XXI. COMMUNICATIONS BIOPHYSICS[*]

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A. WORK COMPLETED

These reports summarize S.B. theses submitted to the Department of Electrical Engineering, M.I.T., May 1966.

1. HIGH SPEED ELECTROMECHANICAL SHUTTER FOR VISUAL NEUROPHYSIOLOGY

An electromechanical shutter capable of interrupting a light beam, 7 mm in diameter, in less than one millisecond was needed for use in a visual stimulator. By overdriving a

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pen motor with a vane mounted on the stylus to interrupt the light, a rise time of 0.7 msec and a fall time of 0.8 msec were achieved.

J. M. Hahn

2. COMPUTER SIMULATION OF SEQUENCE OF ACTIVATION IN FIBRILLATING HEART

A program for simulating a trial fibrillation, similar to one reported by Moe, Rheinholdt, and Abildskov[1] was developed for a PDP-1 computer. A square array of 2500 cells (50 × 50) was used to represent a cylindrical surface. Wave fronts leaving the right edge re-enter on the left. A cathode-ray oscilloscope display was used, with spots of light indicating active cells.

Once a cell has fired, it can activate the adjacent four cells (two on upper or lower edge) in succeeding time intervals that depend on the time at which the inactive cell last fired. If an adjacent cell is in the "absolute refractory" period, it will not fire at all; if it is in the "resting state" it will fire on the next cycle. During the "relative refractory" period delays of 1 to 5 intervals are introduced. Heterogeneity in the population of cells was introduced in a separate program that distributed randomly the length of the absolute refractory period between two limits.

With no randomness present, circus movements were observed with specific excitation patterns, and the failure of stimulation at one or more points to produce sustained activity was noted. These results are consistent, for example, with those predicted by Wiener and Rosenblueth.[2]

When the refractory period was randomized in the range of 10-30 time steps, response to an ectopic focus was quite regular and sustained activity was not observed after the stimulation ceased. The range was then extended to 8-30 time steps, and then spontaneous, apparently turbulent, activity was observed as reported by Moe. New runs were made with an ectopic focus continually firing. The activity appeared to be just as random. The model, then, appears to be unable to distinguish re-entry mechanisms from ectopic foci as the basis of fibrillation. The use of autocorrelation to study the nature of the firing patterns in the model was suggested.

S. J. Hayashi

References

1. G. K. Moe, W. C. Rheinholdt, and J. A. Abildskov, "A Computer Model of Atrial Fibrillation," Heart J. 67, 200-220 (1964).
2. N. Wiener and A. Rosenblueth, "The Mathematical Formulation of the Problem of Conduction of Impulses in a Network of Connected Excitable Elements, Specifically in Cardiac Muscle," Archivos del Instituto de Cardiologia de Mexico 16, 205-265 (1946).

3. CONTROL OF A SERVO RESPIRATOR USING MUSCLE POTENTIALS

The advantages of a respirator which is under full-time patient control is discussed. Efforts to record electromyograms from skeletal musculature involved in respiration are described. The system finally developed derives a control signal from an esophageal electrode which picks up muscular activity from the patient's diaphragm. A simple but effective method of discriminating the muscle activity of the diaphragm from the electrocardiogram is presented. Included is a tentative design of a respirator control system which uses this signal and includes fail-safe features.

J. L. Lehr

4. COCHLEAR POTENTIALS IN GUINEA PIGS WITH SURGICALLY PRODUCED ENDOLYMPHATIC HYDROPS

Cochlear microphonic potentials (CM), DC endolymphatic potentials (EP), and auditory-nerve compound action potentials (N_1) were measured for a variety of stimulus conditions from both cochleas of animals with unilateral hydrops. Comparison of measurements between the normal and operated ears for 14 guinea pigs showed a definite tendency for CM, EP, and N_1 to be smaller in the operated ears, although in a few animals the differences were not significant. Although only fragmentary histological results are available now, there appears to be a correlation between the diminution of the potentials and the degree of hydrops.

These experiments were carried out in cooperation with Mr. Robert Kimura of the Electron Miscoscopy Laboratory, Massachusetts Eye and Ear Infirmary.

R. L. MacDonald

5. TEMPERATURE-AND HUMIDITY-REGULATING APPARATUS FOR A MICROSCOPE-STAGE INCUBATOR

An automatic temperature-controlling device was designed and constructed for a small, partially open incubator mounted on a microscope stage. Also, an independently operating humidity supply designed to maintain high water vapor content of the same incubator is described. Although the basic parts of the temperature-controlling device are applicable to other situations, the microscope-stage incubator places restrictions on the choice of heating and temperature-sensing elements which, being reflected in the overall design, results in a somewhat specialized instrument.

W. A. Plice III

6. A HIGH SPEED ANALOG-DIGITAL CONVERTER INPUT AND COMPARATOR CIRCUIT DESIGN

The design of an input amplifier, sample-and-hold comparator circuit is described in this thesis. The design is described from the initial specifications through to the final design and includes comments on circuitry which was not used in the final device, as well as a description of the completed system. Particular attention was given to the effects of thermal drift and component selection. The final specifications are:

Input dynamic range	1 volt peak-to-peak
Input impedance	100, 000 ohms
Input coupling	DC
Sampling time	0.5 μsec
Hold time	10 μsec
Comparison time	0.04 μsec
Total drift	0.1% for 60°C temperature change

D. G. Tweed

B. PSYCHOACOUSTICS

1. GENERAL REMARKS

The work in psychoacoustics during the past year can be divided into the following categories: (a) binaural unmasking, (b) perception of frequency ratio, and (c) preparation for future research. The work on binaural unmasking has consisted of preparing previous results for publication, analyzing certain aspects of the phase-detector model of binaural unmasking, and performing an experiment to determine the dependance of binaural unmasking on the bandwidth of the masking noise. The research on the perception of frequency ratio has been concerned with the difference between the physical and subjective octaves and with the ability to detect small changes in frequency ratio. The work related to future research has consisted of an attempt to formulate a language in which one can construct a model for short-term memory of sounds, construct an overview of psychoacoustics that will allow one to relate certain topics in psychoacoustics which are now treated separately, and develop instrumentation that is more flexible and efficient. The effort to prepare previous results for publication has resulted in two journal articles[1,2] and a chapter in a book.[3] The work on the phase-detector model of binaural unmasking, the perception of frequency ratio, and the development of new experimental facilities, is outlined below.

N. I. Durlach

References

1. L. R. Rabiner, C. L. Laurence, and N. I. Durlach, "Further Results on Binaural Unmasking and the EC Model" (to be published in J. Acoust. Soc. Am.).
2. N. I. Durlach, "Note on Application of EC Model to Interaural JND's" (submitted to J. Acoust. Soc. Am.).
3. N. I. Durlach, "Binaural Signal Detection: Equalization and Cancellation Theory," Chapter 16 in Modern Foundations of Auditory Theory, edited by J. V. Tobias and E. D. Schubert (to be published by Academic Press, Inc., New York).

2. ANALYSIS OF PHASE-DETECTOR MODEL OF BINAURAL UNMASKING (S. B. Thesis)

The phase-detector model of binaural unmasking was proposed by Webster[1] in 1951 and Jeffress, Blodgett, Sandel, and Wood,[2] in 1956, to account for certain results on the binaural unmasking of tones masked by random noise. It is assumed that there exists a narrow-band peripheral filter (the "critical band") and that the effective masking noise can be regarded as a sine wave of the same frequency as the tone, but with a slowly varying amplitude and phase. The interaural phase of the total signals (signal plus noise) can be shown to depend on the interaural differences in amplitude and phase of the tone and noise, and the amplitude and phase of the noise relative to the tone. The fundamental assumption of the model is that binaural detection is based on observations of this interaural phase. Since the amplitude and phase of the noise are random, this interaural phase is also random. In previous work on the model, the statistical properties of this variable have not been adequately analyzed. In this thesis, an attempt was made to compute the probability distribution function on the interaural phase for a variety of stimulus configurations. The results (which are far from complete) are presented in integral form and require the use of a computer for numerical evaluation.

J. E. Brown III

References

1. F. A. Webster, "The Influence of Interaural Phase on Masked Thresholds. I. The Role of Interaural Time Deviation," J. Acoust. Soc. Am. 23, 452-462 (1951).
2. L. A. Jeffress, H. C. Blodgett, T. T. Sandel, and C. L. Wood III, "Masking of Tonal Signals," J. Acoust. Soc. Am. 28, 416-426 (1956).

3. SUBJECTIVE OCTAVES (S. B. Thesis)

An experiment was performed to determine, for a given reference frequency, the frequency ratios corresponding to a subject's estimate of the 1st upper octave, the 2nd upper octave, and the 1st lower octave. In each case, the estimate was obtained by presenting the subject with a sequence of two alternating tones, one of which was fixed and one of which was variable, and instructing the subject to adjust the variable tone to the required octave. The results indicate that there is a general tendency for the estimates of the 1st and 2nd octaves to exceed the frequency ratios 2:1 and 4:1, respectively. In most cases, the results were consistent with those obtained by Ward on "subjective musical pitch."[1]

D. Assael

References

1. W. D. Ward, "Subjective Musical Pitch," J. Acoust. Soc. Am. 26, 369-380 (1954).

4. JUST-NOTICEABLE DIFFERENCES IN FREQUENCY RATIO (S.M. Thesis)

It is well known that our natural musical scale employs tones whose frequencies are related by simple whole numbers. A sequence of tones in this scale sounds "natural," whereas sequences of tones whose frequencies form more complicated ratios sound "strange" or "unnatural." The purpose of this project was to determine whether or not this phenomenon is reflected in the auditory system's ability to detect small changes in frequency ratio. Specifically, an attempt was made to determine the just-noticeable difference, Δk, in frequency ratio, k, in the vicinity of the octave ($1.90 \leq k \leq 2.10$) and at the major third ($k = 1.25$). The results of this work indicate that in the frequency region 350-1000 Hz and in the frequency-ratio region $1.25 \leq k \leq 2.10$, the Weber fraction $\Delta k/k$ is independent of k and has a value of approximately 0.006.

A. J. Houtsma

5. CBL 16-B: AN INSTRUMENT FOR MULTISUBJECT TWO-ALTERNATIVE FORCED-CHOICE EXPERIMENTS

CBL 16-B was designed to make random selections between two stimuli in a two-alternative forced-choice experiment, and to decode, record, and display the answers of up to 10 subjects simultaneously. The apparatus allows the experimenter considerable freedom in the choice and timing of the stimuli, and permits him to control the feedback of information to the subjects concerning correctness of response. It also allows him to control the probability of presentation and to observe the current and cumulative performance of the subjects. When used in the multisubject mode, presentations are paced by external timing devices. When used in the single-subject mode, the subject may be allowed to pace the presentations himself. Interlock mechanisms prevent the subjects from answering more than once on a given trial. When used in conjunction with a paper-tape punch, CBL 16-B provides a complete record of the experiment suitable for computer analysis. Although this instrument was designed primarily for two-alternative forced-choice experiments with up to 10 subjects, it can also be used in experiments in which the response set consists of more than two elements, provided the number of subjects is appropriately limited.

L. Braida, N. Jordan

6. PSYCHLOPS: A SYSTEM FOR USING THE PDP-4 COMPUTER FOR ON-LINE ADAPTIVE PSYCHOPHYSICAL EXPERIMENTS

A system of computer programs, called "PSYCHLOPS," has been developed for using the PDP-4 computer on-line to conduct psychophysical experiments. Although any sort of experiment may be performed with this system, the power of the computer is not generally needed unless the experiment is adaptive. (An adaptive experiment is one in which the parameters of each stimulus presentation may be a function of the past record of the subject's responses.)

Using the PDP-4 remote console as an interface, the computer can control a variety of units, which in turn generate and shape the stimuli that reach the subject. Output from the remote console's digital-to-analog converter may be used to control a voltage-controlled oscillator, or for any other purpose. Level outputs from a remote console lamp register are used to set a digitally controlled attenuator, and to generate pulses which may be used to control electronic switches, feedback lights, and so on. The subject may signal the computer via the remote console trigger inputs.

The PSYCHLOPS programs handle all of the stimulus presentation timing, and record all responses by the subject. A user of the system wishing to conduct a particular experiment need supply only three things. First, he must give a table specifying all parameters of a stimulus presentation. This table may be altered under program control between stimulus presentations. Second, he must give a machine-language subroutine that computes, after each subject response, the parameters of the next stimulus presentation. Finally, he must give a machine-language subroutine with final output instructions.

When writing his two subroutines, a PSYCHLOPS user has at his disposal a large number of useful subroutines that are included in the system. These subroutines perform such services as table lookup, pseudo-random digit generation, and the formation of DO loops (as in FORTRAN), among others. Also, all output is handled through PSYCHLOPS subroutines. The user may give print or punch output commands at any time, and they will be properly processed by the system, in the program interrupt mode, without interfering with the stimulus and response timing.

To use the system, the user simply assembles his source tapes with the PSYCHLOPS system tapes. The remote console is wheeled over to the analog equipment rack, and connected to the appropriate units. Operation of the system may then be directed via the remote console lever switches, and, if necessary, the computer teletype keyboard.

The system has now been in use for some time, although it is still undergoing final debugging. Preliminary documentation is available. It has proved to be fairly easy to use PSYCHLOPS to conduct complicated adaptive experiments. The ease with which experiments may be altered merely by making small program changes makes the system particularly useful for experiments that are in the developmental stage.

L. Krakauer

C. GENERAL-PURPOSE COMPUTER FACILITY

During the past 18 months, we have undertaken to integrate a medium-sized digital computer (Digital Equipment Corporation PDP-4) into our laboratory facilities. This computation system provides a versatile tool for members of the group who are working on a variety of different projects. The computer is located in the center of the laboratory and has been specially adapted to handle easily real-time, on-line experimental problems. The facility contains an analog-to-digital conversion system, analog display, and analog outputs, a special real-time clock, a magnetic tape system for mass storage, a special switch and digital signal interface, and provisions for operating the computer remotely from the experimental stations. These features offer many of the conveniences of the LINC computer system,[1] but in a substantially larger and more powerful machine.

The full power of the computer can be focused on a particular problem simply by writing an appropriate program. This enables the computer to replace a variety of special-purpose devices, each built to do a specific job of data handling or experimental control. The computer system offers additionally more power and flexibility than are usually obtainable in a special-purpose device for a single application.

As examples of applications in connection with electrophysiological experiments, the PDP-4 computer has been used to perform quite flexible average-response computations with a minimum interval between points as low as 8.3 μsec, up to 16 simultaneous averages, variable time-base averaging, and averaging data simultaneously before and after a trigger or synchronizing pulse. The computer has been used to compute histograms of firing patterns of single neurons with simultaneous computation and display of both interval and post stimulus time (PST) histograms for up to 4 different units. The simultaneous computation of average responses and histograms for single neurons has also been done.

All of these operations can be done in "real time" and the programs are equally well-suited for use during an experiment or for later off-line processing from analog magnetic tape. In many instances, however, the last advantage offers substantial savings of computation time.

In another application, the PDP-4 computer was used to determine the dependence of the amplitude of evoked responses on the phase of on-going alpha activity. Stimuli were randomly presented and EEG and stimulus information recorded on digital magnetic tape. The tape was then scanned for the occurrence of the alpha rhythm. Individual evoked responses were separated according to the phase of the alpha cycle in which they occurred. Average response computations were then made for a particular alpha phase. A family of average evoked responses showed the dependence of evoked response on alpha phase. This type of analysis was possible because the data were temporarily stored, and average evoked responses were computed after decisions on alpha occurrence and phase had been made.

In one psychophysical study,[2] the PDP-4 computer used the cathode-ray tube display to present a visual stimulus to a number of subjects (up to 8) in a forced-choice experiment. Simultaneously, the computer checked individual response keys operated by each subject. The response times were recorded, displayed, and various statistics could be computed. The system can be arranged to present automatically randomly distributed stimuli and to record performance. Similar uses include the computer control of auditory signals in forced-choice experiments.

The computer has also been used in waveform detection problems to analyze electrical activity observed in explanted chick embryo cultures,[3] and to evaluate, manipulate or display data in a variety of ways.

1. Hardware Description

The computer shown in Fig. XXI-1.is a basic Digital Equipment Corporation PDP-4 computer with 8192 words of 18-bit memory (8.333 μsec/cycle). The system includes an IBM compatible magnetic tape unit and a 16-channel analog-to-digital system with an accuracy of 1 part in 256. Also, part of the system consists of hardware multiply and divide, a special real-time clock, and an analog system that drives a cathode-ray tube display and x-y plotter. A special relay, a switch, and a digital signal interface complete the system.

The 8.33-μsec cycle time is moderately fast and sufficient for most purposes. The machine time is accurately controlled, and hence used by program loops as a time base. The 18-bit word memory is usually sufficient for calculations involving analog data (8 bits), and there is no need for multiple precision arithmetic in handling most of the data. The 8192 words of memory are all directly addressible, and allow rather long and involved programs to reside in memory together with a substantial amount of data. This allows a rather elaborate data display program to be used essentially as a subroutine. The magnetic tape system provides mass storage for data and programs, and also permits transfer of data to or from other more elaborate systems.

The A-D conversion system is easily programmed and provides 16 inputs to a single 8-bit converter. The maximum sample rate is 120,000 samples/sec, while the maximum continuous rate of analog conversion to IBM format magnetic tape is 20,000 samples/sec.

2. Remote Operation

A remote console has been constructed to provide convenient and efficient use of the PDP-4 for on-line use in experimental control and analysis of data. This remote console is shown in the left foreground of Fig. XXI-2. Five switch registers (18 bits) are

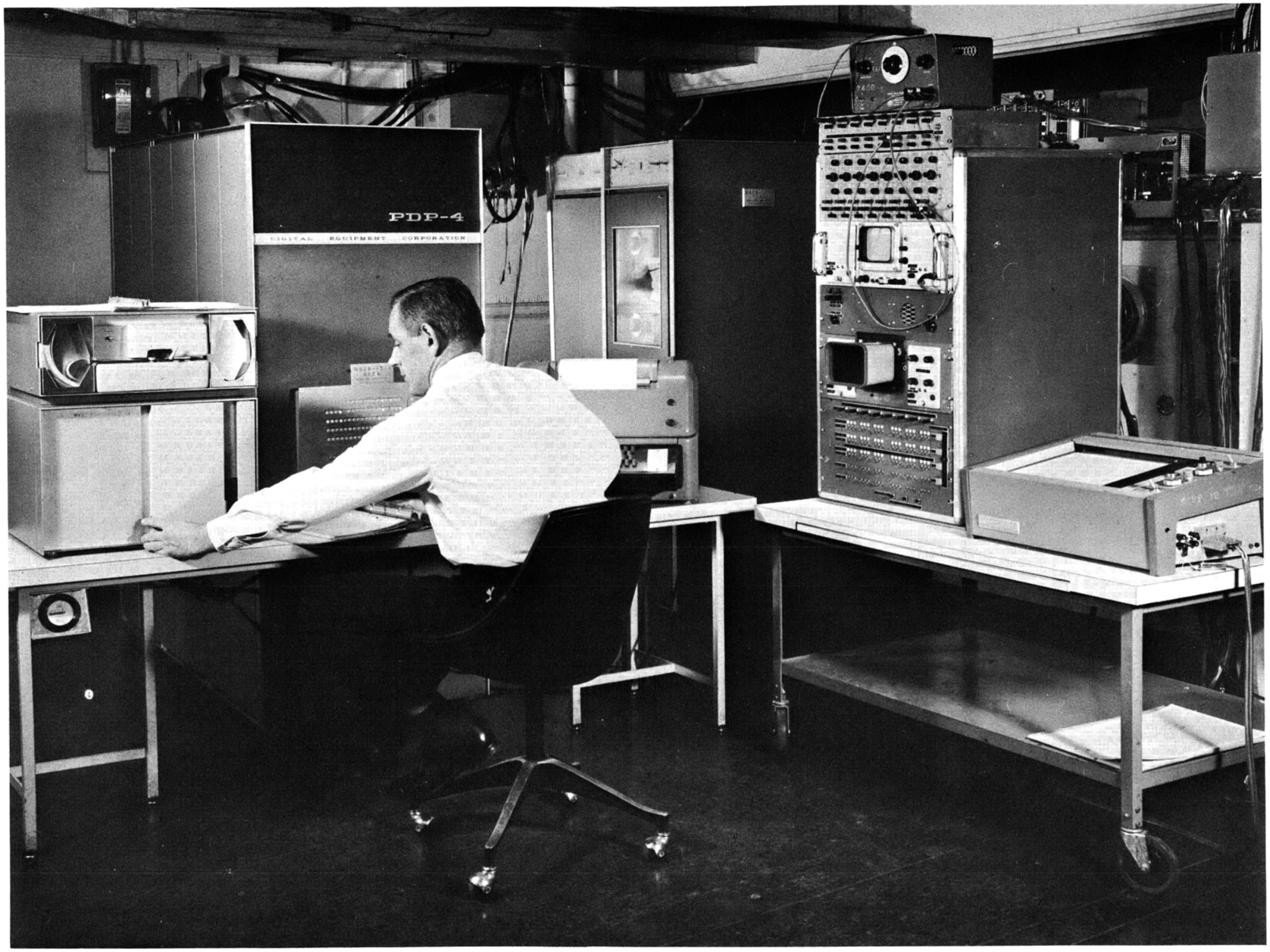


Fig. XXI-1. General view of the PDP-4 computer system.

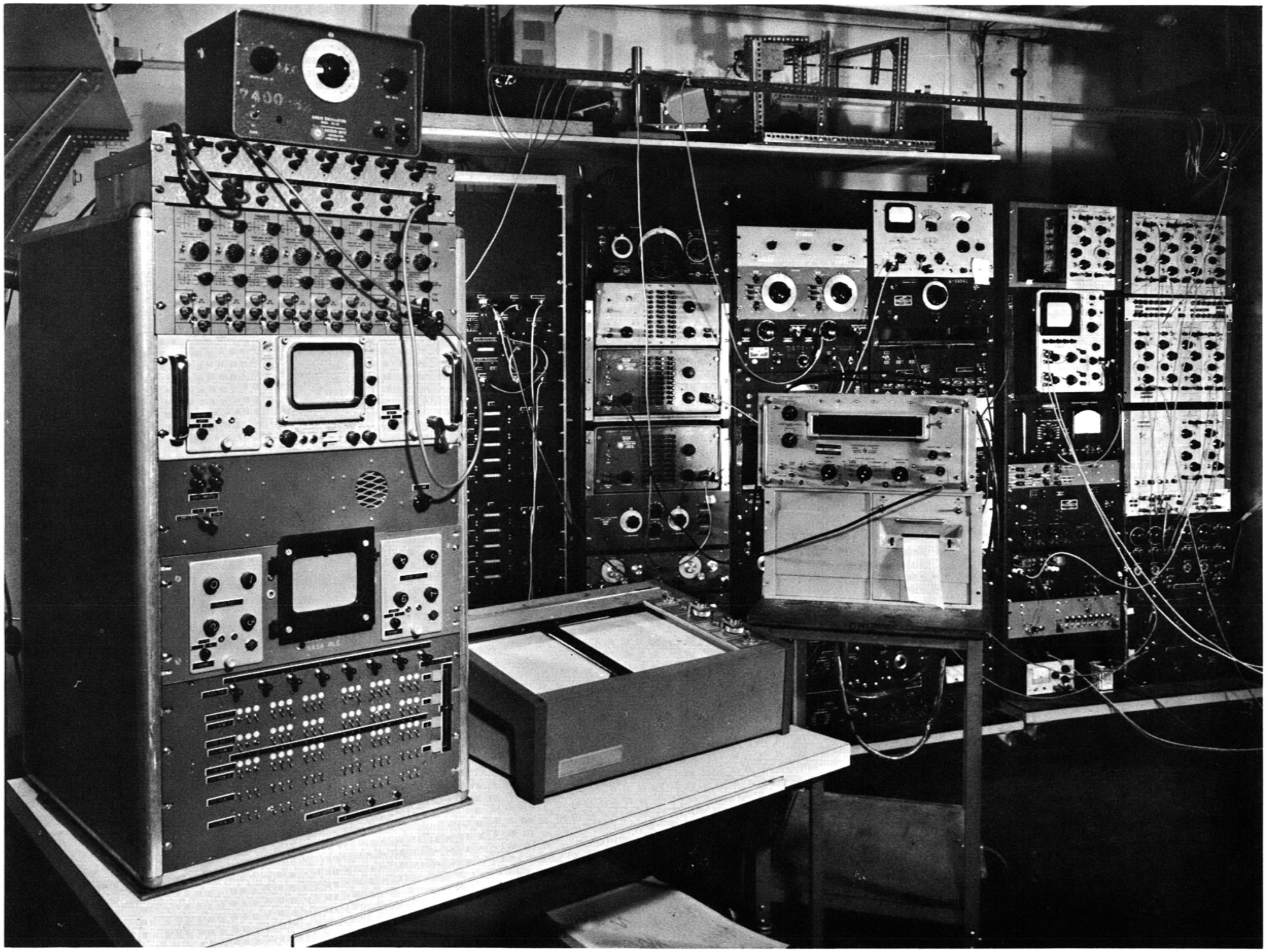


Fig. XXI-2. Remote console (left) as employed in a psychophysical experiment.

provided for the control of experimental parameters. The oscilloscope display presents both alphanumeric text and graphical data. The potentiometers located on either side of the display provide additional controls for various parameters. Connectors are provided on the console for inputs to the A-D conversion system, pulse inputs for synchronizing the computer to experiments, and relay and digital output lines for controlling experiments. Forty-eight indicator lights provide additional output to the operator, while lever and push-button switches may be used to control computer operation. The entire remote console, connected by permanent cabling, can be moved to any of the experimental stations in the laboratory. Programs are generally written to make use of the remote console for input, output, and control.

3. Summary

A PDP-4 computer has been incorporated into the facilities of our group. The computer is used to assist with a number of different experimental problems. A number of special features have been added to make the PDP-4 especially well suited for real-time, on-line use in electrophysiological and psychophysical experiments for both experimental control and data analysis. Because of the flexibility of the computer, it is possible for a number of different users to use the same machine, and thus allow each to have access to a more powerful system than would be easily justifiable for a single user.

R. J. Clayton

References

1. W. A. Clark, "The LINC," a paper presented at the Annual Meeting, National Academy of Sciences, National Research Council, Washington, D. C., April 12, 1962.
2. S. K. Burns, Course 6. 37 Class Notes, M. I. T. , 1966.
3. A. W. B. Cunningham, R. R. Rojas-Corona, J. A. Freeman, and P. H. Levine, "Tissue Dynamics of Brain Tissue in vitro," Quarterly Progress Report No. 79, Research Laboratory of Electronics, M. I. T. , October 15, 1965, pp. 247-261.

D. TISSUE DYNAMICS OF BRAIN TISSUE *IN VITRO*

Few microelectrode studies on the electrophysiology of brain tissue in culture have been published thus far. In 1962, Hild and Tasaki[1] reported cellular membrane potentials (50 mV or less and electrically stimulated action potentials (up to 70 mV) from cells within explants of new born rat or 7-14 day-old kitten cerebellar tissue. More recently, Crain and Bornstein[2] have observed after-discharges lasting 4-5 seconds caused by a single electrical stimulus applied to long-term tissue cultures of neonatal mouse cerebellar and cerebral cortex. These authors present strong evidence that functional, as well as anatomical, connections between nerve cells are present in these long-term brain-tissue cultures, thereby substantiating the potentialities of electrophysiological studies of the behavior of brain tissue in vitro.

For the past few months, we have been conducting microelectrode investigations of spontaneous electrical activity occurring in small pieces (1 mm^3) of living brain tissue in a suitable in vitro environment. In 1959, such spontaneous potentials were first detected by our group, using gross platinum electrodes. These potentials were spontaneous in the sense that we did not knowingly stimulate the tissues, mechanically or otherwise. Subsequent experiments (using gross electrodes) showed that these potentials respond reversibly to anesthetics, changes in the O_2, N_2, CO_2 concentrations[3] in the immediate environment of the explants, the addition of drugs such as strychinne and brucine, and changes in termperature. These changes altered the spontaneous activity in a manner similar to that expected from experience with in vivo preparations.

The microelectrode observations reported here were carried out on 14 day-old chick embryo telencephalic tissue (that used in the gross platinum electrode experiments). Details of the culture technique employed in these experiments have been reported previously.[4]

The culture chamber was a piece of glass tubing, 18 mm in diameter, 4.3 mm high, 1.5 mm thick, with a 4-mm arc-shaped gap in the wall. Round coverglasses, 18 mm in diameter, were cemented on either end of the glass ring to enclose a piece of fritted glass of coarse porosity which filled the chamber, except for a sector opposite the opening in the glass ring. A 40-gauge platinum-wire recording electrode, insulated to its tip with Teflon, lay between the upper coverglass and the frit, with its tip at the angle of the missing sector of fritted glass.

The frit was saturated with nutrient fluid which differed from that previously reported,[3] in that chick serum was used as a source of protein and 1 cc each of a concentrated solution of methylene blue in balanced salt solution, multivitamin solution and amino-acid solution was added to each 100 cc of nutrient fluid. Methylene blue's well-known property of vitally staining the granules in neurons was used, along with phase-contrast microscopy, to identify neurons within the explants. The concentration of methylene blue used here was approximately 1 per cent of that used by others for staining neurons. Previous experiments on the spontaneous activity detected with platinum gross electrodes showed that the presence of such concentrations of methylene blue increased the amplitude of the spontaneous potentials and revived such activity once it had ceased. Methylene blue's known depolarizing effect may be a possible factor in causing these changes. In our experience, spontaneous activity could be detected by the microelectrode in cultures with or without methylene blue.

Approximately 1 mm^3 of the posterolateral aspect of the right telencephalic lobe of 14-day-old chick embryo brain was excised rapidly with the sharp edge of a razor and floated in cold nutrient fluid to remove blood and membranes. Within 15 seconds, the tissue was transferred into the specially designed microchamber (described above) containing warm (35°C) nutrient fluid.

The microchambers containing the excised tissue were transferred immediately after explantation to an incubator at 35°C. The microelectrode insertions were made within 48 hours after explantation. For this, the microchamber was carefully transferred to a specially designed microscope stage incubator,[4] which was maintained as close to 35°C and 100 per cent humidity as possible. Groups of spontaneous potentials similar in form to those previously reported[4] were detected by the platinum gross electrodes within these microchambers.

In any explant, only the cells within a small distance of surface oxygen and of a source of nutrient can survive. Calculation and experiment indicate that with a tissue of respiratory rate of some 100 micromoles of O_2 per gram fresh wt. per hour, such as cerebral cortex, diffusion of oxygen from a solution in equilibrium with an atmosphere of 100 per cent O_2 gives adequate oxygenation to a depth of 0.2 mm.[5] This value is somewhat less if atmospheric O_2 is used. With the use of dimensions of 1 mm^2 for surface area and depth of 0.1 mm for the live portion of tissue, and the volume of pyramidal cell (soma plus apical dendrite) approximated as a sphere of radius 50 μ, the number of living cells in the tissues used here turns out to be 200.

The microelectrodes were 3MKCL-filled glass micropipettes with tip diameters of less than 1 μ, which typically gave the electrodes resistances between 15 and 50 MΩ. A Medistor headstage with negative capacity compensation was used for the first-stage amplification (x10), and its output was fed into both a Dana DC amplifier (x30) and the vertical (AC) amplifier of a Tektronix 502A oscilloscope. The outputs from all 3 devices were recorded on a modified P105 Ampex tape recorder at 7 1/2 ips (1.25 kc).

Placement of the electrode either into the film of nutrient fluid surrounding the explant or into the explant itself was done under direct vision.

The durations of the spontaneous signals detected with a microelectrode were divided into three overlapping classes.

1. Long duration signals lasting from 1/3 to 1 minute.
2. Intermediate-duration signals lasting 50-500 msec, similar to those detected with platinum gross electrodes.
3. Short-duration signals lasting 1 to 2 msec, similar to "extra cellular" and "intracellular" potentials observed *in vivo*.

The general structure of the activity was one of repetitive patterned sequences of the intermediate-duration signals separated by long periods (as long as 12 minutes) of no detectable activity. The long-duration signals only occurred as parts of these sequences. Short-duration signals were detected in the explant, and occurred in bursts or alone. The intervals between these bursts were often regular and comparable to the interval between sequences of the intermediate signals.

Figure XXI-3 shows a typical sequence of intermediate signals detected by a microelectrode in the nutrient fluid around the explant. In this figure the long-duration signal is the long rise off the DC base line which occurs during the sequence. Many consecutive sequences of intermediate signals were detected in the film of nutrient fluid surrounding the explant or within the tissue, and appeared to originate from discrete foci within the explant. A microelectrode placed close to the explant and moved along the periphery of the explant detected activity at some points in the film of nutrient fluid but not in others. The patterned sequences of intermediate-duration potentials detected in this way differ significantly in these different small regions of activity. A 200-300 μ lateral movement of the microelectride tip may make the activity no longer detectable, and return of the tip to its original position reveals the original pattern of activity. The localness of the activity within the explant was suspected from multiple gross electrode studies on similar explants.[4]

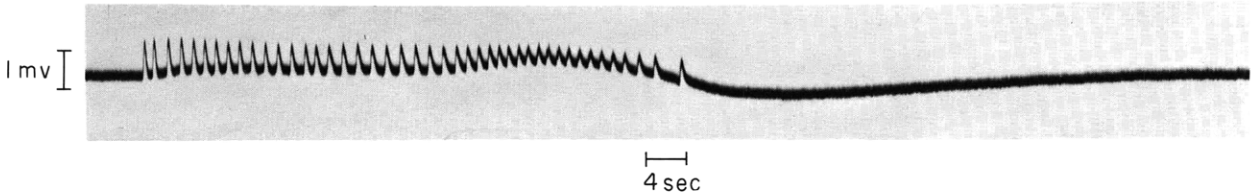


Fig. XXI-3. D-C recording of a typical sequence of potentials of intermediate duration detected in the nutrient fluid around the explant. Positive deflection upward.

Figure XXI-4 shows bursts of extracellular spikes (1-2 msec) detected within the

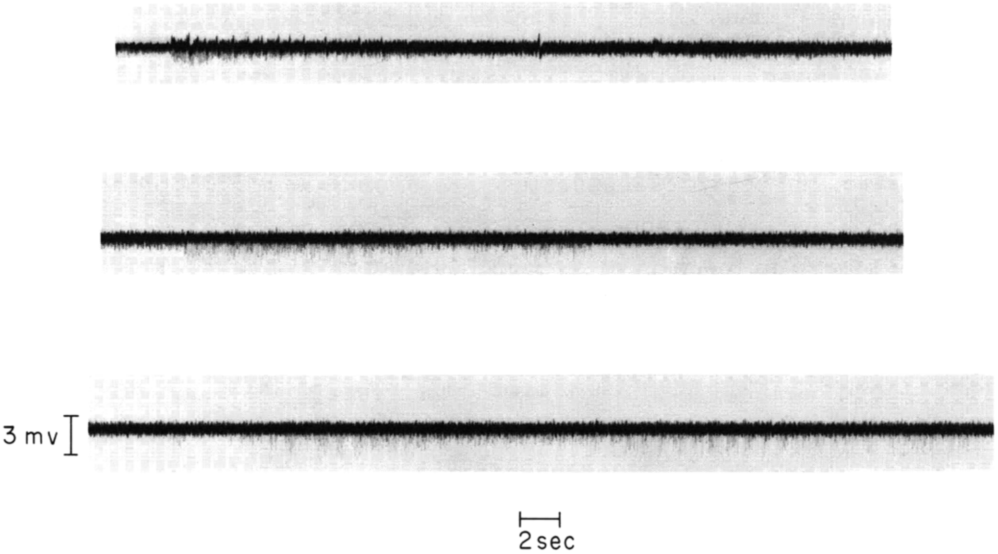
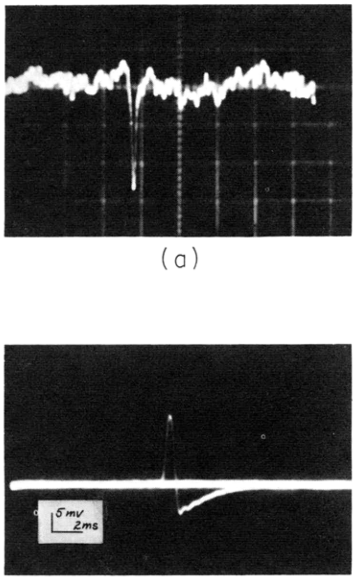


Fig. XXI-4. A-C recording of negative "extracellular" spikes detected within an explant. A sequence of potentials of intermediate duration can be seen occurring with the burst of extracellular potentials in the upper film.

explant. The interval between these bursts was approximately 5-6 minutes. In this figure a sequence of intermediate signals can be seen occurring simultaneously with a burst of short-duration potentials. Figure XXI-5a shows details of a typical "extracellular" spike in Fig. XXI-4. Figure XXI-5b shows an intracellular potential, one of a burst of potentials, detected after visually penetrating a cell whose granules were stained with Methylene Blue. The spike potentials were preceded by a 30-mV DC shift. The discharge pattern of the cell lasted approximately 3 minutes and consisted of a series of bursts of activity whose durations varied. Thus the neurons in these explants appear to be physiologically active.



(a)

(b)

Fig. XXI-5.

(a) Details of a typical "extracellular" spike shown in Fig. XXI-4. Positive deflection upward. Horizontal scale: 5 msec/cm. Vertical scale: 1.25 mV/cm. (b) Details of an "intracellular" potential (AC recording).

To summarize, three types of spontaneous signals arise within the explant from living cells having the appearance of neurons. These signals can be detected with a microelectrode placed in the film of nutrient fluid surrounding the tissue or within the tissue close to groups of histologically identifiable neurons. The intermediate signals occurred in repetitive patterned sequences similar to those previously reported using gross electrodes with similar explants. Since the long-duration signals occurred with the intermediate signals and the intermediate spikes were detected simultaneously with the fast spikes, presumably all three types of activity are related.

A full report on this work has been submitted by the first author to the Department of Electrical Engineering, M.I.T., in June 1966, as an S.M. thesis.

P. H. O'Lague, A. W. B. Cunningham

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E. TIME PATTERN OF COMPLEX BASILAR-MEMBRANE VIBRATIONS AND ITS RELATION TO PITCH PHENOMENA

The tonal residue pitch[1,2] that arises in the perception of complex sounds presents an interesting subject for study for psychologists dealing with the perceptual attributes of hearing, as well as those concerned with the mechanisms of hearing. Understanding of the processes involved in production of the residue effect may help in the solution of a number of audition problems and also contribute to knowledge about the conversion of mechanical sound vibrations into perceptive manifestations.

The residue effect can be demonstrated under a variety of conditions but the most studied[2,3] is that of a sinusoidally modulated pure tone, e.g., a pressure wave described by

$$p(t) = P(1+\cos\omega t)\cos\omega_o t, \tag{1}$$

where typically $\omega_o/2\pi$ is of the order of 600-4000 Hz and $\omega/2\pi$ is the order of 80-500 Hz. The subjective pitch (residue pitch) corresponding to such a complex sound is approximately equal to $\omega/2\pi$, but _not_ precisely so unless ω_o is an integer multiple of ω. To a first approximation, the residue pitch is given by

$$\omega_r = \omega + \frac{\Delta\omega}{n}, \tag{2}$$

where n is an integer, and $\Delta\omega$ is determined by

$$\omega_o = n\omega + \Delta\omega. \tag{3}$$

(Under appropriate circumstances, listeners can identify several pitches for the same pressure wave corresponding to values of n differing from the integer nearest ω_o/ω by ±1.) The pitch given by (2) can be explained by observing that for ω/ω_o not equal to an integer the peaks of the carrier do not occur precisely at the peaks of the modulating waveform. The spacing between carrier peaks near the peaks of the modulating waveform is, in fact, $2\pi/\omega_r$. Presumably, then, the residue pitch is largely determined by this time interval. Physiological manifestations accompanying the process of conversion of the basilar membrane vibrations into neuronal events[4] seem to make such an assumption possible.

More careful measurements have shown, however, that there is a second residue effect[2] resulting in a slightly larger pitch deviation from ω than (2) would suggest. No convincing explanation for this second effect has been proposed. In the following discussion it will be argued that a possible explanation lies in the asymmetry introduced in the sideband energy as a result of the mechanical filtering of p(t) by the middle and inner ear.

In accordance with (1) and (3) we assume that the pressure spectrum of the stimulating signal impinging on the tympanic membrane can be presented (for 100% modulation) as

$$p(t) = P\left\{\frac{1}{2}\cos\left[(n-1)\omega+\Delta\omega\right]t + \cos\left[n\omega+\Delta\omega\right]t + \frac{1}{2}\cos\left[(n+1)\omega+\Delta\omega\right]t\right\}. \tag{4}$$

We shall also assume that for the intensities of interest the middle ear and basilar membrane act as a linear mechanical device. The superimposed effect of the incoming stimulating components can be computed for any particular point of the membrane. The most important point is presumably that which is most sensitive to the central frequency component of the stimulus. In order to perform the computation for the displacement at a particular location on the basilar membrane, the transfer characteristics for the signal components would have to be known. Possible computational models for basilar-membrane displacements has been presented by Flanagan[5] and Siebert.[6] It will be sufficient for our purposes merely to suggest the algebraic form of the result.

At the point which is maximally sensitive to the frequency ω_o presumably the energy in both side bands will be reduced relative to the carrier, but the upper side band will be reduced more than the lower, since the tuning curves are steeper on the high-frequency side. For narrow-band signals we may assume that the phase characteristic is approximately linear and hence choosing the time reference appropriately may express the displacement of the membrane as

$$d(t) = D\left\{\left(\frac{a+\delta}{2}\right)\cos\left[(\omega_o-\omega)t+\phi\right] + \cos\omega_o t + \left(\frac{a-\delta}{2}\right)\cos\left[(\omega_o+\omega)t-\phi\right]\right\}, \tag{5}$$

where δ (which we shall assume is small) represents the effect of the asymmetry in the tuning curve. As a result, d(t) shows both amplitude and phase modulation; specifically, we may write (for small δ)

$$d(t) \approx D[1+a\cos(\omega t-\phi)] \cos\left[\omega_o t - \frac{\delta \sin(\omega t-\phi)}{1 + a\cos(\omega t-\phi)}\right]. \tag{6}$$

The phase modulation in (6) can, we believe, account for the second residue effect as we shall now show. The envelope of d(t) has a maximum at $\omega t - \phi = 0$. In the vicinity of $t = \phi/\omega$ we may write the argument of the carrier approximately as

$$\omega_o t - \frac{\delta(\omega t-\phi)}{1 + a}, \tag{7}$$

and thus the carrier maximum near $t = \phi/\omega$ will occur at

$$\omega_o t - \frac{\delta(\omega t-\phi)}{1 + a} = 0 \tag{8}$$

or

$$t = \frac{-\delta\phi}{\omega_o(1+a) - \delta\omega}. \tag{9}$$

Similarly, the next maximum of the envelope is at $\omega t - \phi = 2\pi$ and in that vicinity the carrier has a maximum at

$$\omega_o t - \frac{\delta(\omega t-\phi-2\pi)}{1 + a} = n2\pi \tag{10}$$

or

$$t = \frac{2\pi n(1+a) - 2\pi\delta - \delta\phi}{\omega_o(1+a) - \delta\omega}. \tag{11}$$

Subtracting (9) from (11) to get the time interval between the peaks (which we assume is the reciprocal of the residue pitch, $\omega_r/2\pi$) we obtain

$$\omega_r = \frac{\omega_o - \frac{\delta\omega}{1 + a}}{n - \frac{\delta}{1 + a}} = \omega + \frac{\Delta\omega}{n - \frac{\delta}{1 + a}}. \tag{12}$$

Compared with (2) this shows exactly the effect desired, i.e., an increased slope in the plot of ω_r vs $\Delta\omega$.

The calculation has, of course, considered only one spot along the basilar membrane – albeit the most sensitive one – as contributing to the perception of pitch. Other nearby areas will certainly contribute, however, and will have a different timing between peaks than that implied by (12). Further studies are in progress.

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F. STATISTICAL THEORY OF FIELDS

In this report we continue to explore some of the consequences of the statistical theory of fields described in Quarterly Progress Report No. 80 (pages 243-247). Our calculations will be based on a soluble neutral scalar field, mainly to illustrate the general dynamical features. It will become quite clear that if the theory is valid other fields can be treated similarly. For each problem only a minimum of statistical features will be introduced to keep the number of parameters as low as possible. For example, in a self-energy problem or the structure of the source, only the total momentum of each mode is assumed to be known, whereas more realistically a knowledge of the average field $\bar{\phi}$ could be added to correspond to coulomb behavior for large distance. In the present calculations this behavior is achieved by a boundary condition on the field.

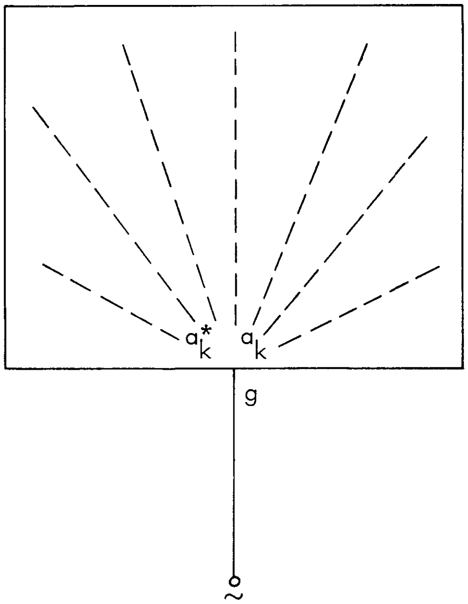

Fig. XXI-6. The cavity.

For simplicity, let us first consider the case of a cavity field. This problem is of importance not only because it is the original area in which the quantum hypothesis was first introduced by Planck but also because it can serve as a model in which the concepts of equilibrium, interaction, coherence, and the processes of production, scattering, detection, and observation, can be examined in their bare essentials. In fact, in our theory the concept of an elementary particle has a close kinship with radiation trapped in a cavity. We start with a cavity of rigidly reflecting walls and provide a means of interacting with the radiation inside the cavity through a coupling placed on the wall (Fig. XXI-6). The coupling can serve as a means of injecting radiation into the cavity, but it can also serve as a detector through which we may examine the state of the cavity. With this wider concept of a source in mind, let us write the Hamiltonian of the system in the rest frame of the cavity. Since the field is real, we have

$$H = \sum_k \omega_k\left(a_k^* a_k + \frac{1}{2}\right) + H_w - \int \sum_k g(2\omega_k V)^{-1/2}\left(a_k^* e^{-ikx} + a_k e^{ikx}\right) F(t,x)\, d^3x, \qquad (29)$$

where H_w is the Hamiltonian of the rest of the system including the walls. Whatever energy is drawn from the cavity will, of course, go into H_w; aside from this, we temporarily ignore the function of H_w and concentrate on the cavity and its coupling.

The following field-theoretical results are derivable[1] through the conventional action principle: (a) Starting from the ground state of the cavity, a prescribed time-dependent function $F(t,x) = F(t)$ will inject into the cavity for each frequency a Poisson distribution $P_n = e^{-N} N^n/n!$, where $N = g^2(2\omega\gamma)^{-1}|F(\omega)|^2$. $F(\omega)$ is the Fourier transform of the function $F(t)$. (b) Poisson distributions are coherent superpositions corresponding to minimum uncertainty wave packets. They can be obtained directly from the ground state by unitary transformations $U(\lambda) = e^{\lambda a^* - \lambda^* a}$, where $|\lambda| = g(2\omega_k V)^{-1}|F(\omega)| = \overline{N}^{1/2}$. (c) The energy transfer to the cavity is $\Delta\mathscr{E} = g^2(2\omega_k V)^{-1}|F(\omega)|^2$, which depends only on the Fourier component of the function $F(t)$. (d) Poisson distributions are localizable, since they are correlated only with the prescribed source at the given point x. (e) The effect of a time-independent interaction $F(t,x) = F(x)$ is to displace the system of states of the cavity into a new system, where $b_k = a_k - g\left(2\omega_k^3 V\right)^{-1/2} F_k$. Here, F_k is the Fourier component $F_k = (2\pi)^{-3} \int F(x)\, e^{-ikx}\, dx$. The number of particles (virtual) is in this case $N_k = g^2\left(2\omega_k^3 V\right)^{-1} |F_k|^2$ and they still obey a Poisson distribution. The total shift in energy is $\mathscr{E}_o = -\sum_k g^2\left(2\omega_k^2 V\right)^{-1} |F_k|^2$. All of these are actually elementary consequences of the solution $|out\rangle = e^{-iW_I}|in\rangle$, where $W_I = \int \sum_k g(2\omega_k V)^{-1/2} (a^* e^{-ipx} + a\, e^{ipx})\, F(t,x)\, d^3x dt$. To see it clearly, take item (a) with $|in\rangle = |0\rangle$ and assume that only one frequency and only $F(t)$ are involved. Then $W_I = g(2\omega\gamma)^{-1}(a^* F(\omega) + aF^*(\omega))$. Using the Baker-Hausdorff formula and the fact that $e^{aF^*(\omega)}|0\rangle = |0\rangle$, we have $|out\rangle = e^{-|\lambda|^2/2} e^{\lambda a^*}|0\rangle = e^{-|\lambda|^2/2} \sum_n \frac{\lambda^n (a^*)^n}{n!}|0\rangle = e^{-\overline{N}/2} \sum_n (\overline{N}^n/n!)^{1/2}|n\rangle$, from which the Poisson law follows.

In connection with our theory we now make the following remarks: (a) Poisson distributions correspond to states of zero entropy. (b) No prescribed interaction term can increase the entropy even if we start from a state of finite entropy. (c) The energy of a cavity in contact with a point source or a δ-pulse necessarily diverges. The proofs are quite elementary. Poisson distributions can be shown to have zero entropy by direct computation. In our context this is almost obvious because we are working under a constraint $S = 0$. The second point corresponds to the circumstance that $\Delta S = 0$, since the transformation is strictly unitary. The third point follows from the fact that for δ-interaction $F_k = 1$, and for δ-pulse $F(\omega) = 1$, which leads to divergent results.[1] For the sake of completeness we may also give, without proof, the case of a Planck distribution plus a coherent state. In this case the distribution is $\sigma = (1 - e^{-2\omega\zeta})^{1/2}\, e^{-\zeta\omega(a^* + \alpha)(a + \alpha)}$

with energy $\overline{\mathscr{E}} = \omega\left(\overline{n}+\frac{1}{2}\right) + \omega/(e^{2\omega\zeta} - 1)$ and entropy $\overline{S} = -\frac{d}{d\gamma}\gamma \ln (1 - e^{-1/\gamma})$, $\gamma\omega = \frac{1}{2\zeta'} = \frac{1}{2\zeta} - \overline{n}\omega$. The characteristic function of this distribution is $C_{\mathscr{E}}(i\xi) = e^{i\xi\overline{\phi}-\xi^2\overline{\mathscr{E}}/2}$, where ϕ is just the sinusoidal waveform.

Let us now consider how our new concepts may help us. We recall that at the beginning of this century there was a problem of ultraviolet divergence for the cavity radiation. This difficulty was removed by Planck with the introduction of the idea of energy quanta. Note, however, that the quantum idea by itself did not remove the difficulty. Rather, the introduction of the quantum concept in connection with statistics accomplished the desired result. The decreasing exponentials that cut off the efficiency of the high-energy quanta are provided by the statistical part. Without the aid of statistics (that is, when all states are equally probable) the field quantization would have led to $\mathscr{E}_\nu = \sum_n (8\pi/c^3)\,\nu^2(nh\nu)$ which diverges even worse than the Rayleigh-Jeans distribution. Thus, quantum field theory does not provide, without the aid of its proper statistics, a solution to the original problem of the cavity radiation, and we should not expect it to give finite results when more elusive concepts such as the virtual particles and their energies are involved.

In our theory the virtual particles are on an equal footing with the real particles, and we must try to remove the self-energy difficulty in a manner similar to cavity divergence. A way of doing this was presented in the previous report. Now we exploit further this simple model with regard to the scattering and production processes.

The apparent spread of the source may be calculated as,

$$\rho(r) = \frac{g}{(2\pi)^3}\int F_k\, e^{+ik\cdot r}\, d^3k = \frac{g}{(2\pi)^3}\int \frac{k^{1/2}\, d^3k\, e^{ik\cdot r}}{(e^{2\mu k} - 1)^{1/2}}, \tag{34}$$

which at large r vanishes, which corresponds to Coulomb behavior. For small distances, $r \sim \mu$, the source behaves in the rest frame as though it were an extended object. This behavior is reminiscent of the usual cutoff theories, but the similarity is illusory. Here the object is a statistical distribution of virtual particles and, in general, this cannot be interpreted as an extended body nor as a smearing of the δ-function.

Clearly, the nature of the source and the behavior of the function F(t, x) are not accessible to direct experimental examination. We may, however, infer from field theory that the source particle itself is a solution of some field equations, and, therefore, describable as coherent or incoherent superposition of waves, $F(t,x) \to \sum_k c_k\, e^{-p_k(\zeta_k+ix_k)}$ or $\int \sum_k \overline{\psi}_k\gamma^4\psi_k\, d^3k$, and so on.

We may now consider the behavior of the source point. Evidently, we cannot imagine it as permanently fixed or in a state of prescribed motion. Our concepts lead us to conclude that the behavior is more like a fluctuation depending on the situation and the particular statistics that it obeys. Here it finds itself in an incoherent superposition of virtual photons, and, like a particle in a heat bath, undergoes an unpredictable jittery motion. From the general entropy law we may infer that the two parts, the virtual cloud and the source particle, should be in a state of statistical equilibrium. If we assign to the source the parameter ζ^{μ}_{ψ} and to the cloud ζ^{μ}_{ϕ}, we may write $\zeta^{\mu}_{\psi} = \zeta^{\mu}_{\phi}$. Although the situation is no longer soluble in the usual sense and the full iteration process is required, we know ahead of time that the integrals are convergent. Let the total energy be

$$\overline{\mathscr{E}} = \overline{\mathscr{E}}_{\psi} + \overline{\mathscr{E}}_{\phi} \geqslant 0, \qquad \zeta^{r}_{\psi} = \zeta^{r}_{\phi} = \zeta, \tag{35}$$

which is to be identified as the observed rest mass. Bare masses, the coupling constant, and the additional statistical parameter, ζ, are then to be related. Since we have three phenomenalogical constants and four theoretical parameters, we must have an additional condition to determine them all. A reasonable assumption seems to be to invoke some partition postualte between the two representations ϕ and ψ. If one interprets this as $\overline{\mathscr{E}}_{\phi} = a\overline{\mathscr{E}}_{\psi}$, where a is a theoretically inferable constant, then the dynamics of the source could be considered reasonably complete, at least as far as the neutral scalar theory is concerned, although for electrodynamics the problem of gauge and extra complications caused by the magnetic moment have to be separately faced.

Coming to problems of more immediate experimental interest, we have examined scattering and production cross sections. Low-energy limits of the cross sections agree with the usual formulas. At extreme high energy, the exponential factors make their presence felt and all contributions tend to zero. This is due to the scarcity of high-momentum virtual particles which mediate the interactions, and can be understood by analogy to cutoff theories. The number of bosons produced in a Bremsstrahlung experiment thus behaves as

$$\overline{n} = \frac{g'^{2}}{(2\pi)^{3}} \int_{0}^{\infty} \frac{\mu\, dk}{e^{2\mu k} - 1}\, d\cos\theta\, d\phi \left[1 - \left(1 - \frac{\Delta p}{m}\cos\theta\right)^{-1}\right], \tag{38}$$

where Δp is the momentum transfer. At low energy we have the usual behavior, whereas at high energy the result is no longer divergent. It seems therefore, possible to test the theory with extreme high-energy scattering and production experiments. For example, deviations from the well-known Klein-Nishina formula (or pair production cross sections) are expected at extreme high energy. The magnitude of the deviations is not exactly deducible at the present stage, since we do not yet know the size of μ and what other interactions are involved for any given particle. All that we may infer within reason is that, if our ideas are valid, the theory is convergent, exponentials are there, and they will make their presence felt beyond some definite limit. This general feature would be of some importance with regard to meson theory. Since the statistical factors seem to provide convergence, irrespective of the strength of the coupling, the strong interaction physics may not necessarily fall outside field theoretical approach.

The theory is expected to lead to differences over the existing theory for bulk material at extremely low temperatures. Preliminary calculations show that critical temperatures for superfluid and superconducting materials would be affected. This comes about mainly because of different weighting over virtual phonons. Differences are, however, not as large as it might be expected at first sight, because of natural cutoff of high-energy phonons at wavelengths corresponding to lattice spacings. A systematic re-evaluation of contributions to specific heats and thermodynamic properties is in progress and might provide testing possibilities for the theory. A reconsideration of the Lamb shift in hydrogenlike atoms indicated that no observable difference is expected over the usual theory. Since the largest contributing factor in Lamb shift (~1015 Mc/sec) is the self-energy difference between a bound electron and a free electron, our statistical weight is expected to reduce the theoretical value $\Delta\mathscr{E}_{\text{Theor.}} = 1058.03$ Mc/sec slightly. Preliminary calculations indicate, however, that the difference $\Delta\mathscr{E}_{\text{Exp.}} - \Delta\mathscr{E}_{\text{Theor.}} = 0.26$ Mc/sec is too large, unless we give unrealistic values to ζ^{μ}. It is probably safer to assume that the present experimental difference is due to some other contribution and that the effect of the theory on Lamb shift is undetectably small. It is doubtful, at present, whether any new features are produced regarding the high-energy diffraction peaks or Regge-pole structure. In particular, the problem of mass spectrum seems as remote as ever; however, the problem of unstable particles seems to take some physical form. If the statistical theory presented here is valid, the ζ^{μ}-parameter, as applied to elementary systems, might be interpretable as a state index, and the conditions of two-way stability and metastability in the presence of all existing fields may have something to do with the mass spectrum. In this case the question of elementary-particle physics would appear to be shifted to the question of elementary fields. In this connection it would be interesting to study the implications of irreversibility as applied to elementary processes to see if new selection rules are implied. For example, it would appear that the β-decay increases entropy, and therefore the inverse process can take place only in relation to other processes which provide the necessary decrease. Similarly, annihilation of protons with antiprotons, which by themselves are stable, emission of a photon, and sending of a single quantum as a signal to some given direction should perhaps be counted as irreversible processes. We should take caution, however, with regard to such far out considerations before we have some experimental tests as to the usefulness of the theory.

We conclude with a few ancillary remarks: (i) The interpretation of $e^{-H(\zeta+it)}|\rangle$ as probability amplitude is perhaps not so forbidding, but $2\zeta = \beta$ as the inverse of temperature would seem to lose its meaning for single particles. We believe this difficulty can be removed by interpreting β, in the case of elementary particles, as an information parameter in the Shannon sense, rather than as actual physical temperature. Note in this connection that in general we need to cast information theory in amplitude form, and construct the probabilities as $\omega = f^* f$, since ordinary information theory is based on objects (switches, levers) of stochastic stability. For objects of stationary stability (consider, for example, the problem of using metastable states of atoms as memory devices), phase information is important, and probability amplitude, rather than the probability itself, would be more useful. Such an extension of information theory is formally possible and reverts essentially to field-theorylike formulas. (ii) The general method may be adapted to wave propagation and dissipation problems by noticing that $\delta(2|1) = -(2|\partial_\mu \Gamma + i\partial_\mu W|1)\delta x^\mu$. The Schrödinger equation analogue of this would be $i\partial/\partial t|\ ) = (H+iK)|\ )$, where H is the Hamiltonian operator, and K is the rate of entropy production. The last quantity is in general not constant; however, it is a positive definite quantity. Evidently, one may construct it as a quadratic function $K = \Sigma\ X^\mu O_{\mu\nu} X^\nu$. It follows that $O_{\mu\nu}$ can be taken as symmetric (Onsager's reciprocity principle), since the nonsymmetric part does not contribute. (iii) Our introduction of statistical weight seems to suggest complex Lorentz transformations. Since the problem of the representations of the ordinary Lorentz transformations is nebulous enough, we should try to avoid this as much as we can. But if we cannot, we should probably swing all the way and interpret all representations statistically in the sense of some random theory. Already, the published statistical interpretations of reflections and the "zitterbewegung" of the electron seem to point in this direction. In this case, the equivalence of Lorentz frames, the problem of normalization, stability, ergodic hypothesis, and so forth will all have to be restated in terms of more general (completed) representations. But if the simpler situation adopted in the present theory in which the imaginary part is identified as the presence of incoherent superpositions is valid, then no extra complication beyond the power of known statistical methods seems to arise.

The present approach has many roots in the past literature of the subject. As early as 1932, Block pointed out the similarity of the Schrödinger equation and statistics by his equation $\partial Z/\partial\beta = -(H/k)Z$, where Z is the partition function.[2] Landau and Lifschitz, Rosenfeld, Guth and Callen discussed the fluctuation relations $\Delta\mathscr{E} \cdot \Delta\beta \geqslant k$; especially Guth pointed out its formal connection with the Heisenberg uncertainty relations.[3] The Green's function method of Matsubara, Schwinger and Martin, and others is well known. These take advantage of the analogy between $i\beta$ and t. Feynman gave the field-theory analogue of the expansion of the partition function.[4] Landau and Lifschitz, and Rosenfeld have also discussed, to some extent, the physical unity and epistomological background of the statistics and ordinary quantum mechanics. Fano[5] and Ter Haar[6] stressed, on the basis of the density matrix, the operational and statistical nature of physical observations. Rosen[7] made an attempt toward a statistical interpretation of the Lorentz transformation. The author[8] has studied the nature of observation, first on the basis of a principle that is reminiscent of the present one, and later in connection with a theory of human perception. The author's old associate and friend, Stanley Schneider,[9] realized, as we do, that the structure of field theory is that of a gas at infinite temperature, and attempted a solution of divergence problems by applying conventional statistical methods to the vacuum. He also realized the role of entropy and considered a special case of the uncertainty relations $\Delta S \Delta n \geqslant k$, where n is the number of particles, and S is the entropy. He concluded on the basis of his ideas that for $v = c$ all cross sections vanish. Therefore, he considered scattering of light by light a decisive test area for his theory. At the time when we exchanged our ideas, he did not have a general principle or a definite conceptual procedure to carry out his program. He had in mind a non-Hermitian Hamiltonian to allow continuous dissipation and decay. Although this idea is not clearly related to his concept of vacuum statistics, it has definite appeal from the point of view of unstable particles, and it might be possible to approach the problem from this angle [see remark (ii)].

To our knowledge, no previous work has attempted a unification of quantum field theory with statistical mechanics by combining entropy and action and introducing microscopically the space of four-dimensional ζ^{μ}-variables, although such an idea is imminently plausible from Gibb's original argument regarding the derivation of the Boltzmann factor $e^{-\beta H}$, and also from the formal analogies between statistical mechanics and field theory.

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