

## XVII. NEUROPHYSIOLOGY\*

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### A. MACHINE DEPENDENCE OF DEGREES OF DIFFICULTY

One may define a degree-of-difficulty relation for total recursive functions by saying that  $f \succcurlyeq g$  ( $f$  is at least as difficult as  $g$ ) if to each program for computing  $f$  there corresponds a program for computing  $g$  such that  $g(x)$  takes no more steps to compute than  $f(x)$  for almost all  $x$ .<sup>1</sup> Unfortunately, such an ordering is highly dependent on our choice of mathematical model for a computer (cf. Hartmanis and Stearns,<sup>2</sup> Sec. III). It is the purpose of this report to so modify our degree-of-difficulty relation as to lessen this machine dependence.

#### 1. Monoid-Induced Machine Equivalence

Let  $S$  be a monoid of 2-variable functions, increasing for  $x$  and  $y$  positive. The associative multiplication is

$$f \cdot g(x, y) = f(x, g(x, y)),$$

and  $S$  contains the identity  $e(x, y) = y$ .

Let  $F$  and  $G$  be two partial recursive functions of a single variable. We say that  $F$   $S$ -bounds  $G$  iff  $F(x)$  convergent implies  $G(x)$  convergent and there exists a function  $p \in S$  such that

$$p(x, F(x)) \geq G(x) \quad \text{for almost all } x \text{ for which } F(x) \text{ is defined.}$$

A machine  $M$  may be thought of as supplied with a collection of programs  $P_i$  ( $i=1, 2, 3, \dots$ );  $\phi_i$  is then the function computed by  $M$  when supplied with program  $P_i$ , and  $\Phi_i(x)$  is the "number of steps" that it takes to compute  $\phi_i(x)$ . (For a given partial recursive function  $f$ , there will in general be infinitely many  $i$  such that  $\phi_i = f$ ; cf. a universal Turing machine.) For such a machine  $M$ , we then say that

DEFINITION 1:  $f \succcurlyeq_M g$  ( $f$  is at least as difficult as  $g$ , using  $M$ ) if and only if, to each program  $P_i$  for computing  $f$ , there corresponds a program  $P_j$  for computing  $g$

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such that  $\Phi_i$  S-bounds  $\Phi_j$ .

In section 3, we shall particularize our choice of S. We observe that Hartmanis and Stearns<sup>2</sup> essentially employ the choice

$$S = \{f \mid f(x, y) = ky, \quad k \text{ a positive constant}\}.$$

Although they treat sequences, whereas we treat functions on the integers, much of their material is, of course, applicable.

We chose S to be a monoid simply so that we might deduce:

THEOREM 1:  $\succsim_M$  is reflexive and transitive.

In describing the machine dependence of the ordering  $\succsim_M$ , we want to know, for each machine M, which are those machines N that give rise to the same ordering:

DEFINITION 2: Two machines M and N are S-equivalent,  $M \equiv_S N$  iff, for all partial recursive functions f and g,

$$f \succsim_M g \iff f \succsim_N g.$$

This equivalence relation is obtained from a partial ordering  $\geq_S$  on machines. We say that M is at least as complex as N (modulo S), and write  $N \geq_S M$ , iff each program  $^N P_i$  for machine N can be replaced by a corresponding program  $^M P_j$  for machine M so that  $^N P_i$  S-bounds  $^M P_j$  ( $^N P_i$  and  $^M P_j$  are programs for the same function). In other words, M is at least as complex as N if, up to elements of S, M can compute any function as quickly as N can. It is now immediate that

THEOREM 2: (i)  $\geq_S$  is reflexive and transitive.

(ii)  $M \equiv_S N$  if and only if  $M \geq_S N$  and  $N \geq_S M$ .

Section III of Hartmanis and Stearns<sup>2</sup> may now be reread as a treatment of equivalence classes under the monoid

$$\{p \mid p(x, y) = ky^{2n}\}.$$

## 2. Turing Machines as Programmed Computers

To fit Turing machines into our present discussion we have to separate the machine from the program. We do this by adopting the following, somewhat nonstandard, model of a Turing machine:

It is a device equipped with a container for cards, a tape scanner-printer-mover, and a tape that is infinite in both directions. The tape is divided into squares along its length and the scanner can look at one square at a time. The device can print the blank, or one of a finite set  $\Sigma$  of symbols, on the square it is examining and shift the tape one square to right or left. The container can hold an arbitrarily large but finite number of cards, together called the program. On each card is printed a single 5-tuple  $q_i S_j S_k M q_l$ . The  $q_i$  denote internal states of the device, the  $S_j$  are tape symbols, and

M is a move L(left), R(right) or N(none). When the device is in state  $q_i$  and scans the symbol  $S_j$ , it prints the symbol  $S_k$ , moves the tape M, and changes its internal state to  $q_\ell$ . If there is no card starting with  $q_i S_j$  in the container when the machine is in state  $q_i$  and scanning the symbol  $S_j$ , then the machine stops. Any program is allowed, subject to the condition that any 2 cards must differ in the initial pair  $q_i S_j$ .

We can associate with each program a partial recursive function  $\phi$  as follows:

The program is placed in the container, an input integer  $x$  is written in some suitably encoded form as a finite string of symbols on the tape, the scanner is placed over the rightmost digit of this string, and the device is put in states  $q_0$ . The device then operates in accordance with the instructions printed in the program. If it never stops, we say  $\phi(x)$  diverges. If it does stop, we let  $\phi(x)$  be the integer which is obtained from the string of symbols on the tape by some standard decoding.

In the following discussion we let  ${}^k T$  be the above-mentioned machine with the constraint that  $\Sigma = \{0, 1, \dots, k-1\}$  (with each of these  $k$  numbers considered as a single symbol) and that the coding of input and output is to be in radix  $k$  ( $k \geq 1$ ). In particular, we shall be interested in machines equivalent to  ${}^{10} T$ .

Now let  ${}^\mu T$  differ from  ${}^{10} T$  only in that  $\Sigma$  is augmented by some fixed finitude of further symbols ( ${}^\mu T$  still uses a radix 10 input-output code).

PROPOSITION 1: (i) If  $P$  is a program that causes  ${}^{10} T$  to compute the function  $f$ , then  $P$  will also cause  ${}^\mu T$  to compute  $f$ , and in exactly the same number of steps.

(ii) If  ${}^\mu P_i$  is a program which causes  ${}^\mu T$  to compute  $f(x)$  in  ${}^\mu \Phi_i(x)$  steps, then there exists a program  ${}^{10} P_j$  which causes  ${}^{10} T$  to compute  $f(x)$  in  ${}^{10} \Phi_j(x)$  steps, where

$$p(x, {}^\mu \Phi_i(x)) \geq {}^{10} \Phi_j(x)$$

on setting  $p(x, y) = \frac{1}{2} (\ell+1)[k(k+1)+(k+y)(k+y+1)] + (3\ell-1)y$   
with  $k = \lceil \log_{10} x+1 \rceil =$  number of digits of input to  ${}^\mu T$

$K =$  number of symbols of alphabet of  ${}^\mu T$

and  $\ell = \lceil \log_{10} K+1 \rceil$ .

PROOF: (i) Is obvious.

(ii) follows on letting  ${}^{10} P_j$  be the following simulation of  ${}^\mu P_i$  on  ${}^{10} T$ :

a. The input string  $x$  to  ${}^\mu T$  is replaced by an input string for  ${}^{10} T$ , each digit,  $d$ , being replaced by an  $\ell$ -tuple,  $do \dots o$ . This can be done in at most

$$\frac{1}{2} (\ell+1) k(k+1) \text{ steps.}$$

b. After  ${}^{10} P_j$  has encoded  $x$ , it acts on each  $\ell$ -tuple of digits just as  ${}^\mu P_i$  acts on each of  ${}^\mu T$ 's symbols. The number of steps required for this portion of the simulation is at most

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$$(3\ell-1) \cdot {}^\mu\Phi_i(x).$$

c. When  ${}^\mu P_i$  stops, its output is an integer  $y$ . Since  ${}^{10}P_j$  simulates  ${}^\mu P_i$ , its tape at this point must contain an encoded  $y$ .  ${}^{10}P_j$  then decodes this to obtain  $y$ , an operation taking not more than

$$\frac{1}{2}(\ell+1) k'(k'+1)$$

steps, where  $k'$  is the number of digits in  $y$ . Since  ${}^\mu P_i$  may, in an extreme case, merely print  ${}^\mu\Phi_i(x)$  digits to the left of  $x$ , the best bound we can give for  $k'$  is  $k + \Phi_i(x)$ .

Our estimate

$$p(x, y) = \frac{1}{2}(\ell+1) [k(k+1)+(k+y)(k+y+1)] + (3\ell-1) y$$

is thus verified.

Q. E. D.

### 3. An Equivalence Class for ${}^{10}T$

Since the purpose of this report is to define computational difficulty to be invariant over a large subclass of machines, a measure of our success must be the size of the machine class containing  ${}^{10}T$ . But this class must depend on our choice of  $S$ . If we choose  $S$  very small, say the set consisting of the single function  $e(x, y) = y$ , then  ${}^\mu T \neq {}^{10}T$ . On the other hand, if  $S$  is too large, e. g., the totality of total recursive functions  $f(x, y)$ , then all machines are  $S$ -equivalent to  ${}^{10}T$  and therefore all total recursive functions are equidifficult. Motivated by Proposition 1, we choose an  $\tilde{S}$  large enough to have

$${}^{10}T \equiv_{\tilde{S}} {}^\mu T \tag{*}$$

but small enough to make the  $\tilde{S}$ -equivalence class of  ${}^{10}T$  interesting. In fact,

$$\tilde{S} = \{q(\log x, y) \mid q(z, y) \text{ is a polynomial, monotone increasing for positive } z \text{ and } y\}$$

Question: Is there a smaller  $S$  satisfying (\*)? Quite obviously, the proof of Proposition 1 can be generalized to show

PROPOSITION 1a:  ${}^k T$  is  $\tilde{S}$ -equivalent to a machine with a base  $k$  code, capable of printing  $\ell$  symbols,  $\ell > k > 1$ . We next state and prove

PROPOSITION 2:  ${}^{10}T \equiv_{\tilde{S}} {}^k T$  for  $k > 1$ .

PROOF: We shall prove this proposition for the special case  $k = 2$ ; a generalization of the proof to any integer  $k$  greater than 1 is quite easy. To simplify the proof, we make use of a machine (similar to  ${}^\mu T$ ) which we call  ${}^\eta T$ : It has a single tape, is capable of printing the 10 symbols 0 through 9, and operates with a radix 2 code. The proof involves showing that  ${}^2 T \geq_{\tilde{S}} {}^{10} T$  and that  ${}^{10} T \geq_{\tilde{S}} {}^\eta T$ . From Proposition 1a we know that  ${}^\eta T \equiv_{\tilde{S}} {}^2 T$ , and hence we may conclude that  ${}^2 T \equiv_{\tilde{S}} {}^{10} T$ .

${}^2 T \geq_{\tilde{S}} {}^{10} T$ : We simulate the program  ${}^2 P_i$ , with  ${}^{10} P_j$  which operates as follows:

a.  ${}^{10}P_j$  takes the input integer  $x$  base 10 and converts it to  $x$  base 2. This can be done in less than  $2([\log_2 x] + 1)^2$  steps.

b.  ${}^{10}P_j$  operates on  $x$  base 2 in precisely the same way as does  ${}^2P_i$ . This takes  ${}^2\Phi_i(x)$  steps.

c.  ${}^{10}P_j$  converts the result base 2 to base 10 in at most  $2([\log_2 x] + 1 + {}^2\Phi_i(x))^2$  steps.

So  ${}^2\Phi_i$   $\tilde{S}$ -bounds  ${}^{10}\Phi_j$  with

$$q(z, y) = 2(z+1)^2 + y + 2(z+1+y)^2.$$

By essentially the same proof we have  ${}^{10}T \geq \tilde{S}^\eta T$ . Q. E. D.

We shall finally state a very general theorem without proof: the proof, though tedious, does not involve any methods other than those contained in the proofs of Propositions 1 and 2.

**THEOREM 3:**  ${}^{10}T$  is  $\tilde{S}$ -equivalent to any machine with a radix  $k$  input and radix  $\ell$  output ( $k > 1, \ell > 1$ ), with a finite number of tapes, each of finite dimension, and with a finite number of scanners on each tape.

In the following example, two degrees of difficulty are compared in the radix 2 machine  ${}^2T$ . By Theorem 3, these comparisons remain valid on a wide variety of machines.

**EXAMPLE:**  $2^x \succ x$

Computation of  $2^x$  involves printing  $x$  zeroes after a 1. Computation of the identity function  $x$  takes only 1 step. Clearly,  $x$  exceeds any given polynomial in  $\log x$  for almost all  $x$ .

We also see why Proposition 2 demands that the radix  $k$  be greater than 1. Certainly  ${}^1T \geq \tilde{S}^{10}T$ , but it is not true that  ${}^1T$  is  $\tilde{S}$ -equivalent to  ${}^{10}T$ . We may see this by considering  $2^x$ . Actually  $2^x$  requires approximately  $2^x$  steps just for writing time on  ${}^1T$ , but only needs approximately  $x$  steps on  ${}^{10}T$ , and  $x$  cannot  $\tilde{S}$ -bound  $2^x$ . Nevertheless, a proof like that for Theorem 3 shows that  ${}^1T$  is  $\tilde{S}$ -equivalent to any machine with a radix 1 input-output code, with a finite number of tapes each of finite dimension, and with a finite number of scanners on each tape.

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#### References

1. M. O. Rabin, Degree of Difficulty of Computing a Function, and a Partial Ordering of Recursive Sets, Hebrew University, Jerusalem, Israel, April 1960. Rabin defines a strict partial ordering  $f \succ g$  ( $f$  more difficult than  $g$ ) as the existence of a program for computing  $g$  such that with any program for  $f$  the computation of  $f(x)$  takes more 'steps' than the computation of  $g(x)$  for almost all  $x$ .
2. J. Hartmanis and R. E. Stearns, On the Computational Complexity of Algorithms (to be published in Trans. Am. Math. Soc.).

## B. SOME RESULTS ON RABIN'S PROBABILISTIC AUTOMATA\*

Consider a finite probabilistic automaton  $\mathcal{A} = \langle \Sigma, S, M, s_o, s_n \rangle$ , where  $s_o$  is the start state;  $s_n$  is the final state;  $S$  is the set of all  $n+1$  automaton states; and  $M$  is a family of Markov transition matrices,  $\{A(\sigma_i)\}$ , which gives for each  $\mathcal{A}$  input symbol  $\sigma_i \in \Sigma$  a corresponding state probability transition matrix  $A(\sigma_i)$ .  $\mathcal{A}$  is said to accept an input tape  $x = \sigma_{i_1} \sigma_{i_2} \dots \sigma_{i_m}$  if and only if  $p_{o,n}(x)$  (the first row,  $(n+1)^{\text{th}}$  column entry of  $A(x) = A(\sigma_{i_1}) A(\sigma_{i_2}) \dots A(\sigma_{i_m})$ ) exceeds  $\lambda$ . Assume everywhere that for each  $\mathcal{A}$  there is some fixed  $\delta > 0$  such that for all  $x$  either  $p_{o,n}(x) > \lambda + \delta$  or  $p_{o,n}(x) < \lambda - \delta$  (Rabin's isolated cut point probabilistic automata).<sup>1</sup> Denote such automata P. A.

Rabin proved that all P. A. accept regular sets of tapes (i. e., the same sets of tapes that finite deterministic automata accept) and that actual P. A. (none of whose  $A(\sigma_i)$  have any 0 entries) accept definite sets of tapes (i. e., the same sets of tapes are acceptable by finite deterministic automata whose present state can only be influenced by the last  $K$  inputs, for some fixed finite  $K$ ). He also showed that actual P. A. are stable in the following sense: For each  $\mathcal{A}$  there is an  $\epsilon > 0$  such that if no entries in the  $A(\sigma_i)$  of  $\mathcal{A}$  are changed by an amount  $\geq \epsilon$ , the perturbed  $\mathcal{A}$  will accept the same set of tapes as  $\mathcal{A}$  did, and with respect to the same isolated cut point.

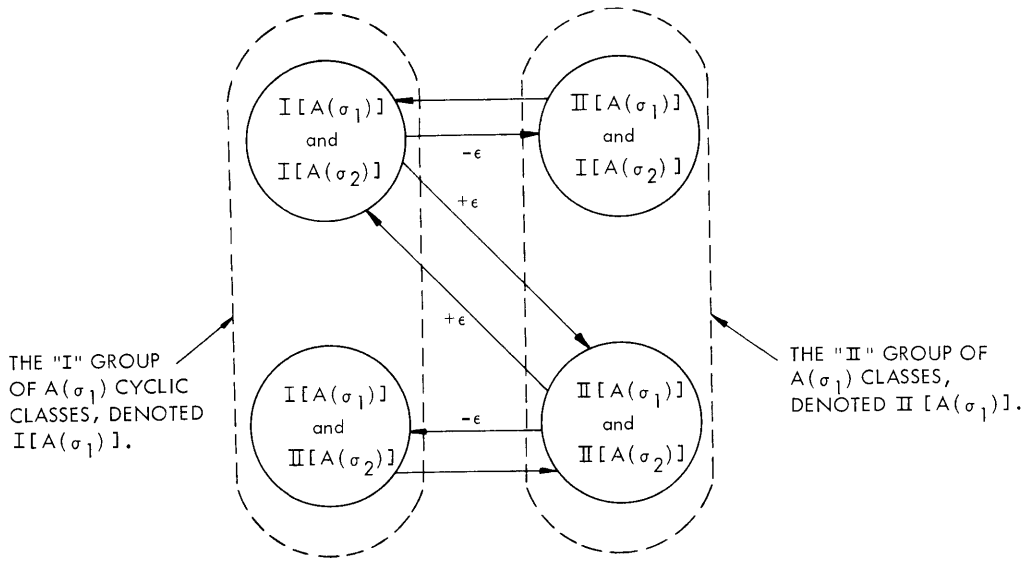
All of our results pertain to nonactual P. A. of a kind for which it is always possible to pass in some number of steps from any one state to any other. (This restriction is for the sake of tidiness and is in no way necessary to the nature of the results obtained.) Denote such an automaton a P. A.\* We show that there is a natural partition of the  $A(\sigma_i)$  for each P. A.\* into a cyclic and an acyclic subset,<sup>2</sup> and that the cyclic subset further partitions into sub-subsets, each of which contains only cyclic matrices having the same cyclic classes.<sup>3</sup> We also show that if any  $A(x)$  contains nonzero submatrices along its diagonal only, thereby indicating that  $x$  is a cycling tape, the cyclic classes of each  $A(\sigma_i)$  for which there is a corresponding  $\sigma_i$  somewhere in  $x$  are identical.

Our first theorem states that if a P. A.\* has only acyclic  $A(\sigma_i)$ , it must accept a definite set of tapes, and Rabin's stability theorem applies.

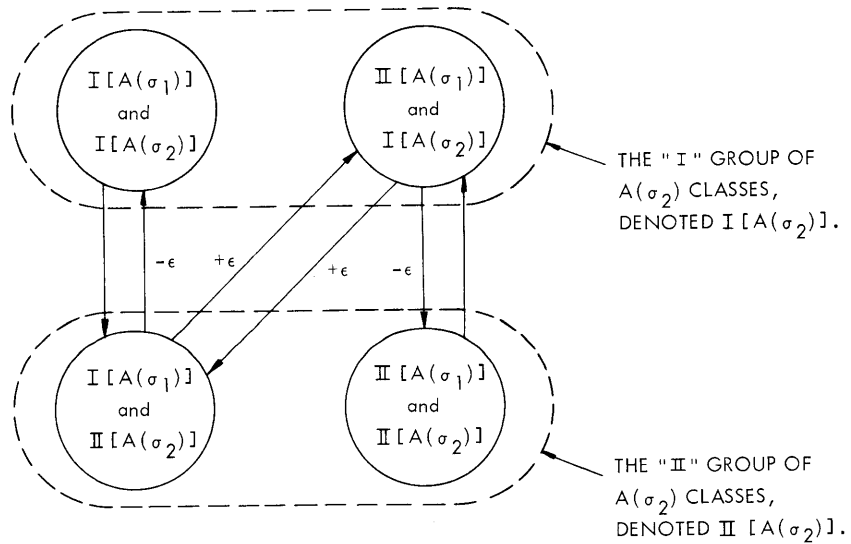
Our second theorem concerns P. A.\* all of whose  $A(\sigma_i)$  are cyclic with the same cyclic classes. We show that such a P. A.\* effectively consists of one part that accepts a definite set of tapes and another part that counts the length of each tape presented to it modulo  $d$ , where  $d$  is the number of cyclic classes. Such a P. A.\*, consequently, accepts a regular, indefinite set of tapes. We prove that Rabin's stability theorem applies mutatis mutandis in this case, provided no new  $A(\sigma_i)$  zero entries are created

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(a) STATE DIAGRAM DEPICTING THE NATURE OF THE INTER -  $I[A(\sigma_1)]$ ,  $II[A(\sigma_1)]$  TRANSITIONS. UPON APPLICATION OF  $\sigma_1$  TO  $\mathfrak{A}$ .



(b) STATE DIAGRAM DEPICTING THE NATURE OF THE INTER -  $I[A(\sigma_2)]$ ,  $II[A(\sigma_2)]$  TRANSITIONS. UPON APPLICATION OF  $\sigma_2$  TO  $\mathfrak{A}$ .

Fig. XVII-1. Instability theorem transition pattern.

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or destroyed as the  $A(\sigma_i)$  vary.

The next theorem concerns a special class among those P. A.\* whose cyclic  $A(\sigma_i)$  have different cyclic classes. A construction is given to show that for every  $\epsilon > 0$  and  $\gamma > 0$ , there exist P. A.\* with associated tapes  $x$  having the following property: If the P. A.\*  $A(\sigma_i)$  entries are allowed to vary by an amount  $\leq \epsilon$ , subject to the requirement that no new  $A(\sigma_i)$  zero entries be created or destroyed in the process,  $p_{o,n}(x)$  can change by an amount  $> 1 - \gamma$  as a consequence (independently of the  $\lambda$  cut point).

Closely related to this theorem is the following one, involving the same assumptions and conditions. Given an  $\epsilon > 0$  and a P. A.\* of the assumed class, there is a cut point  $\lambda_0$  such that all isolated cut points  $\lambda < \lambda_0$  lead to different sets of tapes accepted by the given P. A.\* and its perturbed version.

Rabin's paper<sup>1</sup> concludes by mentioning that H. Kesten produced a P. A. for which there is no  $A(\sigma_1)$  zero-invariant stability theorem. Our main result in the work reported here concerns a suitable generalization of Kesten's example, which is unknown to us at present, since Rabin did not mention it in his paper. It is the following: Every P. A.\* which is unstable in the Rabin sense necessarily has at least one pair of cyclic  $A(\sigma_i)$  which have different cyclic classes. Suppose in some given P. A.\*,  $\mathfrak{A}$ , that they are  $A(\sigma_1)$  and  $A(\sigma_2)$ . Then it is necessary, if stability is to be independent of the isolated  $\lambda$  point, and sufficient for  $\mathfrak{A}$ 's instability that the  $A(\sigma_1)$  and  $A(\sigma_2)$  cyclic classes be partitionable in such a way that the allowed transitions between partitions of states are as shown in Fig. XVII-1 (or an appropriate refinement of Fig. XVII-1 which allows its sequential character to be spread out with certain variations over space). The  $+\epsilon$  and  $-\epsilon$  terms in Fig. XVII-1 show essentially how the allowed perturbations of  $\mathfrak{A}$  must go in order to permit the " $\epsilon$ -wobble" of a clockwise state movement in  $\mathfrak{A}$  to accumulate to the extent that  $\mathfrak{A}$  and its perturbed version recognize the tape  $x = \sigma_1 \sigma_2 \sigma_1 \dots \sigma_2$ ,  $l(x) = f(\epsilon)$ , differently (with respect to any arbitrary isolated  $\lambda$  point, and regardless of where  $s_0$  and  $s_n$  are).

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References

1. M. Rabin, Probabilistic automata, Information and Control 6, 4 (September 1963).
2. Cf. J. G. Kemeny and J. L. Snell, Finite Markov Chains (D. Van Nostrand Company, Inc., New York, 1963). Our cyclic and acyclic matrices are Kemeny and Snell's ergodic cyclic and ergodic regular matrices, respectively.
3. Ibid., see p. 36 for the definition of a cyclic class. Roughly, cycling on an ergodic Markov chain consists of looping from one disjoint cyclic class of states to another around the whole chain.



## C. PROJECT REPORTS

### 1. GENERAL INSTRUMENTATION

#### a. Microelectrodes

We have found a new method for making extremely fine and very stiff microprobes. It is a modification of Hubel's operation on tungsten wire, except that he polishes the wire to a point by electrolysis, whereas we polish it by sublimation in a bunsen burner, and he coats with nonconducting varnish, whereas we coat with glass. Our coating process is a modification of Baker's method, and can be carried out in any microelectrode puller; it has great flexibility, for not only can the thickness of the glass coat be varied at will, but the coat and point can be shaped at the tip in a small reducing flame with really remarkable ease.

#### b. Period-Measuring Device

The forward current through a good diode produces a voltage that is logarithmically related to that current. Thus the discharge of a condenser through a diode in the forward direction ought to yield a voltage whose height measures the logarithm of elapsed time from the instant of connecting the diode plus some constant. We constructed this device some five years ago and have been using it quite regularly to measure logarithms of pulse interval. But in observing the firing rate of certain retinal ganglion cells, it became clear that it would be a good thing to have the ability to compare (on an x-y plot) the present pulse interval with the one just before it, either on a linear or logarithmic scale. This instrument has been constructed, is remarkably stable, and is good over at least four decades.

#### c. Nerve-Impulse Selector

When one is recording from a nerve bundle or from the brain, several different neurons can be identified by differences in height and shape of discharge. It is useful to be able to track one of these at a time. This can be done by making a pulse-height window that passes only transients higher than one voltage but lower than another without distorting shape. This device can be made easily by modifying a very inexpensive commercial pulse generator.

### 2. EXPERIMENTAL RESULTS

#### a. Olfaction

(i) In Quarterly Progress Report No. 72 (pages 253-256) Dr. R. C. Gesteland in collaboration with J. Y. Lettvin and W. H. Pitts showed that there was some reason

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to think that the positive swing of the Ottoson potential in the electro-osmogram is not artefactual as had been supposed, but rather indicates that the receptors have two modes of operation. For any receptor there would be two classes of olfactants, those that cause a signal current to flow and those that cause a shunt of pre-existing signal current. The response to repeated puffs of anisole was the basis for this notion. In the frog nasal mucosa such vapors as those of methanol or ethanol produce no negative Ottoson potential but only a positive swing. If one supposes that the positive swing is not due to a countercurrent but to a shunt, then when methanol is played on the mucosa after the negative Ottoson potential is produced, the size of the resultant dip in the Ottoson potential ought to be a function of the height of the Ottoson potential. This is so. Since there are no synapses in the olfactory mucosa, the result implies that the output of the single receptor is a vector rather than a scalar, that the receptors themselves must be characterized in terms of two variables, and that the classification of olfactants with respect to any receptor must be in terms of something like excitation and inhibition in the same sense as if the olfactants were synaptic mediators to the receptor conceived as a neuron.

While this result is very beautiful, it complicates matters immensely, for now the deciphering of receptor activity becomes the same sort of problem that confronts us in the rest of nervous tissue. By proving that these receptors have two degrees of freedom (a fact that is also evident in Schneider's data on insect olfaction), the already tedious work of deciding what a single receptor does becomes an even more tedious and perhaps fruitless job.

The general strategy of researchers when confronted by a disastrous opening of new vistas is to take refuge in a new theory before making what may be fruitless measurements. Such a theory is discussed below in the section on "General Considerations."

(ii) H. A. Baldwin reports that the olfactory bulb of the frog is beginning to show stimulus-related activity when proper attention is given to preserving blood circulation in that part of the brain. The new tungsten electrodes that have been devised, as mentioned earlier in this report, are plated with a gold ball, 2-5  $\mu$  in diameter, and these have been particularly valuable in studying single-cell responses for several hours.

Two distinct levels of active cells are discernible in the surface of the bulb. Within these levels cells fire at a fairly low rate, and a particular cell may be inactive for long periods of time. Our assumption at this time is that we are recording from the external plexiform layer (tufted cells) and from the mitral cell layer. There is still no noticeable difference in the general activity of both of these layers with respect to location on the surface of the bulb.

The activity of a cell is strongly related to the rate at which air or a stimulant is introduced into the nostril. Cells in general are inactive both with no air and with air introduced at a rapid rate. The "bottled" air that is used for stimulation is passed through both a bone charcoal filter and a water bath. The pump used displaces 0.7 ml

and is operated cyclically, that is, air is drawn through the nasal passage in a manner that might occur during breathing.

We suspect now that the bulb response shows that air is an olfactory stimulant. Both "on" responses and "off" responses are observed with single cells. It may be profitable to explore weak olfactory stimulants of this type rather than strong odorants. Our experience with the preliminary use of odors that are noticeable to our own nose is that they produce general inhibition in the bulb response for brief periods of time. This inhibition may simply reflect the great sharpening effect on odor identification by the bulb, for in a few cells we could show that a few odors produce a weak response and that everything else produces a much stronger inhibition.

b. Vision

(i) Frog retina (work done with Dr. S. Frenk)

Dimming detectors. On studying the off fibers or dimming detectors in the optic nerve, we were struck by the extraordinarily long time constant of change in firing pattern, and this seemed to us very probably to be related to receptor processes rather than built into ganglion cells. Something of this sort had already been studied by Kuffler, Barlow, and Fitzhugh, in 1957, on the cat. The slow changes that they observed in average frequency on adaptation to light or to dark did not seem to them to bear a definite relation to receptor processes, for, in the main, they were dealing with elements that had opponent processes between center and periphery (for example, center excited by "on" of light, periphery excited by "off"). Since we had ganglion cells in a frog which show a weighted function of simply one quality over the entire receptive field, we were in a position to study a much simpler relation. There are in reality two types of dimming detectors, just as the authors quoted found two types of adaptation effects. The first kind shows almost an absolute measure of the state of dark adaptation, that is, it has a firing rate that is greater, the darker it is, and changes to a new frequency with change in level by overshooting and then coming to the new frequency with a very long time constant. The second comes to a fixed rate of firing at any level of illumination and with a shorter time constant after a step to darkness. That is, it is as if the process measured by the first type is differentiated by an operation with a shorter time constant. If, with respect to the first type, we use a dim flash of light as a test and search for the first fluctuations of response produced by that dim flash, we always find them at the same average frequency of firing, a result specifying that the frequency in fact is measuring something related to the dark adaptation of that cell. Tentatively we believe that the "on" fibers described by W. R. A. Muntz for color reception (when he visited our laboratory two years ago) are also divided into similar groups, but we are not yet prepared to establish them.

There are several ways in which to account for these findings, and we shall discuss

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them briefly. In the first place, we may consider that the output of the rods and cones is a linear and faithful representation of the state of bleaching of the visual pigment inside. This is the view that has been proposed by Barlow. It requires that the output of the single receptors be faithful over approximately a six-decade range, if not more. With this view, and with other considerations such as spatial operations between rods and cones neglected, there would be two types of bipolar cells. One type would perceive directly the total amount of bleaching in the receptors either as a current flow from the receptors or as the efflux of some excitatory chemical. The other type would adapt to the current or chemical with a particular time constant, and both of these bipolars would act in both excitatory and inhibitory fashion on the succeeding ganglion cells, and in their combinations produce the responses that we mentioned. This model, although seemingly simple, poses some serious questions. In the first instance, How does one get such an enormous dynamic range in the transmitted signal between receptors and bipolars? Second, Can such a population of bipolars adequately account for the other operations that we observe, say, in the frog retina? But most important of all, if one occludes the circulation to the nervous elements of the retina, leaving only the outer segments of the receptors intact (for they are circulated by the choroid against which they abut), their average response ought to show a linear relation to the level of light, and this is not so.

The same notion we had about the rods and cones of the eye led us to search for the bivariate character of the olfactory response of the frog mucosa mentioned above. That is, we felt that the output of the rods and cones could best be explained by supposing that they too had two degrees of freedom in their responses. One parameter would be the rate at which pigment molecules were bleaching, and the other parameter would be the total number of molecules bleached. If these were arranged internally in the receptor in the same manner as we suggested for the color receptors in Quarterly Progress Report No. 70 (pages 327-337), the signal current from sites on the membrane of the outer segments at which pigment molecules were bleaching would be attenuated (at the level of the cell body and its processes leading to the bipolars) by shunts through the places at which molecules had already been bleached. Thus we felt that we would achieve a reasonable compression of the wide dynamic range of receptors into an easily handled signal well within the dynamic range of the succeeding nervous tissue. But such a schema would require that the bipolar cells attached to the rods and cones be capable of appreciating the two degrees of freedom characterizing the response which are such that they could couple either parameter to the ganglion cells. For one must realize that if one set of ganglion cells gives a signal that depends on the level of light at that state of adaptation, and another set yields a measure solely of that adaptation, there must be two degrees of freedom in the way that receptors affect bipolars except in the linear case (as in Barlow's model). It is idle to speculate further here, for the matter is sufficiently important that we must search for more intimate measures in the system. Yet we shall

say this: Our present studies incline us to believe that the bipolars may be able to appreciate changes in impedance, as well as in current flow occurring in the receptor elements. We advance this notion tentatively.

Frog vision. Four years ago we published our study on frog vision. Since then there has been some reluctance on the part of our colleagues to accept our class 2 fibers for what we claim them to be. The notion of a curved-edge detector as being best characterized by the combination of properties that we gave seems to violate popular notions of simplicity for some reason. Some authors, such as Gaze or Wagner, on testing these elements have announced that they in fact are no more nor less than the classical center "off," peripheral "on" elements that are found elsewhere and in other retinas. The concept that these authors advance is that the receptive field of such cells is organized into two concentric regions, both of which are averaged and then played against each other. Thus, for example, Gaze, after checking for the activity that we found, began using spots of darkness suddenly established in the field rather than moving them in as stimuli, and found responses. Accordingly, he pointed out that the effect of small objects as opposed to large objects in exciting the receptive field was due to the fact that in a small object the darkening of the center on moving the object in was accompanied by a lightening of the periphery on moving the object out of the periphery and into the center, and this coupling gave an enhanced response to a simple center "off," peripheral "on" cell. Neither Gaze nor Wagner had carefully considered the argument for curvature, particularly with respect to an object such as a square of the same size as the receptive field brought in either edge first or corner first. Nor had they observed in their own experiments the curious feature that the center of the receptive field had to be darkened after it was lit and the response could not be established by a simple annular arrangement flashed on. That is, in order to get a firing of the cell it is necessary that the region that is to be darkened be first lit – not established as a relatively dark spot contemporaneously with a relatively light surround. In other words, our experiments showed that the cell detected "edge modified by active dimming" rather than "edge modified by darkness," and so, as a matter of fact, did their experiments.

Accordingly, to show that one could not explain the activity of such a cell by a simple averaging procedure, we devised several easily understandable illusions to show the difficulties. For example, if we position a black spot just outside the receptive field, and diametrically across, in the receptive field, position the apex of a dark triangle in such a way that that apex intersects the periphery and just touches the center of the receptive field, and then move this constellation rigidly coupled so as to bring the black spot into the center of the receptive field, very little response occurs. If, however, the black spot is moved in alone, without the apex of the triangle moving out, the response is large. The apex of the black triangle moving out of the periphery in the outward direction is equivalent to causing an increased lighting in the periphery at the same time

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that the black object darkens the center and ought to enhance the response. In fact, it inhibits it. Thus the mode of describing such a response such as the one that we advanced in Sensory Communication (edited by W. A. Rosenblith. The M. I. T. Press, Cambridge, Mass., 1961), where we proposed that the cell was taking something like a Green's function, still obtains. There must be a local interaction between the quality of "edgedness" and the quality of "darkening."

These comments are not carping. The fundamental dichotomy among the men who are working on the retina is between those who believe that the anatomy in fact is somehow or other related to function, and those who suppose that all that is required is a sort of random connectivity. To characterize ganglion cells by the property of having a center "on", peripheral "off" or vice versa is to suppose that no other parameters are of anything but secondary importance. We have shown, however, that it is other discriminants that more easily characterize cells by groups in such a way as to relate conduction velocity and size of receptive field to function as well. It is not now a question of proof but one of classifying phenomena before a theory has been formed, and so judgment must be held in abeyance.

### 3. GENERAL CONSIDERATIONS

We have been concerned for the last year with a prolegomenon to a theory of nervous action based on neurons as simple relation detectors. The argument goes this way: From the work of Hodgkin and Huxley we know that the nerve membrane at any one point consists of a parallel resistance and reactance to which can be added in parallel either a current generator or a shunt. This is the restatement of what is meant by saying that one has two types of monovalent ions carrying current in a nerve, one an equilibrium ion (either  $K^+$  or  $Cl^-$  whose chemical potentials are in equilibrium with the membrane potential of a nerve) or a nonequilibrium ion (for example,  $Na^+$  whose chemical potential is inverse in sign to the resting potential of the nerve). The studies that have been carried out on excitation and inhibition in cells of cats, frogs, crayfish, and so forth, indicate that the excitation process occurs because current flows between the region in which an excitatory synapse ends, and the axon hillock and inhibition occur because that signal current is attenuated before it gets to the hillock. If one now looks at the structure of a dendritic tree of a neuron, one cannot but be struck by the notion that if each dendrite could be represented by a transmission line with the electrotonic constants of nerve and if excitatory and inhibitory points were represented by nonlinear processes locally in the transmission line, such as current generators and shunts, then the arrangement of excitation points versus inhibition points in the tree would produce results that would depend upon the mutual order. That is, one could not simply take all excitatory events and attenuate them by the sum of all inhibitory events, but rather consider the

constellation of excitatory events occurring in a dendritic tree weighted in particular ways by different weighting functions represented by different constellations of inhibitory events. That is to say, a cell does not take either an average or ratio between excitatory and inhibitory events but rather the sum of all excitatory events weighted not only by distance from the axon hillock but by distribution (rather than sum) of inhibitory events.

This account tells us that the input-output relation in a neuron is not a simple function; instead it must be told enumeratively. When one reflects that for any neuron in the central nervous system there are more than a thousand synapses, the thought of enumerating the various input combinations becomes somewhat horrifying. True, to some extent the situation is not as bad as described because the electrotonic constants are relatively large. But they are not so large that they reduce one to considering average inhibition and average excitation as a sufficient account of the input to the nerve cell.

Thus, the input of a neuron must be described in terms of many parameters, among which are the geometrical relations of the different synapses to each other. But the output of a neuron is describable by simply one parameter, and that is frequency of firing. Such a device, which has a multiparametric input and a single parametric output, is best thought of as a relation-taking device of relatively low resolution, for every frequency in the output represents a confusion matrix on the input where a confusion matrix cannot be represented simply by averaging methods.

Suppose that we had a class of such elements in which  $n$  parameters characterized all possible relations between the various inputs and  $x$  represented the number of devices connected to the inputs, with the sole stipulation that each device is different but takes account in one way or another of every element in the input. All that could be said about such a system is that relational discriminations increase as the number of elements increases, but what the relations are and what the discriminations are remain obscure. Under these circumstances we advanced the notion that the resolution on the input of an ensemble of  $x$  devices increases as  $x^n$  as  $x$  is increased, without defining what is being resolved.

Thus, for example, if we consider our olfactory receptors, let every receptor be more or less excited or inhibited by every possible odorant, or, alternatively, let there be a limited class of odorants for each receptor which will tend to excite it and another limited class that will tend to inhibit it. The response of any single fiber will then not signify what odor is available, but any odor that is presented will have a figure of response in a large ensemble of such elements. The more neurons in the ensemble, the more easily one odor can be picked out from another. But all that one loses on losing neurons in the ensemble is resolution and not quality.

Similarly, suppose that we had a ganglion cell in the retina which had a cone acting as the center of its receptive field which absorbed mainly red light, and an average

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distribution of red, green, and blue cones in the surround of the center; then if such a neuron were organized in the typical center vs periphery arrangement, a uniform red light would excite it and so also would a white spot at the center, and a uniform blue light would inhibit it and so would a uniform green light and so would light in the surround, so that any color response would have a large class of stimulus equivalents produced by form, and any response to form could be imitated by a large class of colors. This ambiguity in response of a single neuron (this establishment of stimulus equivalents at the input), however, yields, when one makes every rod or cone the epicenter of such a neuron, a high resolution both in color and in form space when one considers the ensemble. That is, no form could be mistaken for color and no color for a form, with very many such elements packed together.

Thus, in a certain sense every neuron is more like a monad in the Leibnizian manner of speaking than it is like any other device ever described. Every neuron sees, as it were, an enormous amount of the world that it converts into a purely intensive function of low resolution. As the number of neurons increases, all that increases is resolution of relations between parts of the world, nonlinear relations, out of which comes the notion of quality and form. The notion of a system so arrayed has, we believe, different consequences from the usual notions underlying models of nervous systems. Very practically, it is prescriptive for research into real nerve nets and also suggests a different way of handling the results achieved by such research. But on the epistemological level, it breaks through the mind-body problem by installing something like mindedness in every component element of the nervous system in a manner similar to that proposed by Leibniz (and later Whitehead), so that mind does not suddenly arise, as if miraculously, after one has built to a certain complexity of a machine.

J. Y. Lettvin

## 4. THE NATURE OF BIOLOGICAL MEMBRANES

Our work in this area during the past quarter was largely experimentally oriented and was concerned primarily with arranging laboratory equipment and preparing to make various measurements upon biological and nonbiological membranes. Our significant progress was mainly theoretical and was on two fronts. First, the measurement of bio-potentials on a cellular level invariably involves the use of salt bridges and, consequently, the estimation of liquid-junction potentials. We have devised a new method of solving the equations that relate the liquid-junction potential to the ionic mobilities and activities near the junction. We intend, however, to defer discussion of this matter until experimental evidence is available and to devote the remainder of this report to our second idea.

We propose to offer an explanation of the passive ion-passing properties of a simple



unmyelinated nerve membrane such as that found on a squid axon. We shall confine our presentation to outlining the salient features of our theory and listing a few of the verified predictions that are now available from it.

First, we conceive of a nerve membrane as an organized structure separating two ionic solutions and composed of four distinct layers (protein, lipid, lipid, protein) and we note that experiments have shown that the lipid layers are essential to the membrane's functioning electrically as membrane, whereas the protein layers are nonessential and exert a strong modifying influence only.

Second, we conceive of mass transport across this membrane as taking place by way of small pores called channels, some of which will show a strong specificity for a given transportable entity. In particular, we shall restrict our considerations to two types of channels: (i) a so-called potassium channel, geometrically large enough to pass a hydrated  $K^+$  ion, but too small to pass a hydrated  $Ca^{++}$  ion; and (ii) a so-called sodium-calcium channel, geometrically large enough to pass with some ease hydrated  $Na^+$  and  $K^+$  ions and with some difficulty hydrated  $Ca^{++}$  ions. We shall assume that all cations pass through these two types of channel. We shall also assume that no anions pass through these channels, possibly because of either a slight negative charge on the inside of the channel<sup>1</sup> or a charge distribution with prominent negative extremals but no net charge.

Third, we conceive of a hydrated ion as a core particle of radius  $\overset{\circ}{\rho}$  surrounded by a dielectrophoretically bound shell of water molecules that exchange rapidly with the free water molecules adjacent to the hydrated ion. The hydrated ion will have an effective radius  $\overset{\circ}{b}$  as it floats freely in solution, and an effective radius  $\overset{\circ}{r}$  when it is in collision with a counterion, channel wall or other nonsolvent entity.  $\overset{\circ}{\rho}$  will be arbitrarily taken to be equal to the ion's radius in simple crystalline compounds; for example,<sup>2</sup>  $\overset{\circ}{\rho}_{Li} = 0.60 \text{ \AA}$ ,  $\overset{\circ}{\rho}_{Na} = 0.95 \text{ \AA}$ ,  $\overset{\circ}{\rho}_{K} = 1.33 \text{ \AA}$ ,  $\overset{\circ}{\rho}_{Rb} = 1.48 \text{ \AA}$ ,  $\overset{\circ}{\rho}_{Cs} = 1.69 \text{ \AA}$ ,  $\overset{\circ}{\rho}_{Mg} = 0.65 \text{ \AA}$ ,  $\overset{\circ}{\rho}_{Ca} = 0.99 \text{ \AA}$ ,  $\overset{\circ}{\rho}_{Ba} = 1.35 \text{ \AA}$ , and  $\overset{\circ}{\rho}_{La} = 1.15 \text{ \AA}$ . Since the oxygen atom of the dipolar water molecule tends to be strongly negative whereas the positive portion of the dipole is more distributed, we shall assume that cations are much more strongly hydrated than anions that display relatively little hydration. We speculate, therefore, that the  $\overset{\circ}{r}$  of a number of cations can be derived by subtracting the  $\overset{\circ}{\rho}$  of suitable anions from values of  $\overset{\circ}{a}$ , the distance of closest approach of cation and anion in free solution. Although in theory derivable from a number of different measurements,  $\overset{\circ}{a}$  is basically not a well-understood quantity. By taking a consensus of  $\overset{\circ}{a}$  values as determined by several different methods,<sup>3</sup> however, one can state roughly that  $\overset{\circ}{r}_{Li} = 2.8 \text{ \AA}$ ,  $\overset{\circ}{r}_{Na} = 2.4 \text{ \AA}$ ,  $\overset{\circ}{r}_{K} = 1.7 \text{ \AA}$ ,  $\overset{\circ}{r}_{Rb} = 1.7 \text{ \AA}$ ,  $\overset{\circ}{r}_{Mg} = 3.2 \text{ \AA}$ ,  $\overset{\circ}{r}_{Ca} = 2.8 \text{ \AA}$ ,  $\overset{\circ}{r}_{Ba} = 2.7 \text{ \AA}$ , and  $\overset{\circ}{r}_{La} = 3.1 \text{ \AA}$ . It may sometimes happen that ions of different elements will be clearly distinguishable at close quarters in one or more ways related to their electrical properties:

- (i) Their  $\overset{\circ}{r}$  may differ. At closest approach the smaller ion will, for a given net

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charge, apply the greater electric field to the approached entity.

(ii) Those ions that are most highly hydrated [ $(\bar{r} - \bar{p})$  greatest] will show the smallest rms variation of electric field from point to point over their effective surface. That is, if one chooses a point on an imaginary sphere close to the ion and measures the temporal fluctuation of the electric field there, it will on the average be less than or of different frequency spectrum than that detected at a comparable point near a less well hydrated ion.

(iii) The most probable electric-field distribution about a poorly hydrated ion will have larger lobes than that about a well-hydrated ion. In all three of these ways it should be possible to distinguish calcium, sodium, and potassium ions from one another; it would not be too surprising if they behaved differently in a channel.

Fourth, we assume that the electric field resulting from the transmembrane potential and the presence of ions in channels, plus that resulting from any ionization of the membrane protein, will exert a profound organizing effect on the membrane ultrastructure and that this will be especially noticeable in the lipid layers.

Fifth, we assume that a cation in a channel will be present in hydrated form with an effective radius nearer to  $\bar{r}$  than to the others defined.

We shall now present our model. Consider, first, a sodium-calcium channel. Initially, calcium, sodium, and potassium ions can enter. We shall assume that  $K^+$ , because of its electrical properties, will not interact with the channel walls in such a way as to become strongly bound to them; it may attach, but it will be easily displaced by  $Na^+$  or  $Ca^{++}$ . We assume that  $Na^+$ , by virtue of its somewhat different electrical properties, will bind more strongly but will be dislodged with slight difficulty by  $Na^+$  or with ease by  $Ca^{++}$ , but rarely if ever by  $K^+$ . As a result of its relatively omnidirectional electric field, its size, and its greater charge,  $Ca^{++}$  will be assumed to lock onto the channel walls, block the channel, and, in unison with the transmembrane potential, strongly organize its neighborhood to the point where  $K^+$  cannot dislodge it, and, normally,  $Na^+$  can do so very infrequently. If it is assumed provisionally that sodium ions cannot readily pass the potassium channel, this locking of the sodium-calcium channel by  $Ca^{++}$  accounts for the membrane's low permeability to sodium. If a sudden depolarization is applied to the membrane, however, the membrane ultrastructure may, temporarily, be so disrupted that a sodium ion will with relative ease be able to "unlock" the blocking calcium ion and "tumble" it down the channel into the axoplasm. This sodium ion will then take the calcium's place in the channel. In part as a result of the temporary disorganization of the ultrastructure and in part as a result of the sodium's normal weaker binding, another sodium ion will then easily be able to unlock the first and tumble it into the axoplasm. A multiplication of this effect results in the rising phase of the action potential. It is assumed that  $K^+$ , because of its different electrical structure, will still not be able to function as a "key," to unlock the blocking ion and tumble it into

the axoplasm. A channel will permit an ion to lock into it and block again only when the ultrastructure has had time to effect a partial reorganization and fresh calcium has flowed in from the external medium. This model accounts for the normally observed<sup>4</sup> time course of the sodium conductance.

Next, let us consider a potassium channel. Initially we shall assume that either  $\text{Na}^+$  cannot, because of its geometric dimensions, enter it or that  $\text{Na}^+$  cannot, because of its electrical configuration and that of the channel walls, bind firmly enough to the walls to block the channel; we also assume that  $\text{Na}^+$ , should it be capable of intruding into a potassium channel, will be prevented by virtue of its electrical configuration from unlocking any ions that may be blocking the channel. We assume that a  $\text{K}^+$  ion can lock onto the channel walls, but that it can be easily unlocked and replaced in the channel by another  $\text{K}^+$  ion. We envision serious blocking of a potassium channel to be the consequence of the attachment, in part Coulombic but also strongly dielectrophoretic, of a calcium ion to the outer orifice of the channel. We assume that this  $\text{Ca}^{++}$  can be unlocked and tumbled into the surrounding medium by  $\text{K}^+$  at any time, but that the likelihood of its being so removed is greater (i) when the membrane is partially depolarized so that the electric field trying to pull the  $\text{Ca}^{++}$  through the channel is less; (ii) when a sudden depolarization has occurred so that the local ultrastructure is disturbed, the blocking ion less firmly bound and more easily unlocked; and (iii) when the electrochemical potential gradient of the potassium ions is strongly outward so that more potassium ions, that is, more "keys," will be presented to the locking ion per unit time. Of course, as the ease of unlocking a firmly bound calcium ion rises, that of unlocking a loosely bound potassium ion will also. This model will account for the normally observed<sup>4</sup> time course of the potassium conductance during an action potential.

Now we wish to make a few predictions.

PREDICTION 1:  $\text{Li}^+$ , having an  $\bar{r}$  similar to that of  $\text{Na}^+$  and being well hydrated, should function in sodiumlike fashion.  $\text{Rb}^+$  and  $\text{Cs}^+$ , being poorly hydrated and with an  $\bar{r}$  similar to that of  $\text{K}^+$ , should function somewhat as  $\text{K}^+$ . These are classically observed phenomena.

PREDICTION 2: The potassium concentrations and fluxes will not directly affect the sodium fluxes and vice versa, and it seems unlikely that the inwardly directed fluxes directly affect the outward fluxes. This is a consequence of the locking and unlocking hypotheses. Experimental evidence for the first point has been presented by Hodgkin, Huxley, Keynes, and Frankenhaeuser, and their school, and most recently by Mullin<sup>5</sup>; that for the second seems less favorable.

PREDICTION 3: A sufficiently slow rise of depolarizing current should occasion no action potential, since the membrane ultrastructure will have ample time to adjust to potential changes and will not be suddenly disrupted. This is the well-known einschleichen phenomenon. Slow depolarization by perfusion with low  $\text{K}^+$  solutions should likewise

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occasion no action potential; this has been observed by Narahashi.<sup>6</sup>

PREDICTION 4: As a result of the assumptions on the cation channels, calcium will display a marked influx only in conjunction with an influx of sodium (or sodiumlike) ions. Convincing evidence of this has been given by Hodgkin and Keynes.<sup>7</sup>

PREDICTION 5: A lowering of the external calcium concentration should decrease the rate at which the sodium conductance falls in the wake of a depolarization. This was observed by Frankenhaeuser and Hodgkin.<sup>8</sup>

Finally, we shall present a conjecture.  $\text{La}^{+++}$  has an  $r^{\circ}$  comparable to that of  $\text{Ca}^{++}$ ; again like calcium it is well hydrated. Therefore, it should fit the sodium-calcium channel and lock it. Its greater charge, however, should result in an in-channel dielectrophoretic binding twice that of calcium. Thus, if lanthanum seawater is substituted for normal calcium seawater as a bathing solution for the axon, one would expect a nerve block that will be only slowly reversible upon return of the axon to a bath of normal calcium seawater. The lanthanum should also radically increase the rise time of the potassium conductance by virtue of its stronger binding to the mouth of the potassium channel. We now know this to be so, having done the experiments with Dr. John Moore and Dr. M. Takata at Duke University.

We recognize that our model possesses none of the mathematical elegance and rigor that have come to characterize membrane theory; we failed to use the thermodynamics of irreversible and nonequilibrium processes, since we were unable to see how to apply them to so complex a structure as our membrane. There are no equations in this work, since we were at a loss to formulate meaningful ones. Neither can we assert that our model of membrane action possesses any necessary correlation with the actual mechanism: we don't know. We claim for our model only its simplicity of concept and application and its unrivalled propensity for giving correct predictions.

J. Y. Lettvin, W. F. Pickard

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## D. NEW METHOD FOR TESTING CAMERAS AND LENSES

In recent years spectacular improvements have been made in the performance of wide-aperture photographic objectives, and often the quality of a photograph is governed more by the focussing capabilities of the associated camera mechanism than by the inherent resolution limits of the lens. In particular, one soon discovers that the attenuated image on the ground glass of the reflex camera is poorly suited for rapid and accurate focussing in dim-light situations; if, on the other hand, one uses a range-finder camera, there is the possibility of mechanical inaccuracy of the mechanism. In our experiments with wide-aperture lenses, we have been particularly beset with these limitations and accordingly looked for methods of testing of our camera system which would enable more accurate focal settings than could be achieved by trial-and-error methods.

In Quarterly Progress Report No. 67 (pages 197-204) we described a photographic method for the measurement and testing of the focussing properties of the human eye. Since that method made use of the retinal reflex, we thought that, if it could be adapted to camera tests, it would be quite useful to the photographer who desires to test the focus of his camera in a realistic situation, but who wishes neither to disassemble its mechanisms for optical bench tests, nor to shoot endless rolls of films of elaborately positioned test charts. Experiments have since shown that the previous method is not adaptable to the measurement of the focus of wide-aperture lens systems. Accordingly, we have developed a new method specifically adapted to this purpose.

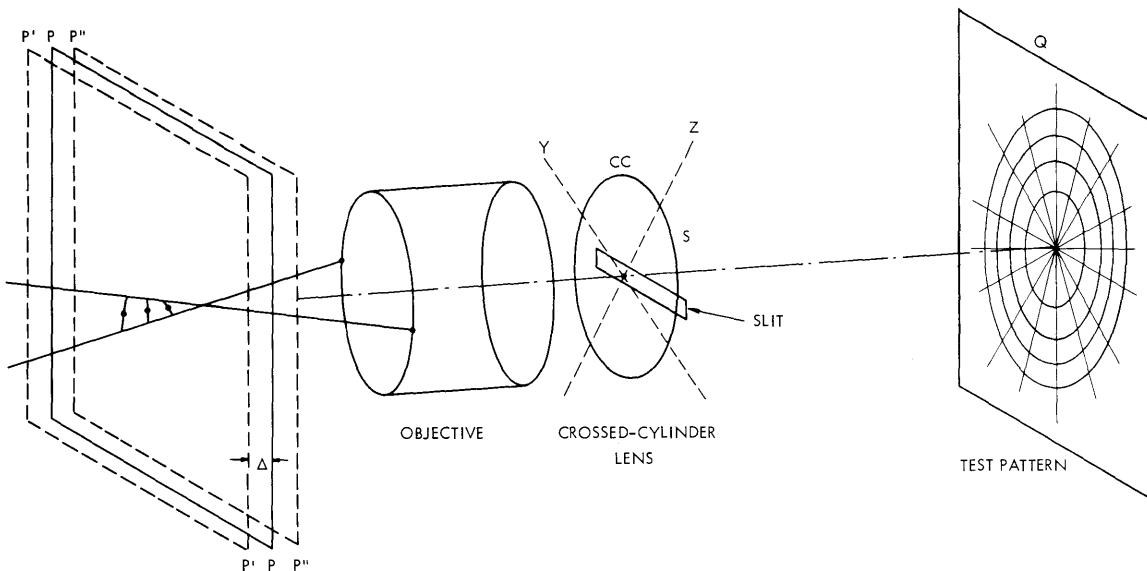


Fig. XVII-2. Arrangement of crossed-cylinder lens and slit for testing the focus of a lens.

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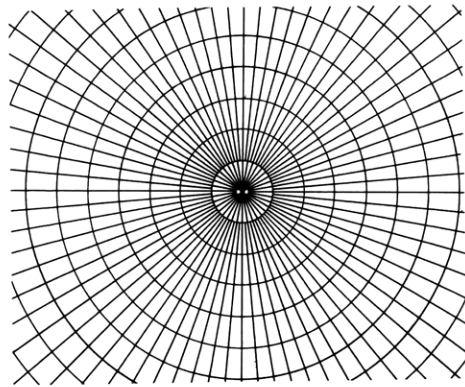
This method makes use of the crossed-cylinder lens, of importance in ophthalmic diagnosis.<sup>1</sup> By this term is meant a spherical-cylinder lens having equal positive and negative refractive powers about two perpendicular axes. When such a lens is placed in front of a perfect photographic objective the combination will exhibit a strong astigmatism. In Fig. XVII-2 we show this combination of lenses; the object plane Q is assumed to be focussed on the image plane P by the objective lens; the inclusion of the supplementary lens splits the focal plane into P' and P". The axes Y and Z of the crossed-cylinder lens have been chosen to lie at 45° to the horizontal. We may note that the action of the crossed-cylinder lens is to defocus equally all lines that might be drawn in the object plane Q because the image of a point source in Q is a circular blur spot in P. By a simple argument we can show that this blur circle is, in fact, an image in miniature of the aperture of the objective lens rotated 90°. Motion of the plane of film from P towards P' transforms this circular blur spot into an ellipse, then into a line at P', and again, with further displacements, into an ellipse.

With these preliminary observations we are in a position to disclose the method: In front of the crossed-cylinder lens is placed a horizontal slit, S, which is at 45° to axes Y and Z. This slit aperture transforms the blur image of a point source in Q to a line segment in P. This line-segment image must necessarily coincide with the previous line-segment images in P' and P", and thus with shift of the film plane must rotate through the vertical at P. In general, the angle of inclination will be given by  $\theta = \arctan\left(\frac{d}{\Delta}\right)$ , where  $\Delta$  is the splitting caused by the crossed-cylinder lens, and d is the displacement of the film plane.

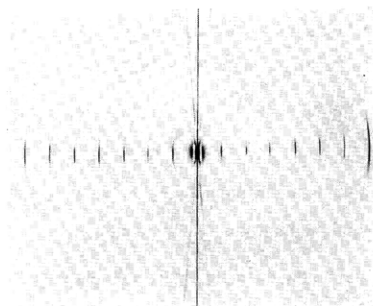
We next consider the imaging of a pencil of lines radiating from a central point in the object space, Q. We assume that the location of the film plane is uncertain with respect to P and P'. The image of that line in the object space whose line-segment images are similarly aligned will appear darkest and most sharply delineated. The angle of the best-imaged line(s) will thus critically reflect the exact location of the film plane vis-à-vis the plane P. Thus, we have a qualitative and quantitative test of focus, the sensitivity of which is inversely proportional to the power of the crossed-cylinder lens. Since the alignment of the slit and crossed-cylinder lens is of importance, we have constructed them as one unit. It should be noted that this supplementary lens combination exhibits a circular asymmetry, for which we have adopted the convention that the image shall rotate clockwise on the ground glass or print when the camera is made myopic. To preclude errors in sign, the supplementary lens combination is supplied with threads that allow attachment to the camera lens in one way. A level may also be attached to the supplementary lens combination to further facilitate alignment with respect to the chart.

### 1. Experimental Procedures

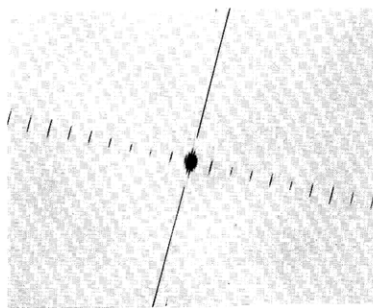
For our first experiments, we have used uncut ophthalmic lenses of powers  $\pm 1/8$ ,  $\pm 1/4$ , and  $\pm 1/2$  diopter, together with a special polar coordinate chart having all radial



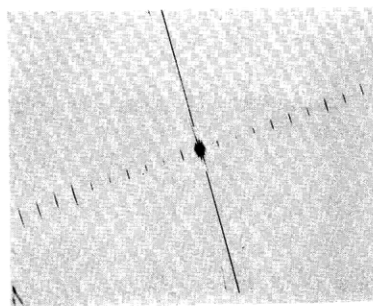
**Fig. XVII-3.** Polar coordinate chart having all radial lines of equal thickness.



(a)



(b)



(c)

**Fig. XVII-4.**

Appearance of chart when photographed through the strong supplementary lens attachment with (a) camera focussed on chart; (b) camera focussed in front of chart; and (c) camera focussed beyond plane of chart.

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and circumferential lines of equal thickness (see Fig. XVII-3). Tests were conducted for the most part with a 4 inch  $\times$  5 inch press camera with a variety of lenses. Kodak Contrast Process Panchromatic was developed to a  $\gamma$  of 4 in D-11.

In Fig. XVII-4a we show the appearance of the polar coordinate chart when photographed through a lens of very good quality, together with the  $\pm 1/2$  diopter supplementary lens. (The camera was first accurately focussed without the supplementary lens in position.) In Fig. XVII-4b we show the result of focussing the camera on a plane in front of the chart; in Fig. XVII-4c we show the result of focussing the camera behind the plane of the chart.

It will be appreciated that this method provides an improved means of focussing by trial exposures those cameras in which the film plane is inaccessible for direct observation. Each trial exposure indicates the magnitude and direction of defocus. The magnitude of the focal error is given by the rotation of the cruciformlike image of the chart and the strength of the supplementary lens combination; measured in diopters, this focal error is independent of the distance from the camera to the chart. This point is important in that it enables us to test the performance of a range finder-coupled camera over a very wide portion of its focussing range by using the same supplementary lens and chart; only the point at infinity is inaccessible to this measurement. In Fig. XVII-5 we show the results of such a test of a poorly mated camera-lens combination. The focal error is evidently due to differences in the range finder mechanisms of the Nikon and Contax cameras.

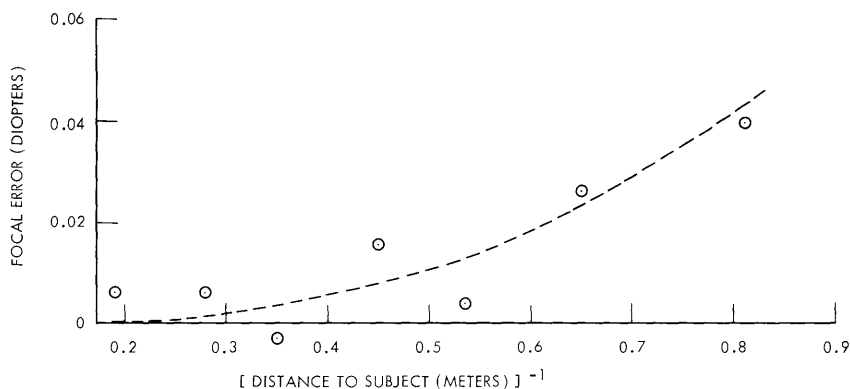


Fig. XVII-5. Focussing errors of a range finder camera. (Nikon SP camera and Contax lens.)

### 2. Test of Alignment of Lens to Film Plane

In tests of a miniature camera, it generally suffices to determine the accuracy of focus of the image at the center of the film plane; one may assume that the machining of the lens mounts is sufficiently precise to ensure parallelism of motion of the lens



and perpendicularity of the lens axis with respect to the film plane. With large-format cameras this assumption is optimistic, and we may note that our method given here permits a simple diagnosis of the nature and extent of such misalignments. Note that we assume that the test chart has in fact been accurately positioned parallel to the plane of the film, and/or that it is sufficiently far away that a small misalignment will not matter. In Fig. XVII-6 we show the pattern that results from an intentional approximately  $5^\circ$

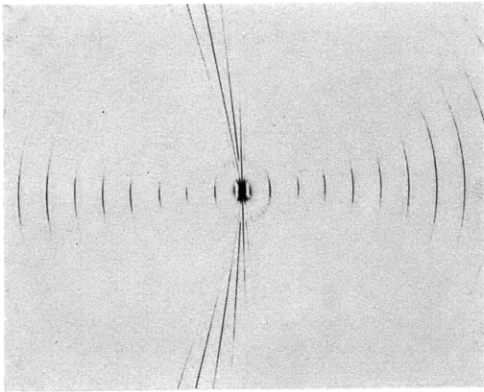


Fig. XVII-6. Results of  $5^\circ$  vertical misalignment of axis of lens with respect to film plane.

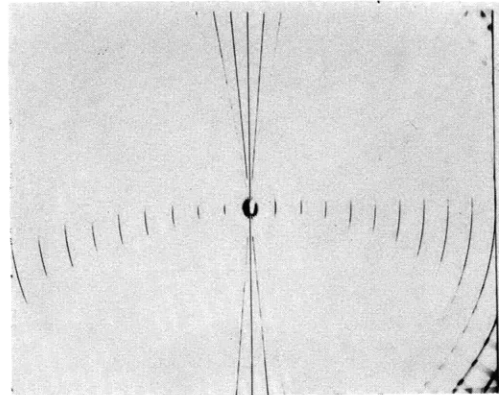


Fig. XVII-7. Results of simulated horizontal misalignment of axis of lens with respect to film plane.

vertical misalignment of the lens axis. In Fig. XVII-7 we have simulated the case of an equivalent horizontal misalignment. (Since the motions of our press camera did not permit a horizontal swivelling of the lens, the chart was tipped with respect to the camera for this exposure.) It should be noted that in each case the test indicates both magnitude and sign of the error.

### 3. Testing of Lens Objective

The result of photographing a polar coordinate pattern through the supplementary lens system described here is to render in sharp focus only those line segments that are similarly oriented with respect to the slit; thus we explain the cruciform patterns of Fig. XVII-4. It should be noted that the horizontal arm of the cross consists of images of tangential line segments, and that the vertical arm consists of images of radial line segments. If the lens objective possesses an astigmatism, the surfaces of sharpest focus for radial and tangential line segments will differ and the result will be a distortion of the cross, since at least one of the two arms will be curved. Should the radial and tangential focal surfaces coincide, but at the same time exhibit curvature, we will

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have a spiral pattern of distortion of the cross corresponding to curvature of field.

In order to permit satisfactory reproduction of lens test results presented here, it was necessary to use a chart with lines not too finely drawn, a supplementary lens of considerable power, together with an objective of (by modern standards) inferior quality. We were able to obtain several examples of lenses having various representative image defects in generous measure, from a set of antique lenses acquired by the author (Fig. XVII-8). These lenses were all of the two-group, four-element modified Petzval



Fig. XVII-8. Selection of antique lenses that we have tested.

portrait type and were characterized by good definition, low spherical aberration and coma, together with large astigmatism and/or field curvature.

In Fig. XVII-9 we show the results of our test of one such lens that exhibits a large and uniform field curvature. In Fig. XVII-10 we show a similar test of a lens that exhibits strong astigmatism, that is, the curvature of the tangential field is almost zero whereas the curvature of the radial field is very pronounced. In Fig. XVII-11 we show a test of a more modern lens, which exhibits reversed curvatures of both the focal surfaces, that is, astigmatism without field curvature.

In these tests we purposely selected a strong power of supplementary lens, to complement the rather large focal surface curvatures of these primitive lenses. It is, however, possible, merely by weakening the power of the supplementary crossed-cylinder lens, to increase the sensitivity so as to permit the testing of arbitrarily high-quality

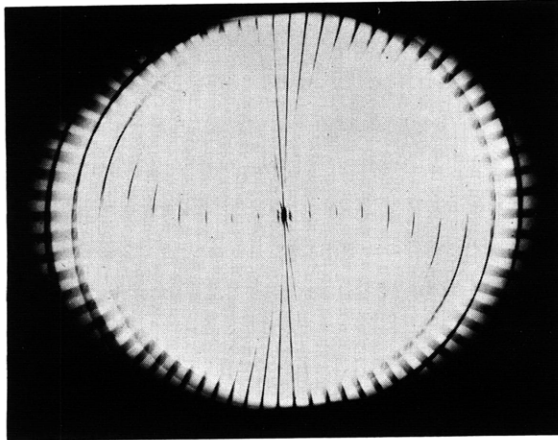


Fig. XVII-9.  
Test of antique lens having pro-  
nounced curvature of field.

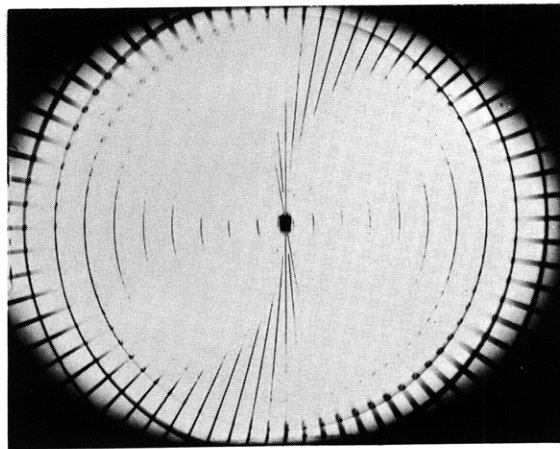
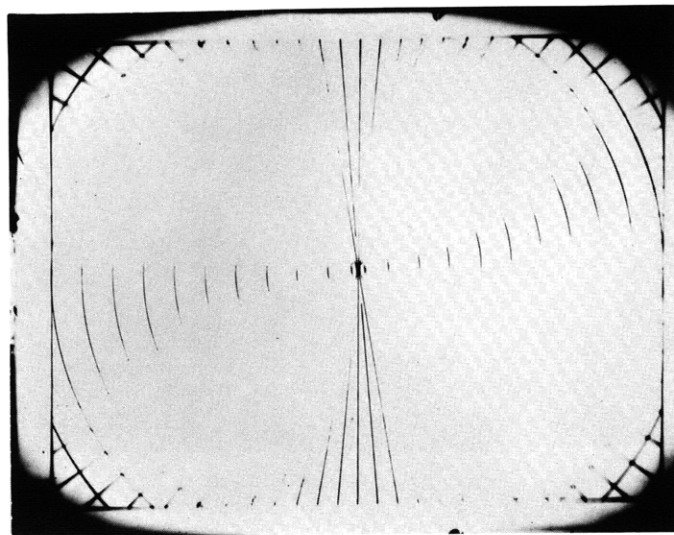


Fig. XVII-10. Test of antique lens exhibiting strong  
curvature of radial field only.

Fig. XVII-11.  
Test of modern lens showing  
astigmatism. Radial and tan-  
gential focal surfaces curved  
in opposite directions.



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lenses – tests at full aperture with a set of 35-mm lens objectives of the highest available quality have not failed to reveal noticeable curvatures of the focal surfaces over the 24 mm × 36 mm field. The results of these tests would, however, be very difficult to reproduce here. Another factor governing our choice is the fact that modern camera lenses tend to be much more highly corrected than the lenses shown here, and only infrequently does one encounter an example of the simpler aberrations, as for example the field curvature of Fig. XVII-9.

B. Howland

References

1. I. M. Borish, Clinical Refraction (The Professional Press, Inc., Chicago, 1954).