \left(1 + \frac{4}{3\delta - 1} \right)$$

which always exceeds $1/3$. For example, for $\delta = 3$, with the intended strength t equal to 2, we have $1 < (t \pm \Delta t) < 3$. To retain $\Delta\theta$ of ± 5 per cent of its intended value reduces these limits to $1.05 < (t \pm \Delta t) < 2.85$, or $\frac{|\Delta t|}{t} = 0.425$.

[When a variation of this size is experimentally produced in the afferent termination in the spinal cord of the cat, it alters the circuit action. Even posttetanic potentiation and convulsive doses of strychnine alter the voltage of signals by less than 10 per cent.]

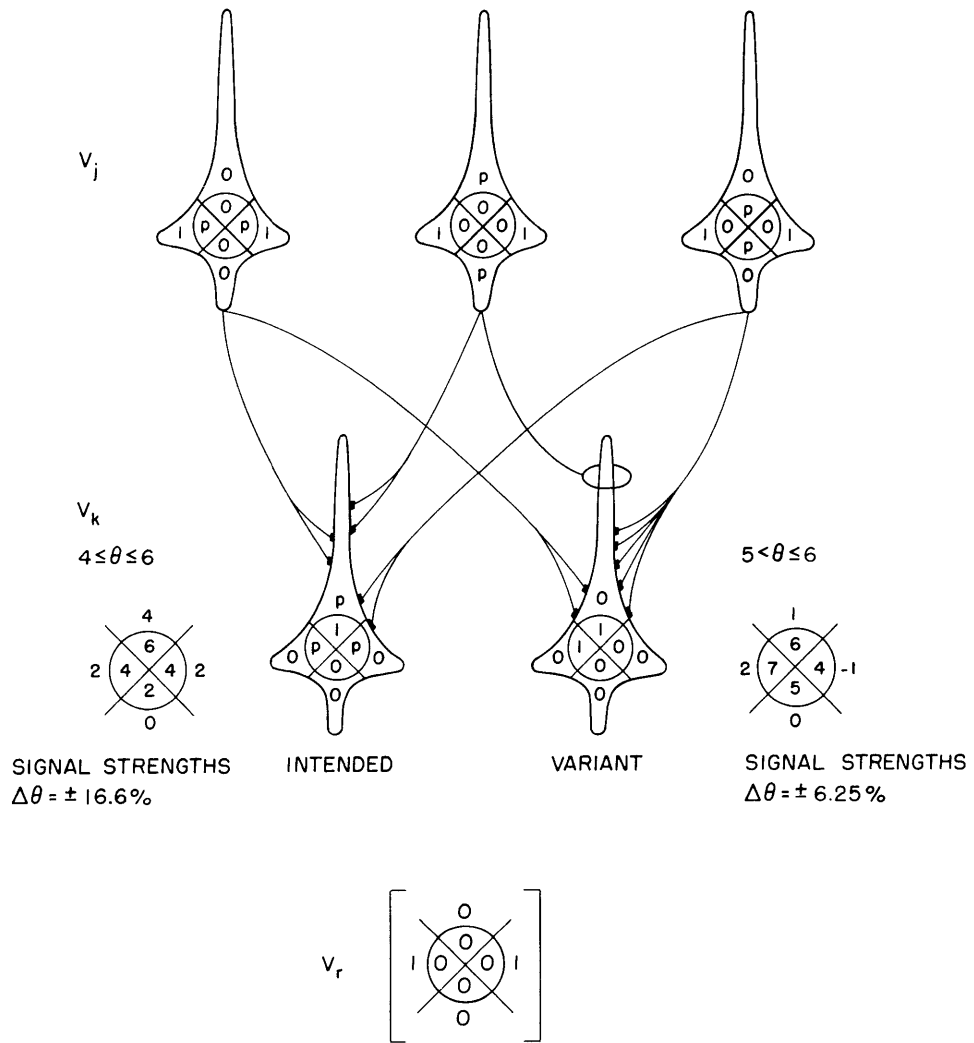If we hold $\Delta\theta$ to a minimum and the signals to their intended strength, we may

Fig. XVI-5.

permit variation, Δs, in the connections, or synapsis, s, to obtain a similar limit.

$$\frac{|\Delta s|}{s} < \frac{1}{3}\left(1 + \frac{4}{3\delta - 1}\right)$$

But it is more reasonable to suppose that, on real neurons, the sum of the afferents, $\sum_{1}^{\delta}(s \pm \Delta s) = \delta s$; whence $\frac{|\Delta s|}{s} = \frac{\delta + 1}{\delta - 1}$ whose limit as δ approaches ∞ is unity. For $\delta = 3$, to the nearest integer, $s \pm \Delta s = 2 \pm 3$ (see V_k of Fig. XVI-5). Note that the range of θ of the permissible variant is from -1 to $+7$, and that $5 \leqslant \theta \leqslant 6$, or $\Delta\theta = \pm 6.25$ per cent.

From the preceding paragraphs it is clear that the number of p's that may appear in any Venn symbol for a given change in θ is fixed only for nondegenerate diagrams, and that, for degenerate diagrams, the fractional change in the jots is generally less than the fractional change in θ. Thus the actual reliability tends to exceed expectation as the specifications of strengths of signals or of coupling (i.e., synapsis) are randomly perturbed. But it would be a work of supererogation to inquire into this in general, for the nature of real or of artificial neurons and the statistical specifications of their connections necessarily determine the weight to be allotted to each factor.

If an educated guess as to real neurons and their nets is now permissible, it must take the general form of a $\Delta\theta$ of ± 5 per cent and a Δt of ± 10 per cent, which leaves Δs, for $\delta \geqslant 3$, less than ± 100 per cent for synapsis for neurons of the second or higher rank. This presupposes that neurons of the first rank are relatively closely specified in synapsis in order to segregate possible errors. This is in harmony with much that is known of the auditory system, wherein pitch, loudness, and direction are initially decoded and thence transmitted over separate channels or in dissimilar codes. It begins to look as though the same were true of vision, of proprioception, and of the stages of afferents from the skin following detection and amplification. Thus by the time information from any source reaches our great central computers we are in a region wherein crude specifications of statistical kinds should insure error-free calculation despite gross perturbation of threshold, of excitation, and even of local synapsis. This conclusion follows from two assumptions: first, that we are dealing with a parallel computer of more than two afferents per neuron; and second, that the functions which their neurons compute are sufficiently dissimilar to insure, at at least one level, incompatibility of error in the functions computed. All else may be safely left in large measure to chance.

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B. PHYSIOLOGICAL EVIDENCE THAT CUT OPTIC NERVE FIBERS IN A FROG REGENERATE TO THEIR PROPER PLACES IN THE TECTUM

Sperry (1) pointed out that the results of his experiments on optic nerve regeneration in adult frogs were consistent with specific reconnection of the optic fibers. He proposed that each individual neuron grew back to its original terminus in the tectum, for the behavior after visual recovery was as if the nerve had not been cut. In addition to the behavioral evidence, he produced scotomata in predicted quadrants by fairly large tectal lesions in frogs that had regrown their optic connections. The implications of his proposal are so odd that, while his elegant experiments were accepted, the interpretation was much disputed. Furthermore, the experiments with tectal lesions cannot be considered conclusive, since, by destroying part of the tectum, the ability of the animal to respond is also impaired. The purpose of this note is to give electrophysiological evidence for Sperry's hypothesis.

We have developed a technique for recording single fibers in the frog's optic nerve and single terminal bushes in the tectum (2). In this work we have found that normally the frog's tectum has the following organization. The fibers of each optic nerve cross completely in the optic chiasma and enter the opposite colliculus after dividing into two bundles. One is rostromedial; the other, caudolateral. They sweep over the surface and are distributed in several layers in the outer neuropil that forms the superficial half (250μ) of the tectal cortex (Fig. XVI-6). Most tectal cell bodies lie below this neuropil and send their main dendrites through it up to the pial surface. The axons of
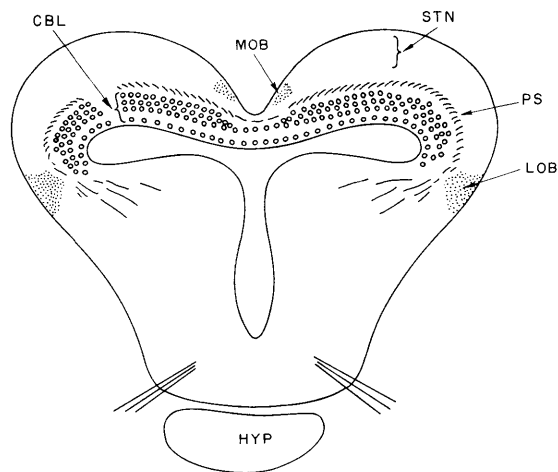

Fig. XVI-6.   Transverse section of the tectum of the frog at the level of the
        oculomotor nerves.
        CBL: cell-body layers   PS: palisade stratum
        MOB: medial optic bundle   LOB: lateral optic bundle
        STN: superficial tectal neuropil HYP: hypophysis

the majority of these cells form a narrow stratum that lies immediately above the compact layers of the cell bodies. The optic fibers end in a systematic way both along the surface and in the depths of the superficial neuropil, mapping the retina in a pattern that is constant from animal to animal. There are three layers of these optic fiber terminals which we have thus far identified only physiologically. Each displays a continuous map of the retina with respect to each of the three following operations on the image at the receptors. The three maps are in registration with each other and show position on the retina according to the cartography of Gaze (3).

In the uppermost layer lie the endings of two sorts of fibers which subdivide into two poorly defined strata. One stratum is composed of those elements each of which is sensitive to moving or maintained contrast within its receptive field. The sharper the contrast, the better is the response. These are equivalent to Hartline's (4) and Barlow's (5) "on" fibers. The other stratum is made up of terminals of units each of which detects a moving or recently stopped boundary within its receptive field, provided there is a net positive curvature of the edge of the darker phase. Such a fiber will not respond, for example, to a straight-edge boundary moving across its receptive field or to a preestablished edge within that field. Both of these strata represent the endings of the unmyelinated fibers of the optic nerve.

The second layer is made up of terminal bushes from "on-off" fibers.

The third layer is composed of endings from "off" fibers.

The layers of endings are distinct in depth, rarely merging even at the transition zones. In this conspicuous order, both along the surface and in the depths, the area of the retina "seen" from any point in the superficial neuropil is at most 10° in radius. Most of the ganglion cells whose terminals appear at that point are crowded toward the middle of that area.

For the purpose of testing Sperry's hypothesis of the specific regrowth of the optic fibers after section of the optic nerve, we cut one optic nerve in several adult frogs (R. pipiens), ensuring the complete separation of the two stumps. At the end of two months the first signs of visual recovery were apparent, but full use of the eye did not occur for another month. When the visual recovery seemed complete, we exposed the colliculi and tested the initially deafferented one for mapping of the retina. We found that the map had been regenerated along the surface, although the ganglion cells from whose terminals we were recording at any point were now spread over an area about two times as large as normal. The separation of operations in depth was also restored, and there was no sign of confusion between the operational layers.

The specific regrowth of the terminals to their proper stations cannot be explained by saying that an initial orderly array of fibers in the optic nerve crudely orders the fibers again at the time of regeneration. The fibers in the nerve simply are not in order ab initio. Any two contiguous fibers can come from as diverse points

on the retina as possible (2, 6).

This finding strongly supports Sperry's hypothesis that optic nerve fibers grow back to their original destinations. They do so in an even more highly specific way than he proposed; the regrowth of the termini is also proper in depth.

[After the preparation of this manuscript we noticed that R. M. Gaze, University of Edinburgh, has presented to the Physiological Society (J. Physiol. $\underline{146}$, 40P, 1959) similar findings in Xenopus laevis. He, however, has not studied the reconstitution of the distribution in depth of the optic fibers.]

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