XXVII. NEUROLOGY*

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RESEARCH OBJECTIVES

Our group is applying communications-engineering concepts, control theory, and servo-analysis techniques to neurological and biological systems. The research spans a field that includes human control mechanisms, mathematical methods for the analysis of nonlinear systems, man-machine systems analysis, the neurophysiology of simple invertebrate receptors, the application of adaptive pattern-recognition techniques for the diagnosis of clinical electrocardiograms, analog and digital computers in data-handling and reduction, computer simulation of biological control systems, and clinical hospital studies utilizing remote on-line digital computer techniques. A study of the interactions between interlocking systems is also being developed in order to learn about the laws of these interactions and to dissect the system through study of various partially overlapping and partially independent pathways.

L. Stark

A. REMOTE, ON-LINE, REAL-TIME COMPUTER SYSTEM FOR BIOLOGICAL EXPERIMENTATION

If the complex details of biological and neurological control systems are to be quantized the requirements for research must include development of more precisely controlled and accurate complex stimulus-response experiments, rapid analysis of characteristically noisy records for the detection of finely detailed responses, and intensive correlation of such experiments with adequate theoretical modeling. In the Neurology Section of the Electronic Systems Laboratory, M.I.T., a digital computer system operating in an on-line, real-time mode has been developed to facilitate these objectives.[1,2] It has been designed to control remote complex multistimulus, multiresponse experiments, transmit experimental data to the computer, rapidly digitize and analyze the pertinent information, and return the results to the experimental sites for real-time display in oscilloscopic, graphical or teletyped form.

The system consists essentially of a transistorized, single-address, general-purpose digital computer (G.E. 225). This machine has a magnetic core memory consisting of 8192 individually addressible 21-bit words, with an access time of 18 μsec. The input devices are, an input console flexowriter, a teletype (8-bit code), an analog-to-digital

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converter with an 18-kc maximum transfer rate (10-bit accuracy) that accepts analog signals in the 0-10 volt range, and a 400 card per minute photoelectric card reader. There are two 250 bits/inch tape handlers with a 55-kc maximum transfer rate. The output devices are a 10 character per second output console typewriter, a 100 card per minute card punch, and a 10-bit digital-to-analog converter that provides a 0-10 volt output. The results of the digital-to-analog conversion may be directly plotted either by a pen recorder, an X-Y recorder or an oscilloscope.

In the laboratory a variety of experimental sites have been connected to the analog-to-digital and digital-to-analog converters of the computer by DC paired telephone lines. This arrangement permits the experimenter to gather data in his own vicinity and to have the computer process it and return to him an analysis displayed in real time. The investigator maintains computer control of the experimental procedure in two ways. (i) A remote G. E. 225 control panel, consisting of program-sensed switches and accumulator register indicator lights, can be located at the experimental site. This panel enables the investigator to run a computer controlled experiment without the necessity of traveling between the experimental site and the computer room. The lights enable him to tell his location in a program at any time so that appropriate action may be taken. (ii) A teletype monitoring system may be used. This provides for remotely controlling the key steps of an experimental procedure, such as computer function generation, data editing, and the real-time analysis and display of results. These sections of an experimental program can be called by teletype from the computer's magnetic tape system into its memory to be executed at the command of the experimenter.

The computer methods of real-time experimental analysis include programs for (a) generation of comb spectra input functions for the gain and phase-shift analysis of a biological system's response; (b) accepting on-line response data evoked by repetitive excitation and automatically computing the average response as an analog-voltage output; (c) Fourier analysis; (d) a variety of statistical analyses (correlation functions, power spectra, etc.); (e) impulse response studies and additional special programs that have been prepared for the acceptance and analysis of data to include pulse interval analysis, delay-line simulation, calculation of Wiener kernels for nonlinear studies, amplitude probability distributions, and various other parametric and nonparametric tests.

Before the organization of this biological data processing system, some less sophisticated experiments were made and they were most discouraging. This was due to extreme variation between single records, large amounts of noise or uncorrelated responses, variable sensitivity to different components of the stimuli, and evidence of complex multi-frequency responses. The use of this system has resolved these data analysis problems and many of the required stimulus accuracy problems. It has further revealed the presence of accurately definable complex responses and has provided us with detailed quantitative information on a variety of biological and neurological control systems. In

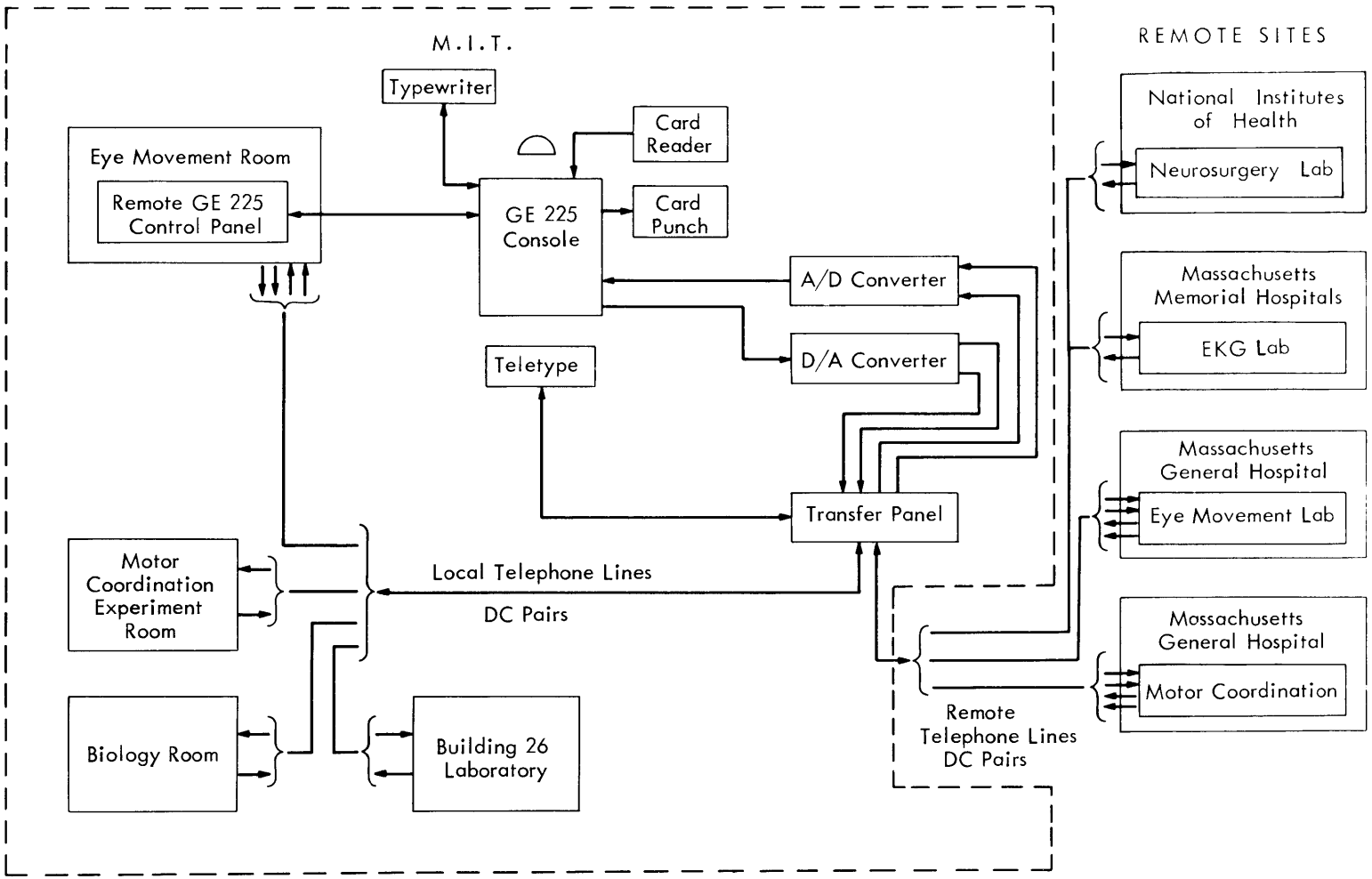


Fig. XXVII-1. Remote hospital diagnostic laboratories connected by telephone lines to computer at the Massachusetts Institute of Technology.

particular, the on-line, real-time digital computer control and analysis of experiments has been applied in studies of the pupil, lens, eye movement, hand motor-coordination and eye-hand tracking control system, and also for computer diagnosis of clinical electrocardiograms by using adaptive matched-filter pattern-recognition techniques.

New dimensions have been given, in particular, to four investigations with the linking of this computer system by DC paired telephone lines to remote hospital diagnostic laboratories for on-line, real-time studies (Fig. XXVII-1). Each of these will be described.

1. Neurosurgical Laboratories of the Massachusetts General Hospital, in Boston. Here, eye goggles with eye-movement reflection photocells for measuring the horizontal position of gaze for one or both eyes are used in diagnostic studies.[3] The connection to

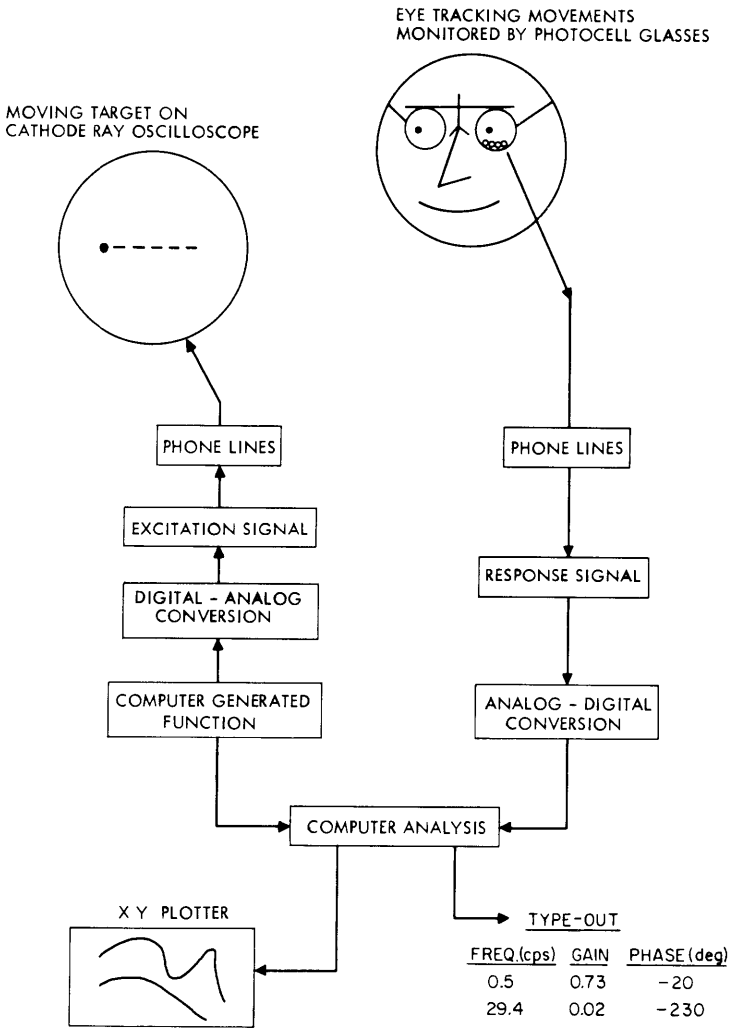


Fig. XXVII-2. Outline of system for remote testing of patient's eye-movement control system.

the computer allows the investigator to conduct a computer controlled experiment, and to receive a real-time analysis and display of the experimental results. Figure XXVII-2 is a diagram outline of the system for remote testing of patients. At the hospital the patient wearing the photocell goggles watches a moving spot on the oscilloscope. The computer drives the spot, measures the angular deflection of the patient's eyes, analyzes the data at each frequency of interest, and then plots or types the analysis, and makes it available to the hospital within a few minutes.

2. Electrocardiography Laboratory of the Massachusetts Memorial Hospitals for real-time computer diagnosis of clinical electrocardiograms (Fig. XXVII-3). These electrocardiograms are transmitted to the computer system where temporal arrhythmia analysis and adaptive matched-filter pattern-recognition techniques are applied for classification and automatic diagnosis.[4] The diagnosis is then returned to the hospital within five minutes. The effect of experimental variation on the pattern classification process is being studied in order to simulate more closely human interpretation of the electrocardiogram.

3. Neurology Laboratory of the Massachusetts General Hospital for engineering studies of the motor-coordination system of the hand.[5] In these studies of hand motor responses, with and without dependence on eye orientation, the computer processes the data with the aim of discovering patterns of neuro-muscular abnormality.

An example of the capability of the system can be seen in a brief outline of a hand-movement study. Here, the requirement for dynamic analysis of a complex unpredictable input is necessary in order to distinguish between behavior attributable to the "neurological system" and to the probable brain prediction apparatus. To meet this need, to reduce hidden errors in analyzing filtered data, and to permit a shorter experiment (and thus less dependence on assumptions about time and variance) the on-line, real-time computer system is used. Briefly, the experimental procedure runs as follows. (a) The function generator capacity of the computer produces a sum of as many as 20 sinusoids, specified as to frequency and amplitude. These are then converted to an analog voltage and fed to a mechanical input to the subject, whose mechanical response, measured as an electrical voltage, is reduced to digital form and stored in the computer in real time. (b) In the analysis routine 25 seconds of tracking are measured. If this seems to indicate a reasonable experimental result, the analysis program then proceeds to determine the alpha and beta coefficients, frequency by frequency. A Bode plot is made, showing the response of the subject to the input. In the conduct of such an analysis it is apparent that this method is sensitive to quantitative differences in the organization and function of the neurological control system for hand movement.

4. Neurosurgical Section of the National Institutes of Health, Bethesda, Maryland. Here, an experimental station has been connected to the computer at M. I. T. for the remote analysis of the dynamics of neurophysiological disease processes. These studies

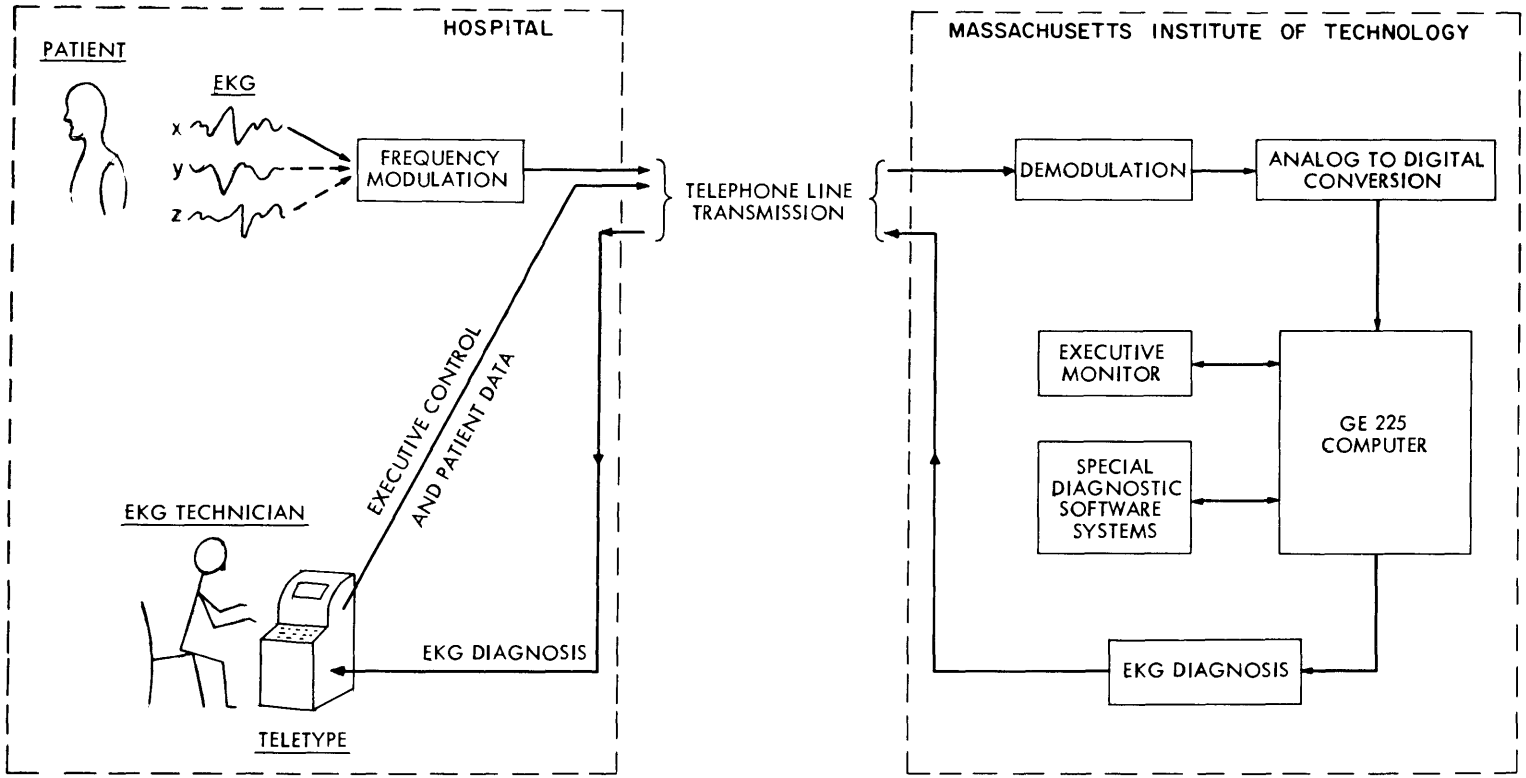


Fig. XXVII-3. Remote electrocardiographic diagnostic system.

are particularly oriented toward gaining insight into the effect of surgical intervention of the progression of disease states that are marked by instability of the muscular coordination control system.

The remote teletype control of the computer at M. I. T. by hospital research workers is a most important feature of this diagnostic system. It provides them with a capability for remotely controlling the key steps of procedures, such as input function generation by the computer, data editing and analysis, and real-time display of the results of the analysis at the hospital. The investigators call these various sections of the diagnostic program by teletype from the computer's magnetic tape system into its memory where they can then be executed at their command.

J. F. Dickson, L. Stark

References

1. L. Stark, R. Payne, and Y. Okabe, OnLine digital computer for measurement of a neurological control system, Communs. Assoc. Computing Machinery 5, 567 (1962).

2. L. Stark, P. Willis, A. Sandberg, S. Stanten, and J. Dickson, in Computers in Biology and Medicine (New York Academy of Medicine, New York, 1964).

3. L. R. Young and L. Stark, A discrete model for eye tracking movements, IEEE Trans. on Military Electronics, Vol. MIL-7, No. 2, p. 113, 1963.

4. L. Stark, M. Okajima, and G. Whipple, Computer pattern recognition techniques: Electrocardiographic diagnosis, Communs. Assoc. Computing Machinery 5, 527 (1962).

5. L. Stark, M. Iida, and P. A. Willis, Dynamic characteristics of the motor coordination system in man, Biophys. J. 1, 279 (1961).

B. ACTIVE DEVELOPMENT IN RESPONSE TO MECHANICAL DEFORMATION IN A MULTI-UNIT SMOOTH MUSCLE

Mechanical deformation of smooth muscle is generally considered as a physiological stimulus for the development of active tension[1,2] and the active tension response to stretch has been demonstrated by several investigators (Bozler,[2] Burnstock and Prosser,[3] and Sparks[4]) using a variety of smooth muscles. The term "active tension response" means that the contractile mechanism is actuated. The term "passive tension response" implies that the time course of tension exhibited by the muscle after stretch reflects only physical viscoelastic readjustments, that is, there is no chemical reaction among the contractile proteins.

Histological and physiological comparison of mammalian smooth muscles has resulted in the division of smooth muscle into two classes, the unitary muscles and the multi-unit muscles.[5] The unitary class is by far the more extensive, and includes the muscles of the visceral organs (intestine, ureter, uterus, etc.) and the muscles of the smaller vascular vessels. The multi-unit class consists of muscles of the iris, ciliary body, nictitating membrane, pilomotors, and the larger blood vessels. The intercellular

spacing of the unitary muscles is an order of magnitude less than that of the multi-unit type, and the cells of the unitary muscles have processes that appear to bridge the intercellular space.[6] The multi-unit muscles have a more extensive innervation than the unitary muscles; groups of fibers of the multi-unit muscles have an innervation pattern that indicates that this type of muscle functions with a number of relatively independent units, similar to the motor units of skeletal muscle. The unitary muscle responds as a single unit in a manner somewhat similar to cardiac muscle. Multi-unit muscle is believed to be under more direct neural control than unitary muscle, in which the innervation sets the environment in which directs mechanical and chemical stimulation acts. In unitary muscle, depolarization spreads from cell to cell with the result that unitary muscle exhibits a much greater electrical conduction than multi-unit muscle[7] does. The mechanism accounting for the spread of depolarization is not fully understood; electrical transmission has been strongly considered, but other mechanisms such as release of chemical transmitters may be present.

The mechanisms associated with the development of active tension in smooth muscle as a result of mechanical stretch are poorly understood, but a description of the sequential events can be given.[5] The mechanical deformation results in a slow, graded, membrane potential in an excitable zone. When the membrane potential is in the excitable zone, spike activity occurs, and the spike frequency is related to the degree of depolarization inside this zone. The spike activity is coupled to the contractile system and results in activation of the contractile mechanism. The mechanical deformation is thought to condition the muscle fibers by bringing them into a sufficiently excitable state for conduction to take place.

Multi-unit smooth muscles do not exhibit an active response to mechanical stretch.[5,8,9] The work of Burnstock and Prosser[3] indicates that vascular multi-unit muscle and nictitating membrane muscle exhibit only a passive tension response to stretch. This report, however, indicates that at least one multi-unit muscle, the iris sphincter of the cat, exhibits active tension development in response to mechanical stretch. Thus the cat iris sphincter, although histologically a multi-unit muscle, has a physiological aspect that is associated only with the properties of unitary muscle. The only known reference on the effect of stretch on the cat iris sphincter is that of Schaeppi and Koella[10] who, in their studies of electrical and pharmacological stimulation of the cat iris, occasionally saw what might have been mechanical activation. These investigators did not undertake a study of mechanical activation in the cat, but their pharmacologic work on pig iris sphincter pointed toward a passive nature for the stretch-induced tension development.[10] Their work also indicates that the type of response to various stimuli depends in part upon the ability of the iris to maintain tone; the pig iris maintains much less tone than does either cat or bovine iris.

1. Methods

Cat iris sphincter rings were prepared by using the technique of Schaeppi and Koella, and were suspended between two platinum-electrode hooks in a nonflowing bath of O_2-saturated Tyrode solution (NaCl 0.8%, $NaHCO_3$ 0.1%, KCl 0.02%, $CaCl_2$%, 0.02%, $MgCl_2$ 0.01%, Na_2HPO_4 0.005%, glucose 0.1%) at 37°C. The width of the iris ring was approximately one-half of the width of the maximally constricted iris. One hook was attached to the core of a solenoid in order to provide quick stretches (~50 mm/sec) of adjustable magnitudes and the other hook was attached to an AC modulated, balanced, strain-gauge force transducer. The solenoid was fastened to a micromanipulator that permitted adjustment of the initial length of the iris sphincter ring. The isometric tension development was measured.

Electrical stimulation, normally consisting of pulses of 1 msec duration, was provided by a standard pulse generator, after either removing one electrode from the bath or replacing the Tyrode solution with silicone oil (Dow Medical Fluid 360).

2. Results

a. Mechanical Stimulation

Quick stretch of the isolated iris sphincter ring resulted in a tension time course (Fig. XXVII-4a) that is generally taken as characteristic of the development of

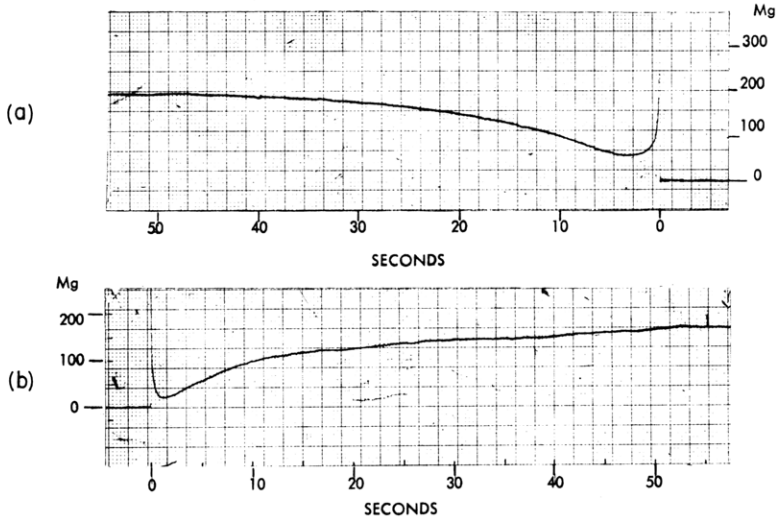


Fig. XXVII-4. (a) Active tension-time course in response to quick stretch of a cat iris sphincter ring from 15 mm to 18 mm. This active tension development is similar to those obtained by Burnstock and Prosser with unitary smooth muscle. (b) A more frequently obtained active tension-time course for cat sphincter did not exhibit a decline of tension.

active tension following mechanical stretch (Burnstock and Prosser[3] in the pig esophagus, cat intestine, etc., Sparks[4] in the human umbilical artery). Figure XXVII-4a represents the typical tension course resulting from mechanical activation in that there is a maximum in the active tension development; for the cat iris sphincter, however, a more frequently obtained response has little or no peak (Fig. XXVII-4b). Preparations exhibited reproducible active responses to stretch for up to six hours. The tension response of a dead iris (Fig. XXVII-5)

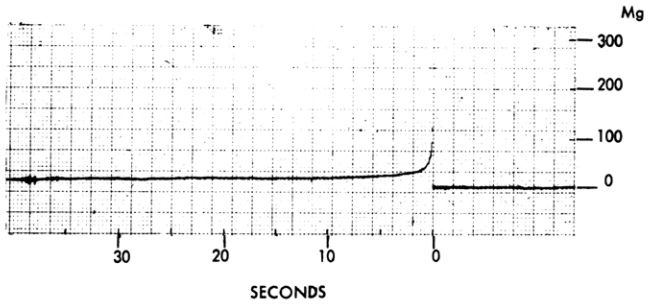


Fig. XXVII-5.

Passive tension-time course is the response to quick stretch of a dead cat iris sphincter. The response reflects the passive viscoelastic readjustments to the initial deformation. The sphincter was stretched from 12 mm to 15 mm.

reflects only the passive viscoelastic readjustments of tension after stretch. Atropine in concentrations of approximately 32 and 64 μg/ml appeared to only slightly prolong the course of active tension development. A depolarizing bathing solution of 1M KCl completely eliminated any active response to stretch, thereby indicating that the stretch effect does not act directly on the contractile mechanism but rather through alteration of the membrane activity.

Preliminary results indicate that the magnitude and rate of increase of the active response is enhanced by increased initial length and per cent stretched. These findings are in agreement with those of Burnstock and Prosser and of Sparks, and if the parallel is complete, a threshold of initial length and per cent stretched may be anticipated. Also, a threshold for rate of stretch is indicated, since slow stretch (2 mm/sec) by hand does not result in an active tension development.

b. Electrical Stimulation

Electrical stimulation, consisting of 1-msec pulses for a variety of frequencies, durations, and voltages, resulted in tension development that was not tetanic, but showed rapid fatigue or relaxation during stimulation after the initial tension rise (Fig. XXVII-6). Cessation of stimulation was followed by a pronounced post-stimulatory relaxation that was greater at lower voltages (around 4 v) and at shorter lengths (around 10 mm). Increase in the frequency of stimulation resulted in a more rapid onset and extent of the

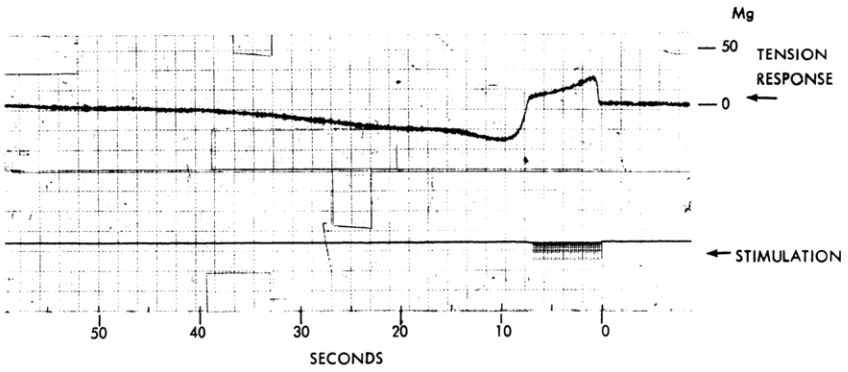


Fig. XXVII-6. Tension response to electrical stimulation of 1-msec pulses of 1.5 v at a frequency of 5 per second. The sphincter length is 9.4 mm. Relaxation during stimulation and a marked post stimulatory relaxation are clearly shown.

relaxation during stimulation. Graded twitch responses to single pulses were obtained with a threshold of approximately 0.5 volt.

c. Interaction of Mechanical and Electrical Stimulation

Of primary interest is the effect of electrical stimulation on the active response to stretch. With preparations in both the normal and atropinized (64 μg/ml) Tyrode bath, continuous electrical stimulation usually diminished or abolished the active response (Fig. XXVII-7). When electrical stimulation was presented after the active stretch response had begun, the rising course of tension was reversed and relaxation followed for the duration of the electrical stimulation (Fig. XXVII-7c). Electrical stimulation also decreased the rate of return of tension following quick release. Although the relaxing effect of electrical stimulation was preserved in the atropinized bath, the initial tension rise associated with electrical stimulation in the normal Tyrode bath was greatly reduced, in agreement with the finding of Schaeppi and Koella on the pig iris sphincter.

3. Discussion

Although the increase in tension obtained after quick stretch of the cat iris sphinter is quite typical of results with unitary smooth muscle, the frequent absence or smallness of the decay of tension after activation has presumably ceased is atypical. The persistence of the tension at the peak level is not without some parallel, for the results of Sparks on the human umbilical artery show that in many instances tension has not begun to decrease after two minutes. The continuance of the active response in the presence of a large concentration of atropine indicates that the active response is not the result

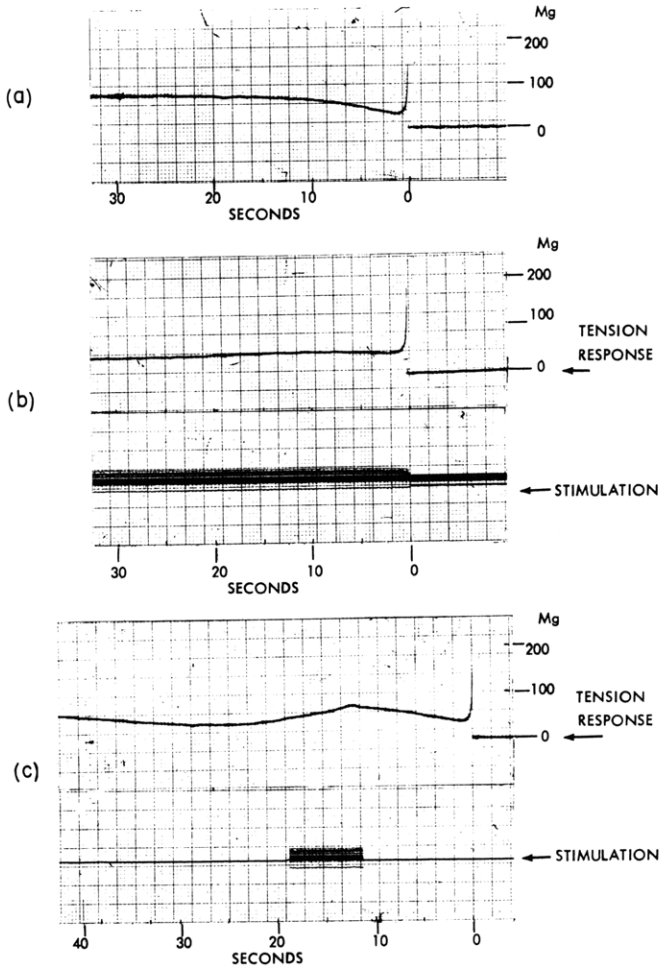


Fig. XXVII-7. (a) Active tension response to quick stretch from 7 mm to 10 mm. (b) Example of total inhibition of the active stretch response by continuous electrical stimulation (1-msec pulses, 2.8 v, 15/sec). The stretch stimuli are the same as in (a). Continuous electrical stimulation either completely or partially inhibited the active response to quick stretch. (c) Electrical stimulation during the active tension response resulted in reversal of the tension increase and subsequent relaxation. Electrical and mechanical stimulation are the same as in (b). All of these responses were obtained with the sphincter in the normal Tyrode bath.

of mechanical stimulation of the parasympathetic neuromuscular junction. The effectiveness of the atropine in blocking neuromuscular transmission is shown by the absence or reduction of tension increase during electrical stimulation since electrical stimulation of the sphincter is taken to be mediated through the neuromuscular junctions.[10] Burnstock and Prosser found that atropine had no effect on the active responses of unitary smooth muscle.

The relaxation following electrical stimulation was also observed by Schaeppi and

and Koella in the pig iris sphincter and they attributed this relaxation to excitation of adrenergic nerve fibers and release of norepinephrine. Perhaps the explanation could be extended to account for the relaxation seen during electrical stimulation. There is disagreement among investigators about whether or not there are adrenergic fibers that are inhibitory to the sphincter.[10] Since in any sphincter preparation there are some radial dilator fibers (adrenergically excited), it is difficult to determine to what extent excitation of the dilator or inhibition of the sphincter occurs. Since the mechanical effectiveness of that portion of the dilator muscle remaining in a sphincter-ring preparation must be severely limited, it is difficult to imagine that dilator excitation alone could account for the extent of the observed relaxation.

The partially inhibitory effect on the active response to stretch of continuous electrical stimulation may be another manifestation of the long term relaxing effect seen with electrical stimulation alone. Alternatively, this result might be taken as parallel to the finding that spontaneously active guinea pig taenia coli relaxes in response to quick stretch, while electrically inactive taenia coli shows an active tension response to quick stretch.[3] A similar situation exists with pig esophagus that has become spontaneously active in a bath containing 1 per cent barium chloride.[3] Excessive depolarization can result in relaxation, presumably because of disruption of synchronous firing.

It is apparent that the blanket assignment to multi-unit smooth muscle of a strictly passive response to mechanical stretch may have to be altered as a result of the present results and of confirmational findings. Also, explanations, based upon a relation between conduction ability and intercellular spacing, have been offered to account for the existence of an active response to stretch in unitary smooth muscle, but they may have to be modified. It is possible that the active response obtained with the cat iris sphincter may be a reflection of the ectodermal origin of this muscle because it may retain to some extent the ability to respond to primitive contractile stimuli although it is ordinarily under nervous control. A study of the erectores pilorum (pilomotor) might yield results similar to ours, for it is also a multi-unit smooth muscle of ectodermal origin.

J. I. Simpson, L. Stark

References

1. W. M. Bayliss, On the local reactions of the arterial wall to changes of internal pressure, J. Physiol. (London) 28, 220 (1902).

2. E. Bozler, The response of smooth muscle to stretch, Am. J. Physiol. 149, 299-301 (1947).

3. G. Burnstock and C. L. Prosser, Responses of smooth muscle to quick stretch: Relation of stretch to conduction, Am. J. Physiol. 198, 921-925 (1960a).

4. H. Sparks, Jr., The effect of quick stretch on isolated vascular smooth muscle (to appear in Circulation Research, 1964).

5. G. Burnstock, M. E. Holman, and C. L. Prosser, Electrophysiology of smooth muscle, Physiol. Rev. 43, 482-527 (1963).

6. C. L. Prosser, G. Burnstock, and J. Kahn, Conduction in smooth muscle: Comparative structional properties, Am. J. Physiol. 199, 543-552 (1960).

7. G. Burnstock and C. L. Prosser, Conduction in smooth muscles: Comparative electrical properties, Am. J. Physiol. 199, 553-559 (1960b).

8. C. L. Prosser, Conduction in nonstriated muscle, Physiol. Rev. 42, Suppl. 5, 193 (1962).

9. E. Bozler, Conduction, automaticity and tonus of visceral muscles, Experientia 4, 213-218 (1948).

10. U. Schaeppi and W. P. Koella, Reaction of isolated pig iris sphincter to electrical stimulation and acetylcholine, Am. J. Physiol. 206(2), 255-261 (1964).

C. EFFECT OF EYE MOVEMENTS ON THE VISUALLY EVOKED RESPONSE

1. Introduction

The elevation of the visual threshold associated with saccadic eye movements[1-6] has been referred to as saccadic suppression.[6] Attempts to elucidate the physiological mechanisms underlying this phenomenon would be greatly facilitated by knowledge of the physiological changes, if any, that occur in the visual system during suppression. Such information is difficult to obtain from human subjects, since the studies have to be carried out during therapeutic neurosurgical procedures. An examination of the evoked response in the EEG during saccadic suppression would be the closest contact one could obtain with the physiological mechanisms involved.

Physiological studies of oculomotor and visual mechanisms can, however, be easily carried out in an experimental animal such as the cat. Although it is not known whether saccadic suppression occurs in the cat, there is evidence that small eye movements occurring with the presentation of a test light flash result in a cortical evoked response (CER) that is smaller than the CER produced with the eyes motionless.[7] But no attempt has been made to determine the parameters of this effect, nor have the experimental conditions under which this phenomenon was seen been clearly defined. If this influence of eye movements on the CER can be shown to behave similarly to saccadic supression, any physiological mechanisms and/or anatomical structures known to be involved might, by analogy, play a role in the saccadic suppression seen in man. Thus, the experiments that we are carrying out are intended to help elucidate the physiological substrate of saccadic suppression.

2. Method

In brief, the experiment consists of obtaining average CER to flashes of light presented with the eyes motionless and comparing these to average CER obtained with flashes presented when the eyes are moving. Any change occurring in the CER can then be assumed to be due to some interaction between the oculomotor system and the visual

system. The temporal aspects of any interaction can be studied by varying the time during the movement when the flash is presented, a method similar to the one used to determine the time course of saccadic suppression.[4] Also, by studying this interaction with eye movements produced in a variety of ways (vestibularly, by direct stimulation of the oculomotor nucleus, by stimulation of various brainstem sites, etc.), the role played by oculomotor mechanisms can be investigated.

The experiments are being carried out on decerebrate cats, since eye movements are relatively easy to obtain in such a preparation.[8] The animal is placed in a Horsley-Clark stereotaxic headholder in an electrically shielded cage. The left cortex is exposed, and the CER is recorded with a platinum-surface electrode and an AC coupled amplifier. Averaging of the evoked responses can be done either photographically, by using a monitor oscilloscope and a Polaroid camera, or with the G. E. 225 computer.

Eye movements have been produced by electrically stimulating various brainstem sites.[8] Spontaneous eye movements are often present in this preparation, once the effects of the anesthesia have worn off. A semiconductor light sensor system with infrared light reflected off the eye, similar to one developed in this laboratory,[9] is used to record the eye movements.

Light flashes are presented to the right (contralateral) eye with a General Radio Strobotac. The flashes can be triggered in a variety of ways. When eye movements are being produced by electrical stimulation, a pulse from the stimulator can be used as a trigger for the strobe; in this case, delaying the pulse allows the flashes to be presented at various times during the eye movement. When spontaneous eye movements are

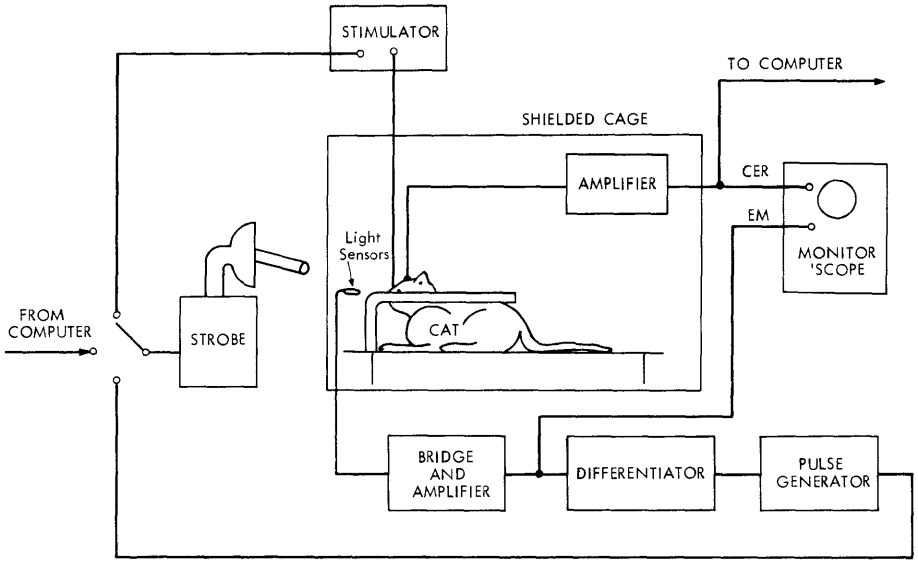


Fig. XXVII-8. The experimental system.

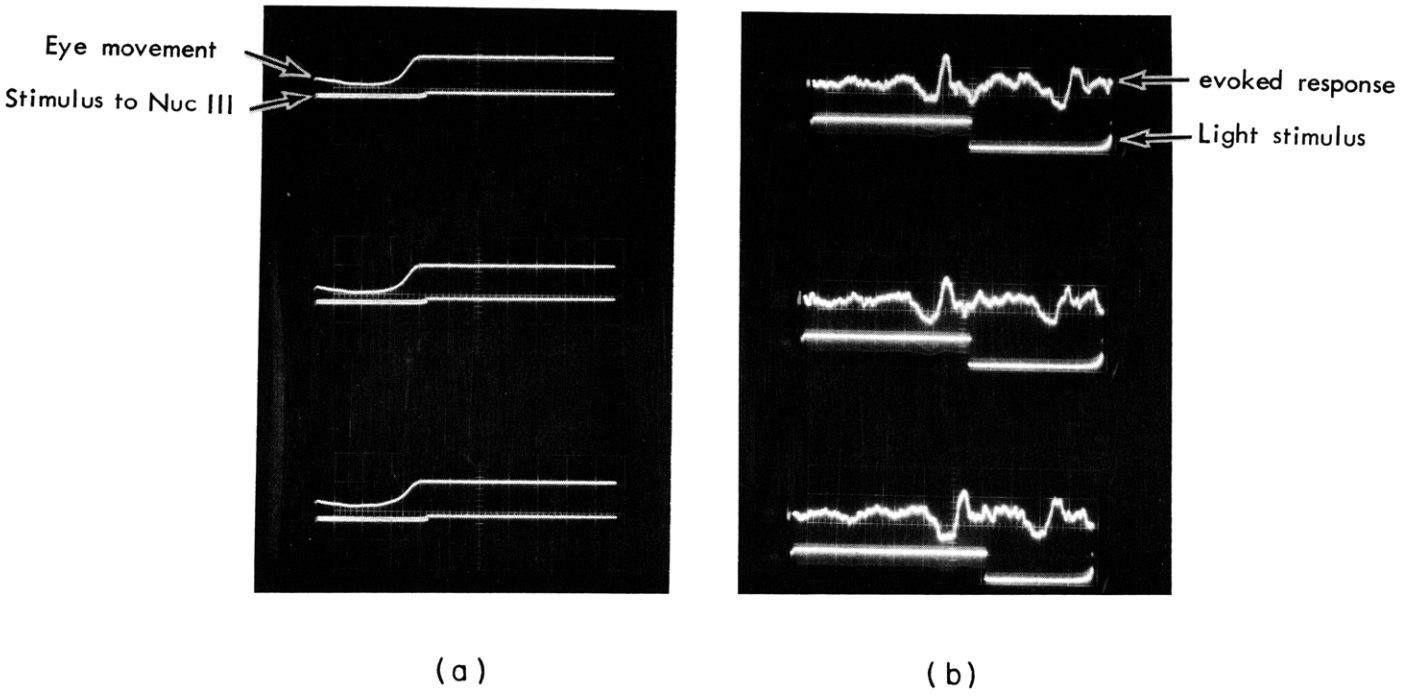


Fig. XXVII-9. Eye movements and CER produced by stimulation of the oculomotor nucleus.

present, the eye-movement response signal can be differentiated and the derivative used to trigger a pulse generator; this, in turn, triggers the strobe. Finally, any desired pattern of trigger pulses can be outputted from the computer.

A block diagram of the experimental arrangement is shown in Fig. XXVII-8.

3. Results

Samples of eye movements produced by stimulation of the oculomotor nucleus are seen in Fig. XXVII-9 along with typical CER.

In the only complete experiment carried out thus far, the CER output could only be recorded on a Sanborn recorder, and no averaging was done. Measurements of individual responses produced a very small and not significant difference between responses occurring with the eyes still and those occurring with the eyes moving, the latter being smaller. The signal-to-noise ratio of the responses was very poor, however, and the lack of averaging makes these results almost meaningless. Nevertheless, we have now devised a system which can be used to carry out this experiment.

4. Discussion

The spontaneous cortical activity that is usually present in our decerebrate preparations makes it essential that some averaging technique be utilized to extract the visually evoked response from the spontaneous cortical noise. The use of the G. E. 225 computer should solve this problem and enable us to complete these studies.

J. Michael, L. Stark

References

1. R. W. Ditchburn, Physical methods applied to the study of visual perception, Bull. Inst. Phys. 10, 121 (1959).

2. P. L. Latour, Visual threshold during eye movements, Vision Res. 2, 261 (1962).

3. F. C. Volkmann, Vision during voluntary saccadic eye movements, J. Opt. Soc. Am. 52, 571 (1962).

4. B. L. Zuber, J. A. Michael, and L. Stark, Visual suppression during voluntary saccadic eye movements, Quarterly Progress Report No. 73, Research Laboratory of Electronics, M. I. T., April 15, 1964, pp. 217-221.

5. B. L. Zuber, Anne Horrocks, M. Lorber, and L. Stark, Visual suppression during the fast phase of vestibular nystagmus, Quarterly Progress Report No. 73, Research Laboratory of Electronics, M. I. T., April 15, 1964, pp. 221-223.

6. B. L. Zuber, Anne Crider, and L. Stark, Saccadic suppression associated with microsaccades, Quarterly Progress Report No. 74, Research Laboratory of Electronics, M. I. T., June 15, 1964, pp. 224-249.

7. A. Fernandez-Guardiola, T. Harmony, and E. Roldan, Modulation of visual input by pupillary mechanisms, EEG clin. Neurophysiol. 16, 259 (1964).

8. R. F. Faulkner and Jane E. Hyde, Coordinated eye and body movements evoked by brainstem stimulation in decerebrate cats, J. Neurophysiol. 21, 171 (1957).

9. L. Stark and A. Sandberg, A simple instrument for measuring eye movements, Quarterly Progress Report No. 62, Research Laboratory of Electronics, M.I.T., July 15, 1961, pp. 268-270.

D. COMPONENT ANALYSIS OF THE ABDOMINAL PHOTORECEPTOR WALKING-MOVEMENT SYSTEM IN THE CRAYFISH

Several aspects of the abdominal photoreceptor walking-movement system of the crayfish have been previously investigated in this laboratory. In these studies, the transfer function of the photoreceptor, considered as a light-intensity-to-frequency transducer, was evaluated.[1] It was found that the detailed timing of the nerve signals coming from the photoreceptor carry no useful information.[2,3] Rather, it is felt that only the average frequency carries the light-level information.

The system has been defined as follows. Two photosensitive cells, one in each half of the sixth abdominal ganglion, send a signal to the infraesophageal ganglion through their axons. The remaining nervous structure has been considered as a decoding unit that can be activated by either one of the photoreceptor cells. The output is the walking movement. The light receptor walking-movement system was also found to have a probabilistic output.[5] That is, there is only a certain probability of getting a walking-movement response to the light stimulation of the sixth abdominal ganglion.

The purpose of this report is to present a more detailed scheme of this system and to show further steps in the processing of the stochastic characteristics of the nerve signal.

1. Method

In a first group of experiments, the directional discrimination of the sixth abdominal ganglion of the crayfish was studied by recording the electrical response of the nerve axon of one photosensitive neuron when it was stimulated by a beam of light coming from a bundle of optical fibers that were used to carry the stimulating light. When the tip of the bundle of optical fibers was 1 mm above the ganglion, a spot of light, 2 mm in diameter, was produced. This spot was used to explore the photoreceptive response to different positions of the light source.

In the second group of experiments crayfish walking movements were investigated following (a) enucleation of the eyes; (b) periesophageal ring transection; and (c) transection immediately below the infraesophageal ganglion. Enucleation of the eyes was accomplished by cutting the stalk of the eyes, periesophageal ring transection by uncovering ventrally the region below the rostrum and cutting the two branches of the ring under the microscope, and infraesophageal section by uncovering the region between the origin of the food-handling legs and transecting the ganglionic chain. Survival of the

animals, after the surgical procedures, was almost 100 percent if, instead of removing skeleton pieces, one uncovered the region, fractured it, and allowed the fractured lips to regain their original position following the procedure.

The walking movements were recorded by having one of the legs of the animals pull a lever with a mirror attached to it. A beam of light, reflected by the mirror, stimulated a photocell, once during each walking swing of the legs.

The voltage generated by the photocell triggered a waveform generator which produced a pulse with each swing. This pulse was displayed on a paper recorder. The animals were secured on their backs to a small table and immersed in a tank of water at 20°C. Constant bubbling of air through the water provided adequate ventilation. The animals and the recording device were located in a dark chamber. The light that stimulated the animals came from a filament projector lamp and was allowed to pass through a hole into the chamber. When required, the light stimulation was automatically switched on by a clock device for 30 seconds, every 15 minutes. In another group of experiments the electrical signals from single fibers were recorded at different interganglionic regions. The methods of microdissection, electrical recording, and computer processing have been described previously.[3,4] The single-fiber preparation in the ventral chord has also been described.[4] Access to the fibers in the esophageal ring was made by producing a circular window, 6 mm in diameter, in the exoskeleton below the rostrum. The uncovering and isolation of the ring was easily done by pushing the green glands backward with cotton plugs.

2. Results

a. Directional Light Discrimination of the Photoreceptor

In the experiment designed to study the directional discrimination of light by the 6th abdominal ganglion photoreceptor, the displacement of the light spot away from the middle line produced only a small asymmetry in the average frequency steady-state response of the fiber, recorded with respect to the symmetrically opposite position of the light (Fig. XXVII-10).

b. Ablation and Nerve-Section Experiments

The extirpation of the eyes, during the first twelve hours after surgery, produced prolonged and frequent walking that in nonrestrained animals consisted of exploratory walking along the walls of the tank with the help of their antennae. The abdominal region and the uropods of the telsom showed characteristic extension. If the number of walking-movement trains were counted in arbitrarily set time intervals, no clear periodicity could be observed by adding the number of movements of intervals counted in a cyclic manner. Figure XXVII-11 shows in shaded bars the probability of getting a walking train in each interval of 21 arbitrary cycles of 35 minutes' duration. Each of the non-shaded

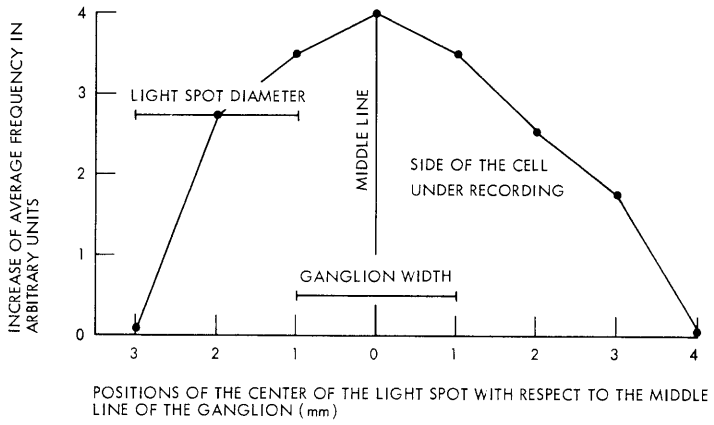


Fig. XXVII-10. Increase in average frequency discharge of one of the photosensitive cells of the 6th abdominal ganglion in response to different positions of a stimulating spot of light. Ordinate: the steady-state average frequency response of the right photosensitive neuron. Abscissa: position of the center of the tip of a bundle of light fibers carrying the light. Also represented is the approximate width of the 6th abdominal ganglion and the diameter of the light spot. Note the slight asymmetry of the response to the changes of light-spot position.

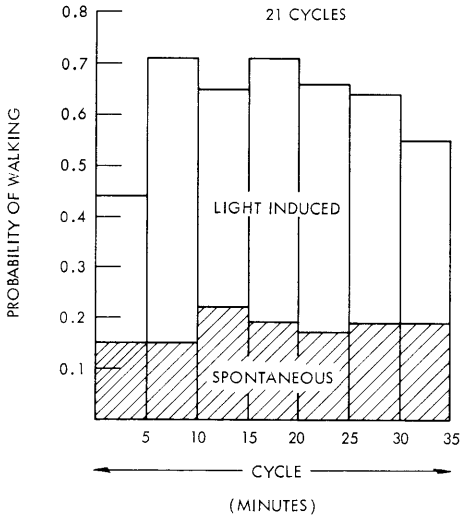


Fig. XXVII-11.

Effect of light stimulation in blinded crayfish on the probability of walking. The 12 hours and 15 minutes of walking recording was divided into 21 cycles of 35 minutes each. Each cycle was subdivided in 7 numerated periods of 5 minutes each. Shaded bars represent the probability of production of walking, each numerated period. Nonshaded bars represent the probability of light-induced walking in each numerated period. Note the absence of cyclic walking activity and the increase of the walking probability with light stimulation.

bars represents the probability of getting a response to a 30-sec light stimulation produced approximately every 15 minutes. The animals with periesophageal ring transection remained motionless most of the time with a permanent flexion of the abdominal region. If they were mechanically stimulated in the dorsal abdomen they would walk for awhile, and then remain in one place for a very long period. Without displacing themselves, however, they displayed spontaneous walkinglike movements of the legs when lying on one

side. These walking movements can be reliably evoked by light stimulation; however, they are not deterministically produced.

A typical experiment showed that the probability of a light-evoked walking movement in a blind animal changed from 0.57 to 0.77 after the periesophageal transection. The animals with a transection below the infraesophageal ganglion remained motionless after the operation. They only showed weak, coordinated movements of the legs when mechanically stimulated on the ventral thoracic surface. Light stimulation produced no leg movements.

c. Single-Fiber Experiments

If the periesophageal ring branches are disconnected from the supraesophageal ganglion, it is possible to pick out from these branches one fiber (B) whose average frequency discharge increases with light stimulation of the 6th abdominal ganglion. This fiber can be found in either of the two branches of the periesophageal ring, even when one of the photoreceptor fibers has been suppressed by abdominal ventral chord hemisection. The response of these fibers is completely deterministic, and its average

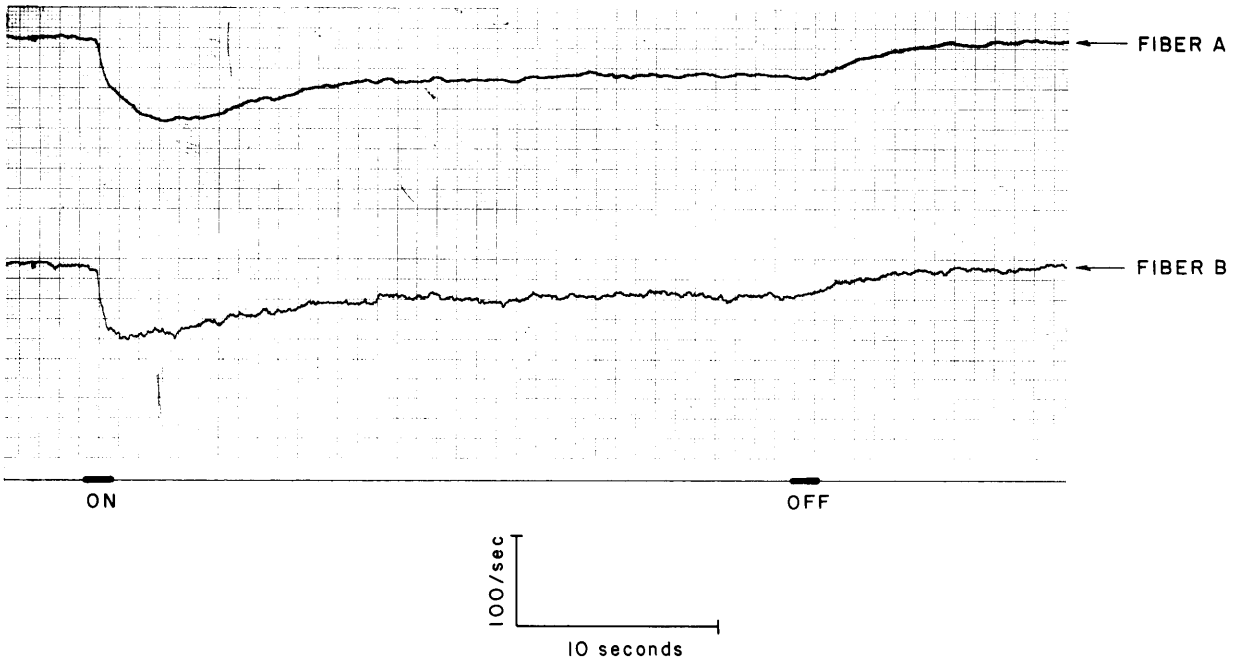


Fig. XXVII-12. Simultaneous recording of the average frequency light response of one nerve fiber (A) coming from the 6th abdominal ganglion photoreceptor, and a nerve fiber (B) in the homolateral side of the periesophageal ring which is disconnected from the supraesophageal ganglion. Note the similar time course of the response.

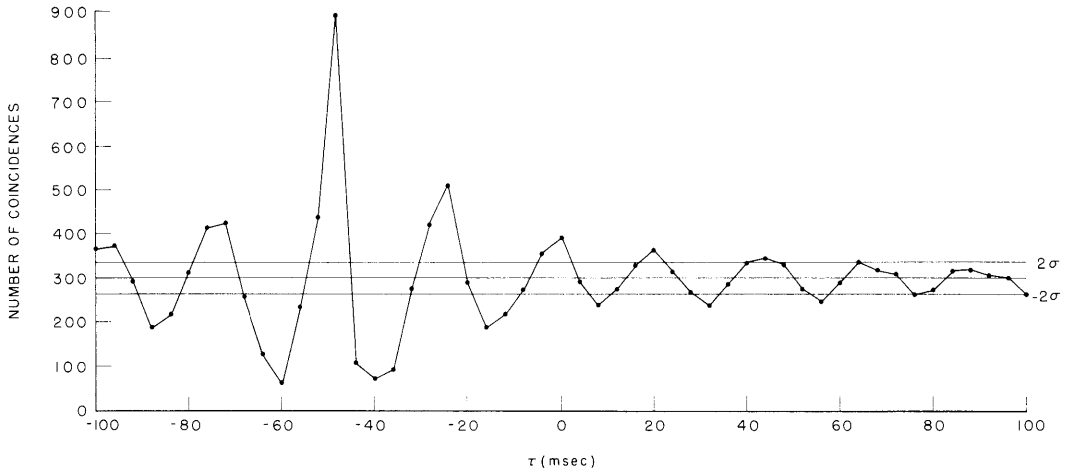
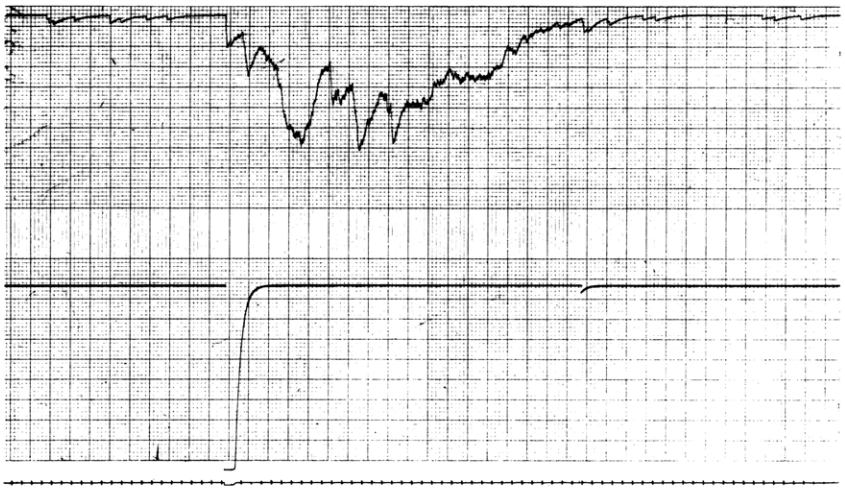


Fig. XXVII-13. Crosscorrelation function between fiber A and fiber B. Note the positive correlation at $\tau = -48$ msec, and the oscillatory nature of the function corresponding to the close values of the average frequency discharge of the two fibers.

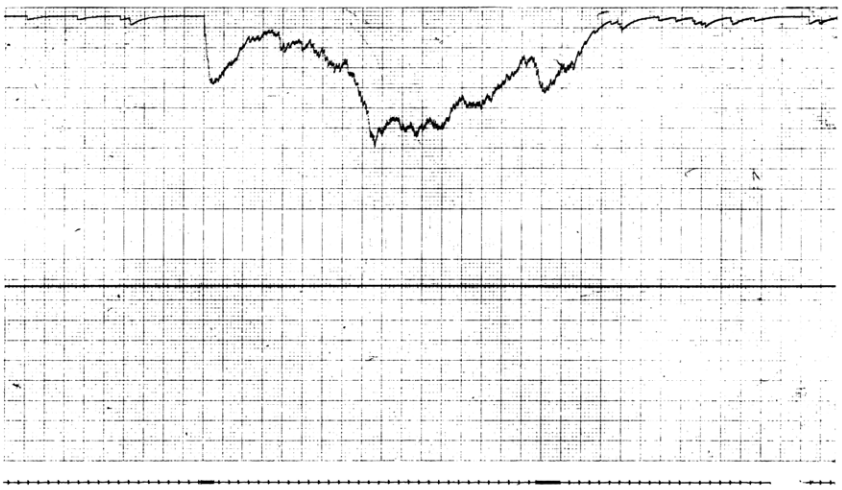
frequency is very close to that of the photoreceptor cell fiber (A) (Fig. XXVII-12). Cross-correlation studies between (A) and (B) pulse trains, during light stimulation, show its higher positive correlation at t = -48 msec, the distance between the electrodes being 5.5 cm (Fig. XXVII-13). Illumination of the main eyes has no effect on the discharge of fiber (B) when the fiber is isolated without sectioning any other fibers in the periesophageal ring.

In those preparations, in which one of the branches of the periesophageal ring are disconnected near the infraesophageal ganglion, the branch now attached to the supraesophageal ganglion shows several fibers (C) with a different response pattern to light stimulation of the photoreceptor. This pattern, in an average frequency recording, can be described as an increase of frequency which fades out before the light stimulation is turned off. A ringinglike phenomenon can be seen superimposed on top of this over-all increased frequency (Fig. XXVII-14a). In most of these (C) fibers stimulation of the main eyes causes them to discharge in a similar fashion to that already described but with additional "on" and "off" bursts (Fig. XXVII-14b). In some experiments it was found that the diffuse stimulation of the lower surface of the eyes inhibits the (C) discharge produced by 6th abdominal ganglion light stimulation.

The crosscorrelation analysis between (B) and (C) pulse trains (Fig. XXVII-15) shows that there is positive crosscorrelation at $\tau = 8$, 4, and 0, the highest correlation being one-third of the pulses at $\tau = 0$. Rather, it is more likely at $\tau = -2$, because of the grid size used (2 msec). A (C) discharge can be obtained even with hemisection of either side of the abdominal ventral chord. The reliability of the response of these fibers, although



(a)



(b)

Fig. XXVII-14. (a) Average frequency response of a fiber coming from the the supraesophageal ganglion (fiber C) in response to light stimulation of the 6th abdominal ganglion. Note the over-all increase of frequency, its transitory nature, and the superimposed ringinglike effect. (b) Response of the same fiber to stimulation of the eyes. Note the "on" and "off" bursts.

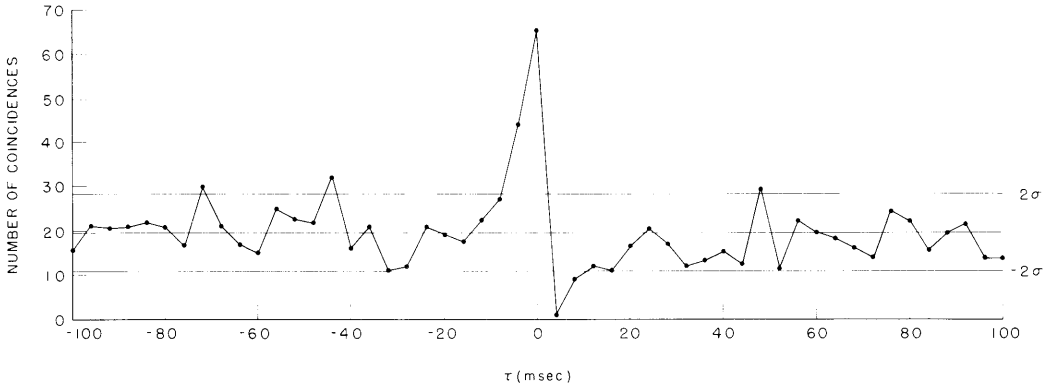


Fig. XXVII-15. Crosscorrelation function between fibers B and C. Note the positive correlation at τ = 49 and 0 msec.

not yet numerically evaluated, is higher than any walking response studied thus far, but the probability of the response is clearly sensitive to the interval between two subsequent stimulations of the 6th abdominal ganglion.

3. Discussion

In previous reports[2,3] dealing with the detailed timing of the nerve signal from the 6th abdominal ganglion of the crayfish, we assumed, on morphological evidence, that light stimulation of the ganglion produced the same effective stimulation of both ganglion cells. The results presented here show that such is the case, since relatively large deviations of the light-stimulating spot did not produce substantial differences in the average frequency response of one of the cells, even when the light was moved toward the contralateral half of the cell side during recording.

From the experiments with ganglionic chain transection below the infraesophageal ganglion, one sees that coordinated movements of the legs can be elicited without the infraesophageal ganglion. Actual walking movements are only possible, however, with the control of the infraesophageal ganglion as shown in the periesophageal ring transected preparation.

The higher probability of getting a walking-movement response to light stimulation in the periesophageal ring transected preparation with respect to the blinded preparation shows that there is a tonic inhibitory influence of the supraesophageal ganglion upon this response. From the experiments in which (B) fiber activity was recorded, it is clear that the infraesophageal ganglion region is the place at least where the signal crosses the middle line of the animal. This might explain the walking-movement response bilaterally produced by the activation of a single 6th ganglion photoreceptor cell.

Considering that the speed of conduction of the photosensitive fibers is approximately 3.8 meters/second, it is tempting to suggest the presence of at least one synapse between

(A) and (B). this would account for the difference between the calculated delay (14.4 m/sec), with (A) and (B) considered as the same fiber, and the actual delay (48 msec) that was found. More experiments, of course, will elucidate the point.

Considering (C) fibers as inhibitors of the walking-movement system in the infraesophageal ganglion would account for the tonic inhibitory effect of the supraesophageal ganglion and for the common observation of walking-movement suppression by the illumination of the eyes in the intact animal.

The small correlation values of τ that were found between (B) and (C) suggest a very simple neuronal circuit that might be monosynaptic.

From the experimental data, we feel that the infraesophageal ganglion acts as a center that gates a true 6th abdominal ganglion photoreceptor walking-movement reflex. The gating depends on several inputs coming from other receptors. Of these receptors, the eye would have the highest priority.

J. Negrete, Guillermina N. Yankelevich, L. Stark

References

1. L. Stark, and H. T. Hermann, The transfer function of a photoreceptor organ, Kybernetik 1, 124-129 (1961).

2. J. Negrete, G. N. Yankelevich, G. Theodoridis, and L. Stark, Signal information carried by a train of nerve pulses, Quarterly Progress Report No. 74, Research Laboratory of Electronics, M.I.T., July 15, 1964, pp. 255-261.

3. G. Theodoridis, J. Negrete, G. N. Yankelevich and L. Stark, Photosensitive neurons of the crayfish sixth ganglion as a dual system, each neuron carrying same signal information, Quarterly Progress Report No. 75, Research Laboratory of Electronics, M.I.T., October 15, 1964, pp. 197-209.

4. J. Negrete, G. N. Yankelevich, G. Theodoridis, and L. Stark, Light inhibitory effects in the crayfish sixth ganglion, Quarterly Progress Report No. 74, Research Laboratory of Electronics, M.I.T., July 15, 1964, pp. 252-254.

5. H. T. Hermann and L. Stark, Random-walk response of the crayfish, Quarterly Progress Report No. 61, Research Laboratory of Electronics, M.I.T., April 15, 1961, pp. 230-234.

E. DYNAMICS OF HUMAN HORIZONTAL EYE-MOVEMENT MECHANISM

1. Introduction

This is a progress report on an investigation of the human horizontal eye-movement mechanism. The investigation, which is still in progress, includes not only a study of the input-output properties of the system, but also an exploration into its physiological elements, in the interest of obtaining a realistic mathematical representation of the system. The interpretations presented here are not final, rather they are the ones deemed most reasonable when based on information available at this time. Additional observations,

no doubt, will lead to further alterations in the system representation.

2. Input-Output Properties

The first part of the investigation consisted solely of a study of input-output properties. As the simplest mathematical representation to deal with is a linear one, an initial question was, Is the system linear?

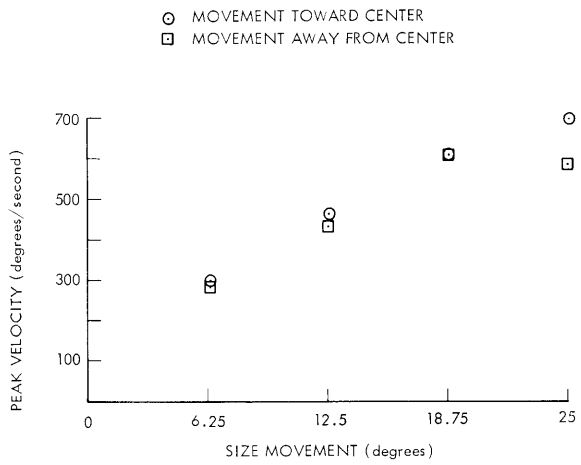


Fig. XXVII-16. Peak velocities attained by the eye during response to instantaneous change in target position.

In the horizontal eye-movement mechanism one observes that the peak velocities, as well as the average velocities, experienced by the eye in response to instantaneous position changes by the target do not increase proportionately as the size of the movements increase. Rather, there is a saturation effect (Fig. XXVII-16). Also, the velocity peaks occur later in time as the size of the movement increases (Fig. XXVII-17). Either of these findings alone rules out the possibility that the system is linear. Additional evidence of the nonlinear behavior of the system is the fact that movements of the same size are faster if the movement is toward the center than if the movement is away from center (Fig. XXVII-16). A known system that exhibits this behavior is a second-order, overdamped, linear system driven by a nonlinear bang-bang controller (Fig. XXVII-18). The phase trajectories for such a system (Fig. XXVII-19) are, however, quite different from those of the horizontal eye-movement system (Fig. XXVII-20). The trajectories of Fig. XXVII-20 more closely resemble those of a second-order, overdamped, linear system driven by a bang-linear controller (Fig. XXVII-21). In such a system, the controller

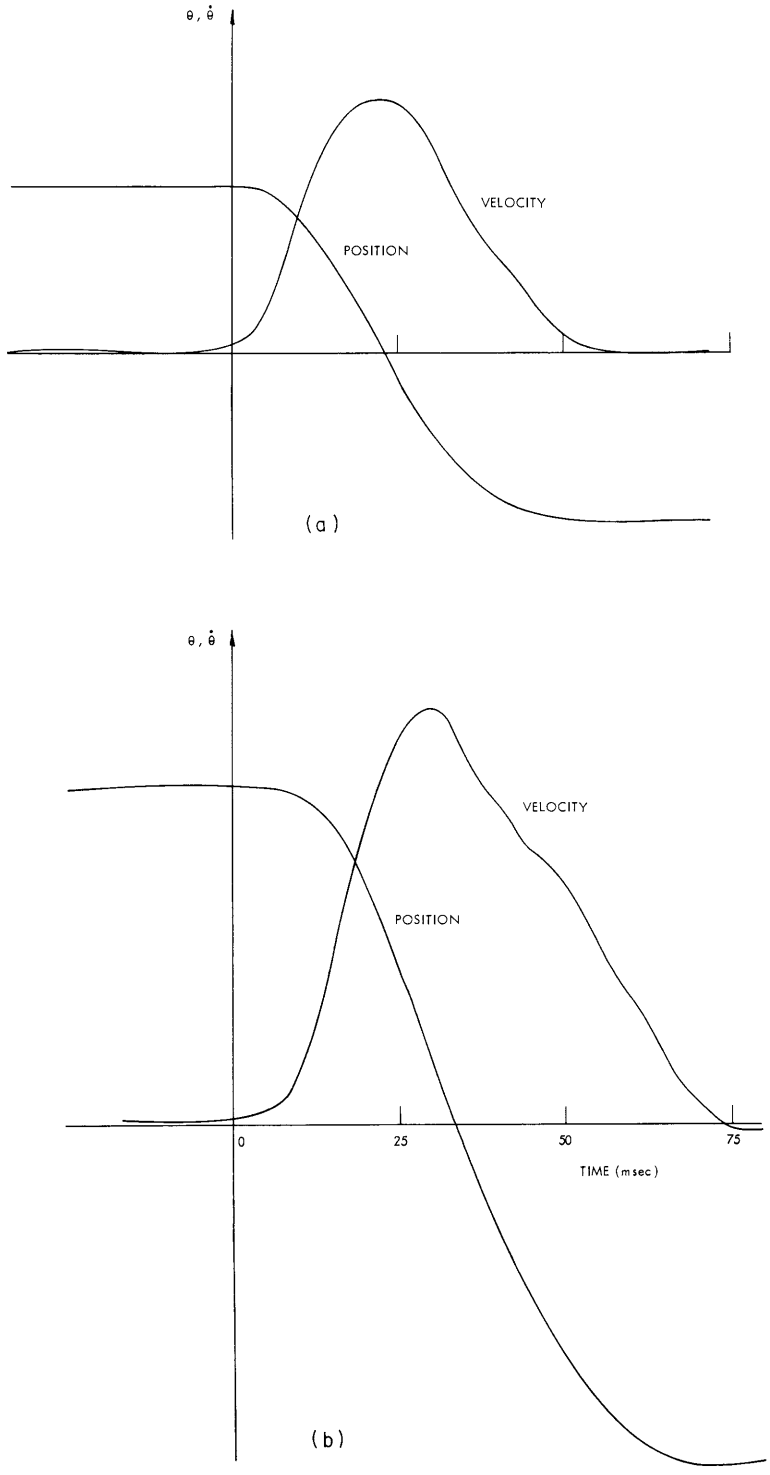


Fig. XXVII-17. Transient response of the eye to instantaneous change in target position. (a) 12.5° step. (b) 25° step.

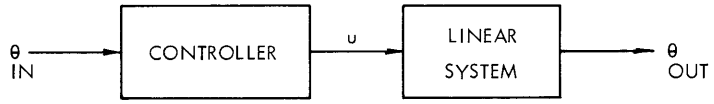


Fig. XXVII-18. Controller driving a linear plant.

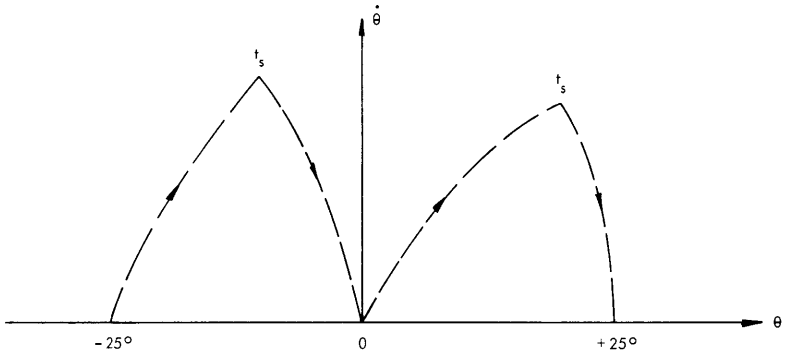


Fig. XXVII-19. Phase trajectories for overdamped second-order linear system driven by bang-bang controller.

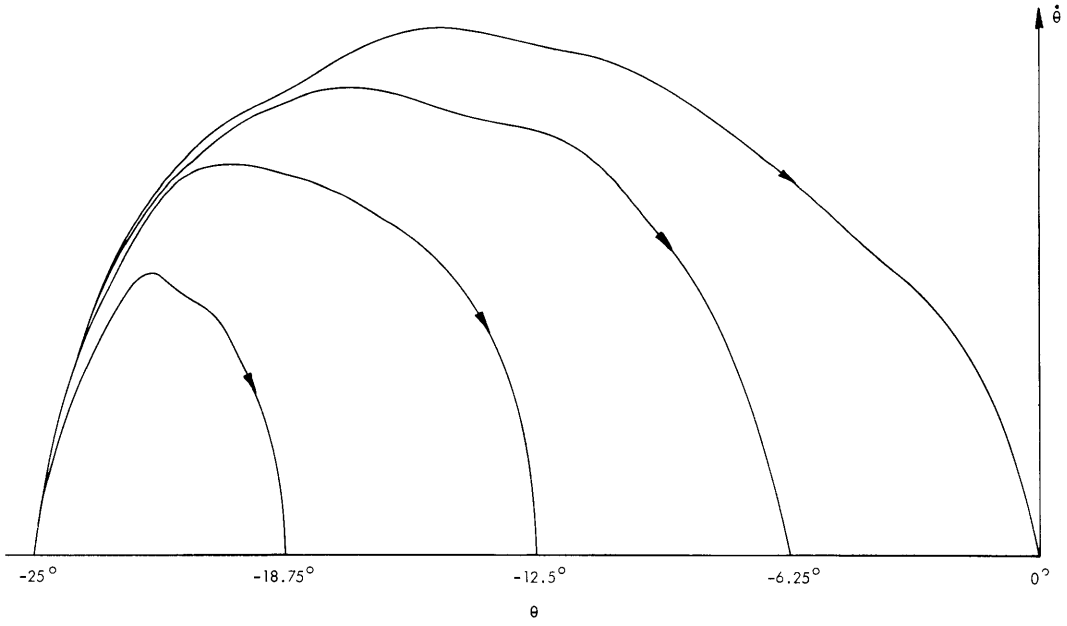


Fig. XXVII-20. Phase trajectories – horizontal eye-movement system.

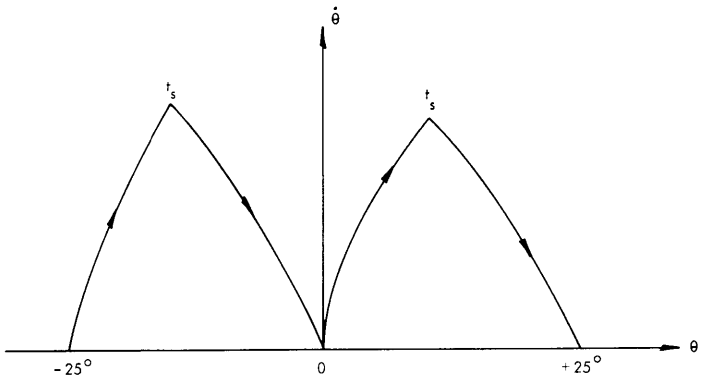


Fig. XXVII-21. Phase trajectories for overdamped second-order linear system driven by Bang-linear controller.

initially gives U the value $\pm\theta_{max}$ and at a time indicated in Fig. XXVII-21 as t_s switches U to θ_{in}. Based on input-output properties alone, the bang-linear model appears to be a reasonable representation. It retains, at least qualitatively, the significant features mentioned above. But our interest goes beyond matching input-output properties. We want our mathematical model to be realistic. That is, we would like to know what various model parameters represent in the physical system. For this reason, and as a check on our first impressions, the physical structure of the eye-movement system has been investigated.

3. Physical Structure

The physical structure of the horizontal eye-movement system is pictured in Fig. XXVII-22. Although there are 6 muscles controlling the eye position, only the lateral and medial recti are shown, as these are primarily responsible for horizontal movements.

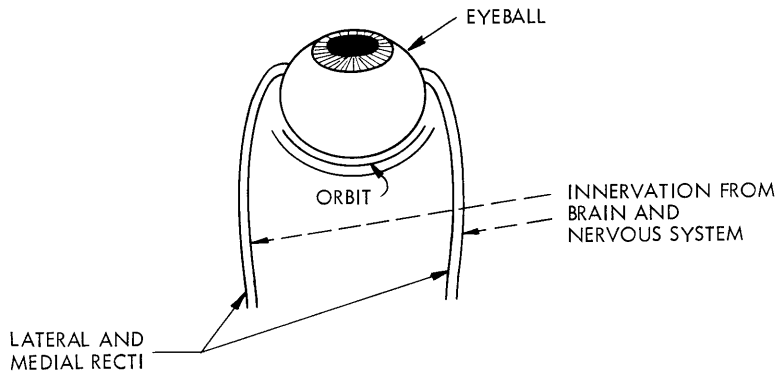


Fig. XXVII-22. Horizontal eye-movement mechanism.

(a) Eyeball. For the eyeball, its physical properties, density ≈1 gm/cc and diameter ≈2.2 cm,[1] together with the assumption that the eyeball is a rigid sphere, yield a moment of inertia about an axis through its center of 2.7° cm sec^2. It is well known that the eyeball is not rigid, but is largely composed of a vitreous humour. Thus a more accurate model for the eyeball might be a series of spherical shells connected successively by springs and dashpots. For simplicity and also because the effect of this inertia is expected to play a very small role in the over-all behavior, we choose to retain the cruder rigid-sphere assumption. The validity of this assumption will be checked when the over-all model is completed and corrections will then be made if necessary.

(b) Active Muscle. The static length-tension characteristic[2-4] for a lateral rectus muscle is shown in Fig. XXVII-23. The corresponding curve for the medial rectus is almost identical. The operating range is from 2 cm to 4 cm, with the "straight ahead"

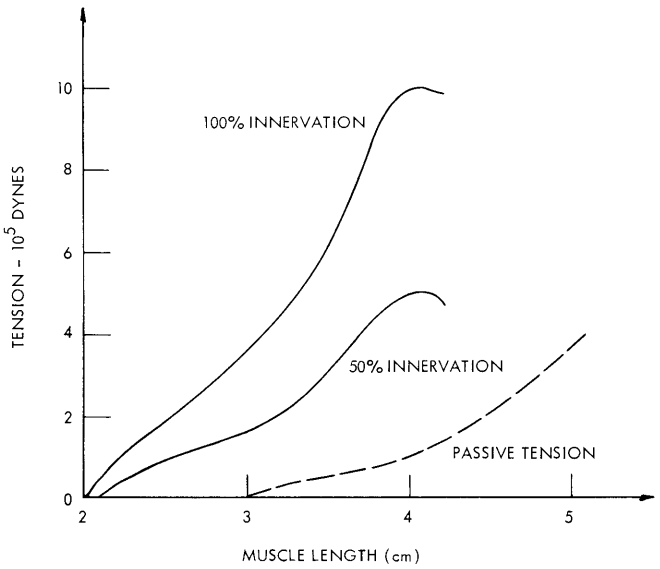


Fig. XXVII-23. Static muscle characteristics.

eye position corresponding to 3-cm length. The 2-cm and 4-cm lengths correspond to angular displacements from straight ahead of ±1 radian (recall that the eyeball radius is approximately 1 cm). The accepted value for maximum eye movement is approximately 50°. The fact that it is slightly smaller than the value based on muscle characteristics is probably due to the checking action of check ligaments. The length-tension curves are approximated by straight lines with a slope of 6×10^5 dynes/cm, or approximately 6×10^5 dynes/radian. This characteristic, of course, can be represented by a spring. The varying degrees of innervation are represented by shifts of the equilibrium position of the spring. This positioner will be called the contractile element, and is

shown with the spring in Fig. XXVII-24.

The transient response during an isometric contraction of a medial rectus muscle[5] is shown in Fig. XXVII-25. This is the response obtained when the muscle is innervated but not allowed to shorten. This behavior demonstrates that there is a dynamic effect

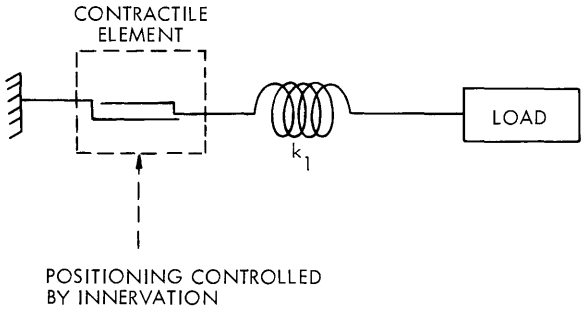


Fig. XXVII-24. Active muscle – static model.

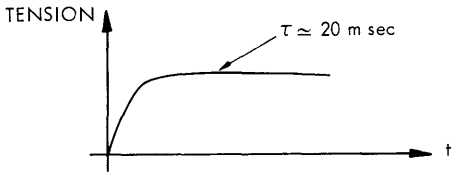


Fig. XXVII-25. Transient behavior of medial rectus during isometric contraction.

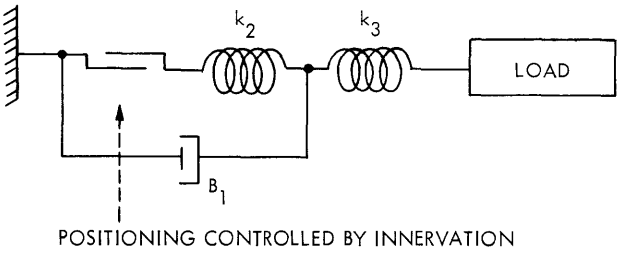


Fig. XXVII-26. Active muscle – dynamic model.

within the contractile element, and that the shortening is not instantaneous but can be approximated by a first-order transient with time constant 0.02 second. This can be represented by an additional spring and a dashpot within the contractile element, as shown in Fig. XXVII-26. The parameters must obey two relations:

$$\frac{K_2K_3}{K_2K_3} = 6 \times 10^5 \text{ dyne-cm/rad}$$

$$\frac{B_1}{K_2 + K_3} = 0.02.$$

The damping coefficient B_1 plays another role as a limiter on rate of energy

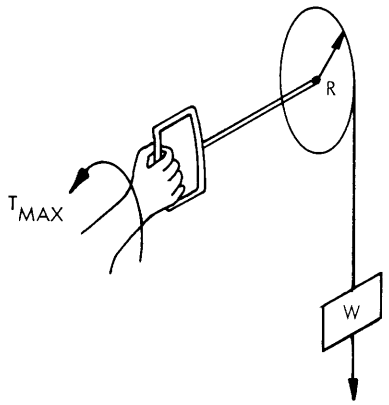


Fig. XXVII-27. Isotonic contraction experiment.

conversion (chemical to mechanical). From an isotonic contraction experiment performed on an arm muscle in the region of T_{max} (see Houk[6] and Fig. XXVII-27),

$$T_{max} = RW + B_1\theta_{\text{steady state}}$$

$$B_1 = \frac{T_{max} - WR}{\theta_{\text{steady state}}} .$$

With appropriate scaling, we obtain $B_1 = 4.8 \times 10^3$ dyne-cm sec/rad. Thus $K_2 = K_3 = 12 \times 10^5$.

(c) Passive Tension. Besides the active behavior of the muscle, there is a passive tension illustrated by the broken line in Fig. XXVII-23. This effect can be represented by a spring parallel to the active muscle with a stretch coefficient of $K_4 = 1 \times 10^5$ dyne-cm/rad, and with a compression coefficient of zero. That is, if the eyeball is pointed θ radians to the right (left) of center, the passive tension of the left (right) muscle pulls with a torque of $\theta \times 1 \times 10^5$ dyne-cm. Here the passive tension of the right (left) muscle plays no role at all.

(d) Eyeball to Orbit Friction. A final source of friction is the interface between the eyeball and orbit labeled B_2 in Fig. XXVII-28, A measurement of this parameter has not yet been obtained.

(e) Electromyograms. Electromyograms[7-9] indicate that during a saccadic eye movement, the innervation signal driving the muscles is piecewise constant. At first, the agonist undergoes a very large burst of activity while the antagonist is highly inhibited. As, or just before the movement is completed, the level of innervation in the agonist is reduced and the level of innervation in the antagonist is increased, the system attaining a level of innervation characteristic of the new eye position. This controller action is different from the bang-linear behavior predicted earlier,

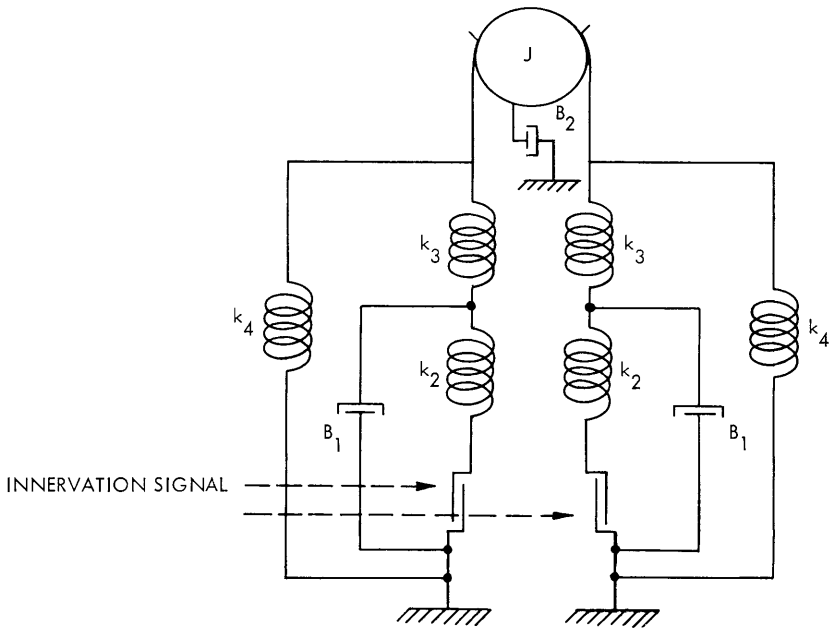


Fig. XXVII-28. Over-all model of horizontal eye-movement system.

in that the time of the switch in the control variable occurs much later during the movement. This fact alone does not eliminate the possibility of bang-linear control, but if one assumes that the large burst of activity maintained throughout most of the movement is the same for all movements, call it $\pm\theta_M$, then the phase trajectories for the movements (a) -25° to -18° and (b) -25° to 0° must coincide until time t_a. This is the time at which the level of activity switches from the high level to the level characteristic of the desired position θ_{in} and, according to the electromyograms, occurs late in the movement. The phase plots (Fig. XXVII-20) show that these trajectories do not coincide until time t_a, but deviate from each other quite early in the movement. One must conclude from this that the value of the control variable maintained during most of the movement, while sufficient to drive the system beyond θ_{in}, is not the same for all movements. That is, maximum effort is not being applied.

It is impossible to quantize the levels of nervous stimulation indicated in the published electromyograms. One can only make comparative judgments. With this amount of information one is led to believe that the over-all system is overdamped, and that the initial burst of nervous stimulation sends the system output (eye position) from its initial position θ_o, toward a value (θ_c) beyond the desired value θ_{in}. As the system in its transient behavior approaches θ_c, it must sometime pass through the point θ_{in}. At or slightly before this time, the stimulation level switches to a value corresponding to θ_{in} and holds the output at this point.

The faster movement toward center than away from center can be attributed to the

passive tension of the muscles. The saturation effect has not been localized. It may be due to a nonlinearity that has been deleted from the model in the gross linearizations, or it may be due to the controller behavior, as the functional relationship between θ_c and the size of the movement has not been determined.

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References

1. E. Wolff, Anatomy of the Eye and Orbit (W. B. Saunders Company, Philadelphia and London, 1961), p. 30.

2. T. C. Ruch and J. F. Fulton, Medical Psychology and Biophysics (W. B. Saunders Company, Philadelphia and London, 1960), p. 108.

3. W. D. Zoethout, Physiological Optics (The Professional Press, Inc., Chicago, 1947), p. 308.

4. G. M. Breinin, The Electrophysiology of Extra-ocular Muscle (University of Toronto Press, Toronto, Ontario, 1962), p. 122.

5. F. H. Adler, Physiology of the Eye (C. V. Mosby Company, St. Louis, Missouri, 1959), p. 363.

6. J. C. Houk, Jr., S. M. Thesis, Department of Electrical Engineering, M. I. T., 1963, p. 27.

7. E. Tamler, E. Marg, A. Jampolsky, and I. Nawratzki, Electromyography of human saccadic eye movements, A. M. A. Arch. Ophthalmol. 62, 678 (1959).

8. J. E. Miller, Electromyographic patterns of saccadic eye movements, Am. J. Ophthalmol. 46, 183-186 (1958).

9. H. Davison, The Physiology of the Eye (Little, Brown and Company, Boston, 1963), p. 235.