

1967

Progress Report No. 3

Biomedical Computer Laboratory

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PROGRESS REPORT

No. 3

1 July 1966 - 30 June 1967



Biomedical Computer Laboratory
Washington University, School of Medicine
St. Louis, Missouri

BIOMEDICAL COMPUTER LABORATORY
WASHINGTON UNIVERSITY SCHOOL OF MEDICINE

PROGRESS REPORT NO. 3

1 July 1966 - 30 June 1967

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I. INTRODUCTION

This progress report from the Biomedical Computer Laboratory (BCL) summarizes work done during the period from July 1, 1966 through June 30, 1967. The Biomedical Computer Laboratory collaborates with research investigators throughout the Washington University School of Medicine in the application of advanced computer techniques to research problems in biology and medicine.

One class of applications requires strong coupling of the computer to its environment. These applications often involve the use of a LINC (Laboratory INSTRument Computer) or a PC (Programmed Console). We have pursued these applications both by bringing signals from the laboratories to BCL by means of either analog tape recordings or telephone lines and in some cases by taking the computers to the laboratory.

A second class of applications requires the use of advanced information processing techniques. This portion of our research program is conducted within the administrative framework of BCL although extensive use is made of both the personnel and the IBM 360/50 at the Washington University Information Processing Center. This work is directed toward development and evaluation of new computational methods in support of biomedical research.

A third class of applications requires a computer strongly coupled to its environment and also the advanced information processing capabilities available on large central machines. We are striving to meet the demands of this particularly difficult class of applications by connecting a laboratory style computer to our IBM 360/50 via telephone lines.

A final class of applications requires extensive computational manipulation. These "computational services" aid many investigators in their research through the use of established numerical and statistical procedures. During the past year this work has been carried on on both the IBM 360/50 and the IBM 7072 at the Washington University Information Processing Center. These computational services are supported by a variety of sources, including the Medical School, various grants and contracts held by investigators at the Medical School, and the Information Processing Center itself.

On April 11, 1967, the formation of the Washington University Computer Laboratories was announced. This federation of computer research activities includes the Biomedical Computer Laboratory, the Computer Systems Laboratory and the Computer Components Laboratory.

The Computer Systems Laboratory is under the direction of Professor W. A. Clark and will be active in the design and development of a compatible set of "macromodules" from which arbitrarily large, complex, or specialized computer systems can be assembled.

The new Computer Components Laboratory is under the direction of Professor W. N. Papiian and is a part of the School of Engineering and Applied Science. It will perform applied research and development work in materials, devices, and circuits for advanced information processing systems.

II. SOURCES OF SUPPORT

During the period covered by this report the primary source of support for the Biomedical Computer Laboratory was two grants from the National Institutes of Health:

FR 00161 Biomedical Computer Laboratory Facility
FR 00215 Biomedical Information Processing Research

Collaboration with other investigators often involved work already supported by other grants. Most of this support was from the National Institutes of Health:

AC 00108 Investigation of Lead Intoxication in Children
AI 04646 Immunochemical Basis of Penicillin Hypersensitivity
AI 09881 Immunochemistry of Penicillin Hypersensitivity
AI 00219 Training in Allergy and Immunology
ES 00139 Center for the Biology of Natural Systems
FR 00218 Computer Technology Center for Biology and Medicine
GM 13925 X-Ray Studies of Enzyme Structure
HE 00082 Clinical and Experimental Research in Respiration
HE 08594 Homotransplantation of the Heart
HE 09019 Mechanism of the Heart Beat
HE 10389 Physiology and Treatment of Shock
MH 12889 Content Analysis of Interaction Psychotherapy
NB 02168 The Etiology of Reduced Visual Function
NB 03856 Auditory Communication and its Disorders
NB 06833 Interdisciplinary Stroke Program
NB 06947 Bioelectric Studies of Cerebral Cortex

Two National Science Foundation grants, an Atomic Energy Commission grant, and an IBM contract helped to support portions of several projects:

NSF G 22296 Expansion of Computing Center

NSF GB 5888 X-Ray Structural Studies of Malate Dehydrogenase

AEC AT(11-1)-1653 Parathyroid Scanning

IBM Contract Study of Computer Requirements for the Biomedical Sciences

Finally, portions of many projects were supported by:

St. Louis College of Pharmacy
Washington University School of Applied Science and Engineering
Washington University School of Medicine

The sources of support for each of the research projects reported in Section V are listed there. All government support is listed by grant number only.

III. PERSONNEL

EMPLOYEES

Personnel employed by the Biomedical Computer Laboratory during the period covered by this report were:

Director

Jerome R. Cox, Jr., Sc.D.

Assistant Director

George S. Whitlow, Jr., B.S.

Assistant Director for Engineering

V. William Gerth, Jr., M.S.

Research Associates

William E. Ball, Sc.D.*
Richard A. Dammkoehler, M.S.
Tom L. Gallagher, D.Sc.
William Holmes, Ph.D.
James M. Vanderplas, Ph.D.*

Research Assistants

Andrew L. Bodicky, B.S.
A. Maynard Engebretson, M.S.
Ramasami Ganesan, M.S.
Donald H. Glaeser, M.S.
David Gurwitz, M.S., since August 1, 1966
Rexford L. Hill, III, M.S. since February 1, 1967
Monte Deh Lien, B.S., since September 16, 1966
Robert G. Loeffel, B.S.
Donald J. Manson, Ph.D.*, since March 20, 1967
Michael D. McDonald, B.S.
Floyd M. Nolle, B.S.
Elizabeth Van Patten, B.S.
David Velten, B.S.

Visiting Scientist

Roy E. Bentley, Ph.D., August 12 to September 16, 1966
On leave from the Institute of Cancer Research, Belmont, Sutton,
Surrey, England.

Programmers

Madhu Bhide, A.B.
David A. Bridger, B.S.*
Sharon R. Davisson, B.S., since July 18, 1966
M. Taghi Farvar, B.S., since October 1, 1966
J. Philip Miller, A.B.
Shirley J. Smith, M.S., since June 15, 1967

Technical Assistants

Michael Hudson, B.A., since June 7, 1967
Clayton Lee Myers, B.S.

Engineering Assistants

Harry Agress, Jr.
David A. Brown, B.S.
Richard E. Hitchens

Programming Assistants

Bruce Brodie, P.S., since June 7, 1967
Dale Dierberg, B.A.
Mark Drazen, since June 21, 1967
I. Richard Hirsh, since June 12, 1967
Susan P. Kahn
Peter J. Kirwin
Davis M. Swan, B.S.
Patricia L. Talmage
Trilochan Wadhwa, M.S.

Electronics Technicians

H. Dieter Ambos, since July 8, 1966
Charles R. Buerke, since October 27, 1966
Fred L. Francis
Charles E. Mitchell
Kenneth F. Rath*
Stephen M. Rhode, since March 1, 1967

Technical Supervisors

James W. Dusoe, since August 1, 1966
Norman T. Kinch*

Office Clerk

Larry W. Lewis

Secretaries

Merry M. Ambos, since September 12, 1966
Carol J. Boulware*
Brigitte R. Clark*
Joann P. Cowley, since February 27, 1967
Marianne Ladd, since July 13, 1966
Janet Litzinger
Sheryl L. Sharp, since June 14, 1967

* Indicates at least 50% of the individual's effort is supported by another laboratory or department.

Changes in Personnel

During the period covered by this report the following personnel resigned or completed their work at the laboratory:

Harry Agress, Jr., terminated September 9, 1966
Carol J. Boulware, hired July 1, terminated July 31, 1966
Brigitte R. Clark, terminated September 15, 1966
Joann P. Cowley, Terminated April 30, 1967
Sharon R. Davisson, terminated April 30, 1967
James W. Dusoe, deceased January 21, 1967
M. Taghi Farvar, terminated June 15, 1967
Tom L. Gallagher, terminated March 31, 1967
Richard E. Hitchens, terminated September 30, 1966
Susan P. Kahn, terminated September 2, 1966
Norman T. Kinch, terminated July 31, 1966
Peter J. Kirwin, terminated September 9, 1966
Larry W. Lewis, terminated September 15, 1966
Janet Litzinger, terminated September 16, 1966
Robert G. Loeffel, terminated October 31, 1966
Charles E. Mitchell, terminated December 16, 1966
Clayton Lee Myers, terminated August 31, 1966
Kenneth F. Rath, terminated September 30, 1966
Davis M. Swan, terminated May 31, 1967

STUDENTS

During the period covered by this report the following students have worked in the laboratory or with laboratory staff members:

M. E. Dodge, B.S., Medical Student
William Glenn, B.S., Medical Student
F. S. Letcher, B.A., Medical Student
W. E. Long, B.S., Graduate Student
L. Medgyesi-Mitschang, M.S., Graduate Student

RESEARCH COLLABORATORS

During the period covered by this report the following investigators from other laboratories, departments, or institutions, collaborated with BCL staff members on problems of joint interest:

Washington University

H. Agress, Jr., Neurosurgery
L. J. Banaszak, Ph.D., Physiology and Biophysics
J. M. Barnes, B.A., Pediatrics
S. J. Birge, M.D., Metabolism
R. Burstein, M.D., Obstetrics and Gynecology
H. R. Butcher, Jr., M.D., Surgery
R. P. Eaton, M.D., Metabolism
J. M. Enoch, Ph.D., Ophthalmology
S. Goldring, M.D., Neurosurgery
G. C. Johns, B.S., Computer Systems Laboratory
S. P. Londe, M.D., Surgery
H. L. Mack, Jr., Information Processing Center
J. C. Morris, M.D., Surgery
G. C. Oliver, Jr., M.D., Medicine
C. W. Parker, M.D., Medicine
E. J. Potchen, M.D., Nuclear Medicine
W. E. Powers, M.D., Radiology
G. Psathas, Ph.D., Social Science Institute
A. Roos, M.D., Anesthesiology and Physiology
P. E. Stohr, M.D., Neurosurgery
L. J. Thomas, M.D., Anesthesiology
Teresa Vietti, M.D., Pediatrics
H. C. Wasserman, M.D., Obstetrics and Gynecology
R. B. Woolf, M.D., Obstetrics and Gynecology

Center for the Biology of Natural Systems

D. M. Gates, Ph.D.
LaVerne E. Papian, M.S.

Central Institute for the Deaf

D. H. Eldredge, M.D.
N. P. Erber, B.S.
I. J. Hirsh, Ph.D.
A. F. Niemoeller, Sc.D.
C. S. Watson, Ph.D.

St. Louis College of Pharmacy

R. L. Schnaare, Ph.D.

Temple University, Philadelphia, Pennsylvania

K. C. Tsien, M.S.

University of Chicago, Chicago, Illinois

H. A. Fozzard, M.D.

IV. PHYSICAL RESOURCES

On April 15, 1964, the Biomedical Computer Laboratory was formed and the original staff moved into 5,463 square feet (gross) of laboratory space at 700 South Euclid Avenue just across the street from the main building of the Washington University School of Medicine. Equipment then available for laboratory applications of digital computers included the LINC (Laboratory INSTRument Computer). This small stored-program computer has been designed specifically for use in biology and medical laboratories where there is a requirement for strong coupling between the computer, the investigator, and other experimental equipment. At that time there were six LINC's in the Washington University medical community. Four more have been added since then for a total of ten. Two belong to BCL, five to our sister laboratory, the Computer Systems Laboratory, two to the Department of Neurology, and one to the Central Institute for the Deaf. Last year the Programmed Console was designed at BCL to function as a combined stored-program digital computer and remote display console for the IBM 360/50 installed during May, 1966, at the Washington University Information Processing Center. BCL's computational facilities now include two specialized Programmed Consoles built at the laboratory. A third is under construction at this time. In addition, six Programmed Consoles have been built by SPEaR, Inc. from plans and specifications developed at BCL. These six are now on loan for evaluation as an aid to radiation treatment planning at radiology centers in Baltimore, Maryland; Bethesda, Maryland; Houston, Texas; Philadelphia, Pennsylvania; St. Louis, Missouri; and Toronto, Canada. Other laboratory facilities include a data transmission distribution system, a well-stocked electronics shop, a large inventory of electronic and computer test equipment, a variety of digital system modules, and both analog and digital tape recorders.

During these past two years the laboratory space has been increased by 3389 square feet on the second floor of the building just south of the original space. Facilities for computational applications are housed here and direct communication with the IBM 360/50 at the Washington University Information Processing Center is provided via phone lines, an IBM 1050, and a Programmed Console.

V. RESEARCH PROJECTS

The reports which follow are grouped around the seven major research areas in which the Laboratory has been engaged during the past year. This organization is different than that used in the first two progress reports but should enable the reader to appreciate the interrelation among the various tasks with greater ease.

Each report lists the personnel active in the research and their affiliations. The academic degrees of all BCL personnel are omitted in these lists since this information can be found in Section III. Unless otherwise specified all organizations and departments listed are part of Washington University. The support for each of these research projects is also listed by grant or contract number. The title of the grant or contract and the funding agency can be found in Section II.

Throughout the following, references to other reports herein will be made by project number alone. References to either of the two previous BCL progress reports will be abbreviated, e.g., (see PR 2, A-1).

A. The Programmed Console

The Programmed Console (PC) was designed at BCL in late 1965 to function as a combination stored program digital computer and display console. The following research reports describe work done this year to complete the development of equipment and programs to make the entire system useful in the work on radiation treatment planning. Those unfamiliar with the system may wish to consult last year's report (see PR 2, A-1).

A-1. Engineering Evaluation of the SPEaR Programmed Console

Personnel: V. W. Gerth, Jr., BCL
J. R. Cox, Jr., BCL
A. M. Engebretson, BCL
F. M. Nolle, BCL
D. Gurwitz, BCL
H. D. Ambos, BCL

Support: FR 00161

Each of the five PC's built by SPEaR, Inc. for the Radiation Treatment Planning project (see PR 2, E-1) was delivered to BCL for detailed evaluation. The machines were exercised with all test and operational programs to check for malfunctions. Particular emphasis was given to data transmission, A/D conversion, oscilloscope display, and Datamaster use. As a result, a few

minor discrepancies were discovered and resolved in cooperation with SPEaR. Probably the most significant improvement was the addition of a counter driven by central clock pulses for the timing of the data transmission interrupts. This modification increased the reliability of data transmission over phone lines and with the Datamaster.

Beyond these modifications, two new engineering developments for the SPEaR PC were a CALCOMP interface and a means for expanding the number of interrupts.

A-2. Test and Alignment Procedures for the Programmed Console

Personnel: V. W. Gerth, Jr., BCL
P. J. Kirwin, BCL

Support: FR 00161

Test and alignment procedures have been written for the Programmed Console to aid in general preventive maintenance and trouble shooting. A set of functional test programs provides for the recognition of malfunction of the instructions in the PC order code not directly related to peripheral equipment. Other programs are used to test the memory, keyboard, oscilloscope, analog system, and Datamaster. A test procedure has also been developed to test the PC console functions. The alignment procedures provide step by step methods for alignment of the analog system, the display scope, the Datamaster, and the variable time delays in the central processor.

A-3. The Datamaster

Personnel: A. M. Engebretson, BCL
H. D. Ambos, BCL
J. R. Cox, Jr., BCL
G. C. Johns, Computer Systems Laboratory

Support: FR 00161
FR 00218

The Datamaster is used with the PC for storing digital data on a strip of magnetic tape attached to a 3½ x 9 inch card. Seven Datamasters built from modified Bell and Howell Language Master units have been tested to date. In these units the cards are driven between a rubber capstan and a small pinch roller. A spring loaded head assembly provides positive contact between the head and the magnetic tape.

Several instances of unreliable operation of the Datamaster have occurred over the past year. The main problem has been maintaining a constant card speed. In the data transmission logic of the PC, resynchronization occurs at the beginning of each 14-bit word (consisting of a leading "1", 12 data bits,

and a trailing "0"). Errors in transmission and loss of synchronization will occur if the card speed varies by more than $\pm 4\%$. The original Language Masters do not in general satisfy this requirement, but the installation of a hysteresis motor in place of the original induction motor has improved matters substantially. In addition, the driving force exerted on the back of the card by the rubber capstan seems unfortunately to be not much greater than the retarding force of the head against the magnetic tape. Differences in the condition of the surfaces of the head and tape or differences in the head pressure can change the speed of the card by 1 or 2 percent which when compounded with other sources of variability causes the $\pm 4\%$ margin to be exceeded. Speed jitter, which is a relatively high frequency random variation around the average speed, seems to be caused by point to point variations in the coefficient of friction between the head and the magnetic tape and by small nodules of adhesive under the tape. As a nodule passes under the head, the head springs outward with a resulting increase in pressure against the surface of the tape.

In spite of these difficulties, a Datamaster with properly adjusted head pressure and alignment can reliably record and play back Datamaster cards. Only a very few cards are sufficiently irregular to cause trouble and they may be rejected at the outset. However, a consequence of the speed problem is that cards recorded on one machine will not work reliably on another.

We feel that to obtain operation that will allow interchangeability of cards between Datamasters a new transport should be designed with emphasis placed on increasing the surface area between the capstan and the card, increasing the dimensional stability of the capstan, reducing the friction between the head and the tape, and providing for convenient alignment of the head assembly.

A-4. PC Closed Circuit Television System

Personnel: D. Gurwitz, BCL

Support: FR 00161

The Programmed Console closed-circuit television system is designed to increase the display capabilities of the PC by increasing image size and by making the image available at more than one location. The system consists of a Concord Model MTC-12 camera, a specially constructed housing for affixing the camera to the PC oscilloscope, and a GE model CBM 72 D Educational TV monitor. The 8 cm x 8 cm image on the oscilloscope is transmitted to the monitor and there displayed as a 13" x 13" image. Several monitors may be used simultaneously.

A-5. Calibration System for Position Transducer

Personnel: A. L. Bodicky, BCL

Support: FR 00161

A position transducer is used with the PC to enter graphic information. The one we now use is manufactured by Data Equipment Company under the trade name "Rho-theta transducer". Two potentiometers produce voltages proportional to the extension of a radial shaft and the angle of rotation of the shaft. Calibration constants relate these voltages as quantized by the PC to the actual extension in $\frac{1}{4}$ mm units and the angle in radians/1024. A third constant to give the minimum distance from a stylus at the end of the shaft to the center of rotation is also required. With these three constants a polar-to-cartesian transformation may be carried out.

A precisely scribed calibration plane has been constructed from plate glass. Data taken on a polar grid with 26 circular segments and 19 radii can be stored in the PC. These 494 points are then analyzed to produce a minimum mean square estimate of the three constants. Programs are in preparation to accomplish this task automatically.

A-6. PC Monitor

Personnel: M. D. McDonald, BCL

Support: FR 00161

The PC monitor is a system of general purpose, functionally independent subroutines developed to aid the PC programmer. The Monitor is in six sections:

Monitor Subroutines

- A routine to set up index registers for the monitor.
- An initial loader for the autonomous mode.
- Read and write routines for the Datamaster.
- Data transmission routines for the LINC.

Character Subroutines

- Half-word routines (HW) to facilitate the loading of 6-bit characters, i.e., one-half a PC word.
- Character Compare subroutine (CHACOM) to permit comparison of an unknown 6-bit character to a series of specific characters with appropriate transfer of control if a match is found.
- Questions and Answers subroutine (Q & A) to display text on the PC scope and accept and display information supplied dynamically by the user at the PC keyboard.

Word Compare Subroutines

A routine to compare the accumulator to storage (CAS), make an algebraic comparison between two 12-bit numbers, one in the accumulator, the other anywhere in memory. The return is trichotomous.

Sampling Subroutine

A sampling subroutine (SAM) to digitize the signal found on the currently selected analog input channel. The 12-bit unsigned number corresponding to the voltage present is left in the accumulator.

Arithmetic Subroutines

Single-precision, fixed-point, signed multiply and divide subroutines (MUL-DIV).

Floating-Point Subroutines

Two sets of single-precision floating-point subroutines, one slow (FLOPS), one fast (FLOPF). The fast routines restrict the user to performing one operation per call to the subroutine, e.g., one add, one multiply. The slow routines allow the user to perform any desired sequence of operations within any one call.

A-7. PCAP and LAP6 Routines

Personnel: M. D. McDonald, BCL

Support: FR 00161

PCAP, the Programmed Console Assembly Program on the LINC, and several associated PC-oriented LINC programs have been modified so as to operate under the LINC Assembly Program No. 6 through the Free Meta command. Two conversion routines are included, one to assemble a program in the LAP6 working area, another for programs in LAP6 files. There are also two special transmission routines for reading PC binary from the LINC to the PC.

A-8. PC Communications Programs

Personnel: E. Van Patten, BCL

Support: FR 00161

The basic communications program for the PC in the autonomous mode reads and writes Datamaster cards in a fixed format. Up to 277 12-bit words are stored on a card. Of these, the first 20 constitute an identification header, the next 256 words are data, and the final word is the

checksum used to verify that a card has been read properly. This format has proven adaptable to storing either data or program instructions.

The method of initializing operation of the PC when it is not connected to another computer utilizes a "cold start card". This card consists of the basic communications program plus a bootstrap program. This latter program checks the accuracy of the load, reads the subsequent card and passes control to the program contained on it.

A supplementary routine added to the Datamaster communications program handles PC exchanges with the LINC. It makes it possible to store or retrieve information on LINC tape. Only 256 word blocks are transmitted in either direction.

A-9. PC Utility Program (UTIL)

Personnel: E. Van Patten, BCL

Support: FR 00161

UTIL is a convenience program for copying Datamaster cards, for transferring information from LINC tape to cards, and for bringing a program into the PC from LINC tape and putting it into execution. Appropriate switch settings and instructions for feeding cards are displayed on the oscilloscope.

B. Computer Applications in Radiation Treatment Planning

A major project within the Biomedical Computer Laboratory during the past year has been the application of the Programmed Console to problems confronting the therapist in radiation treatment planning. The reports of work done on this project have been grouped together within this section but reference should be made to Section A of this report and to last year's report.

Although each of the projects has been strongly influenced by our colleagues from the five institutions participating in this project, only those at Washington University are listed under personnel. We do not attempt to show the indirect support provided by the five participating institutions.

A Programmed Console was displayed as a scientific exhibit at the 52nd Annual Meeting of the Radiological Society of North America, November 27 through December 2, 1966, at Chicago, Illinois. Programs designed to aid the radiotherapist in treatment planning for external beams were demonstrated using the autonomous mode and Datamaster cards for program storage. Hard copy of the treatment plans developed with the Superimpose Beams program were plotted with an incremental plotter (see B-3).

The PC was also demonstrated in the collaborative mode (see C-1) by means of a long distance duplex data line between Chicago and the IBM 360/50 at the Washington University Information Processing Center in St. Louis. The PC served as a remote input-output console for the Radioactive Implanted Sources Program running in the IBM 360/50 (see B-6).

Many of the therapists present were able to try the treatment planning programs first hand. They easily adapted to the operation of the PC after a minimum of orientation. The demonstration received the cum laude award from the convention judges.

Between February 27 and March 10, 1967, the following participants in the Radiation Treatment Planning project met at BCL:

M. D. Anderson Hospital and Tumor Institute
Houston, Texas

Dr. Fred Durrance
Dr. Joseph Castro
Miss Marilyn Stovall
Mr. J. Pat Hughes

National Cancer Institute
Radiation Branch
Bethesda, Maryland

Mr. Dwight Glenn
Mr. Fred Faw

Ontario Cancer Institute
Toronto, Ontario, Canada

Dr. Jack Cunningham
Mr. Joe Milan

Temple University Hospital
Philadelphia, Pennsylvania

Mr. K. C. Tsien
Dr. John Wright

University of Maryland
Radiobiology Laboratory
Baltimore, Maryland

Dr. Eugene Robinson
Mr. Joe Rose

Washington University
Mallinckrodt Institute of Radiology
St. Louis, Missouri

Dr. William Powers
Miss Helen Fotenos

The primary purpose of the meeting was to acquaint the participants with the PC and the system of programs that had been written to aid in treatment planning. A second important purpose was to obtain reactions to the equipment and programs so that changes could be made where needed.

Discussed in detail during the first week were the PC system design, the PC order code, the operation of the Datamaster, the system of test programs, the system of programs for treatment planning, data transmission techniques, the collaborative mode of operation, and simple programming techniques. During the second week the physical and mathematical basis of the programs Superimpose Beams, Enter Isodose Chart and Radioactive Implanted Sources were discussed. Participants demonstrated their understanding of the operation of their systems and discussed possible changes and future work on the last two days of the meeting.

A Programmed Console was demonstrated before a special week-long meeting held at the Institute of Cancer Research, Royal Marsden Hospital, in London, on April 3-7, 1967. A demonstration of radiation treatment planning in the autonomous mode was given on the first day before a group of seventy radiation physicists and radiologists, mostly British. They returned in smaller groups during the rest of the week for individual instruction in the use of the system. The general consensus was that the PC could be economically justified for application in the larger British treatment centers, when full use is made of the collaborative mode for all computer calculations currently employed in radiology.

Papers presented:

T. L. Gallagher and W. E. Powers, "Programmed Console - An Aid to Radiation Treatment Planning", Presented at the 8th Medical Symposium sponsored by the International Business Machines Corporation, Poughkeepsie, New York, April 3-6, 1967 (To be published by IBM).

T. L. Gallagher, "Small Computers for Radiation Therapy and as a Communicative Device", Presented at the National Conference on Computer Applications in Radiology, Columbia, Missouri, April 10-12, 1967.

T. L. Gallagher, "Use of Communicating Devices for Radiation Therapy Planning: Autonomous and Collaborative Modes of the Programmed Console and its Aid to the Therapist in Treatment Planning", Presented at the Conference on the Use of Computers in Radiology, Chicago, Illinois, October 20-23, 1966.

W. E. Powers, T. L. Gallagher, V. W. Gerth, W. F. Holmes, J. R. Cox, Jr., "Programmed Console for Radiation Therapy Planning", Presented at the 1966 Annual Meeting of the American Association of Physicists in Medicine, Chicago, Illinois, December 3, 1966.

Publication:

W. E. Powers, T. L. Gallagher, V. W. Gerth, W. F. Holmes, J. R. Cox, Jr. "Programmed Console for Radiation Therapy Planning", Submitted to Radiology.

B-1. Superimpose Beams Program

Personnel: W. F. Holmes, BCL
W. E. Powers, M.D., Radiology

Support: FR 00161
IBM Contract

Treating tumors by ionizing radiation depends on the greater damage incurred by tumor tissue compared with healthy tissue, when given equal doses. Since the difference in sensitivity is rather small, radiation therapy requires that the dose be controlled within narrow limits -- too much will destroy essential tissue, too little will leave a remnant of tumor that continues to grow. It is common practice to position several beam sources around the patient so that the radiation overlaps in the tumor region, giving a higher relative dose than would be possible with one beam. When planning a treatment, the radiotherapist usually starts with a life-size outline drawing of the patient, showing the tumor and critical healthy structures. In order to calculate radiation intensities with the patient, there is a chart for every beam used in treatment, showing radiation intensity contours underneath the skin. If only one beam is used in treatment, the radiation intensity can be seen immediately by laying the beam's chart on the patient outline. However, two or more beams require a superimposed contour diagram which may take an hour to calculate, since position, angle, relative source strength, and type of beam may all vary. It is thus only practical to calculate a few of the possible arrangements. A beam superposition program has been written for the Programmed Console which performs the calculations in a few seconds, enabling a therapist to try many treatment plans in his search for the optimum. The program works in the following way:

1) A Datamaster card containing patient information (see B-2) is entered. The patient's outline and identification are displayed on the oscilloscope.

2) Selected beams are entered on Datamaster cards (see B-4 and B-5). Each contains identifying information and radiation intensities from which a contour chart can be calculated. The beams are numbered and entered in a table showing relative source strengths. These are typed from the keyboard and may be changed at any time.

3) The beams are displayed along with the patient outline. Each beam is represented by a numbered "T" figure, which shows the width and depth of the beam. Using knobs and keys, the beam T's may be moved about the surface of the patient, and pointed in any direction.

4) A movable square is used to select a region for radiation contour calculations. The square can be enlarged so as to cover the whole patient, or shrunk down to give a more detailed picture.

5) Radiation intensities for the superimposed beams are calculated within the square. Intensity contours may then be seen by typing in their values; the contours are calculated and displayed on the storage oscilloscope.

(The previous steps are repeatable in any order, until the most satisfactory plan is obtained).

6) Numerical values for each beam's position, orientation, and relative source strength may be displayed. This information, along with the radiation contours and the patient outline, constitute a complete record of the treatment plan. It may be photographed or plotted lifesize on an incremental plotter (see B-3).

B-2. Enter Patient Contour Program

Personnel: M. D. McDonald, BCL
J. R. Cox, Jr., BCL

Support: FR 00161

The Enter Patient Contour program was written to allow the user to enter into the PC the outline of a patient by tracing the outline with the stylus of the position transducer (see A-5). This contour may subsequently be used by the Superimpose Beams program (see B-1).

Information from the transducer is supplied to the computer as two voltages, one (ρ) proportional to the extension of the arm, the other (θ) proportional to the angle from the instrument's base line. The voltages, ρ and θ are transformed digitally to a value of x and y which reflect the actual position within $\pm 1/4$ mm.

The user must first specify the patient identification and then indicate with the transducer the location of three points. The first two points are

used to define an axis, i.e., the line from which the program determines θ_0 , the one angle through which all points will be rotated. If drawn as part of the contour, this line would appear on the oscilloscope as parallel to the base of the scope with the first entered point on the left. The third entered point is the origin, a point the coordinates of which will be subtracted from all input points so that the origin itself will appear at the center of the scope.

The user then either supplies the spacing between sampled points or indicates that points are to be taken only upon command from the keyboard. At this time the contour and one or more internal structures may be traced with points appearing on the scope as they are sampled. The spacing between points may differ from outline to outline, and each outline may be left as drawn or closed by having the first sampled point also placed as the last point.

The entire figure may be viewed and scaled; the scaling factor (between .25 and 15.75 in increments of .25) appears on the scope. Lastly, the contour may be plotted lifesize on an incremental plotter, and/or written on a Data-master card. The card then contains the patient contour in the correct format for the Superimpose Beams program.

B-3. A Program for Plotting Radiation Treatment Plans

Personnel: A. M. Engebretson, BCL
D. J. Manson, BCL

Support: FR 00161

A program has been written for the PC which provides a permanent record of radiation treatment plans using an incremental plotter (CALCOMP Model 565). This program is entered after the treatment planning program (see B-1) and uses pertinent data which remains in the memory. The resulting plot includes the patient's name, the patient contour, the position and orientation of each beam, the window in which isodose curves are plotted, the labeled isodose curves themselves, a list of the labels along with the corresponding values, and a table listing information about each beam.

B-4. Generation of Beam Dose Tables from Isodose Charts

Personnel: R. E. Bentley, Visiting Scientist, BCL
T. L. Gallagher, BCL
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S. R. Davisson, BCL
W. F. Holmes, BCL
D. M. Swan, BCL

Support: FR 00161
FR 00215
IBM Contract

To use the Programmed Console for radiation treatment planning, a table of doses is necessary to describe each different beam used. These tables present the dose at the intersections of a radial grid made up of a series of lines at evenly spaced depths in the patient, intersecting a series of rays emanating from the source of radiation. The radial shape is chosen over a rectangular one because it provides both greater accuracy in making linear interpolations and greater ease in correcting for change in source-to-skin distance or for oblique incidence at the skin surface. While formulae for computing doses from basic beam parameters are becoming more reliable, much of beam dose data must still be obtained from isodose charts. A computer program is being written to reduce the isodose lines to a dose table. The position transducer (see A-5) is traced over each isodose line on the chart. The digitized data is used to interpolate between adjacent isodoses, obtaining dose values for those grid points lying between the two lines. Values beyond the outermost isodose line are extrapolated. The method of interpolation should be accurate within 2 millimeters in distance or 1% in dose. At the core of this program is a subroutine that samples the voltages produced by the position transducer and makes the appropriate polar-to-cartesian transformation. In order to maximize the speed of the subroutine the number of multiplications is minimized and the calculations carried out completely in single-precision fixed-point arithmetic. As the stylus of the position transducer is moved along an isodose contour, a table is stored of just those points needed for interpolation to the radial grid.

First results from this program yield dose tables less accurate than anticipated, but the source of error is unknown. To aid in the diagnosis of this difficulty and to provide an early useful result, a FORTRAN routine is in preparation that will use the collaborative mode of operation of the Programmed Console. This approach should make it possible to eliminate from consideration any computational errors due to inadequate precision in the routines for the PC.

B-5. Enter Doses

Personnel: E. Van Patten, BCL
W. F. Holmes, BCL

Support: FR 00161
IBM Contract

Beam cards for the Superimpose Beams program (see B-1) may also be prepared directly from the values of the doses at the radial grid points. These doses may be obtained by manual methods from isodoses, by computation from beam generation formulae, or directly from doses measured in a phantom. The Enter Doses program prepares the beam cards from data typed on the PC keyboard. Some error checking is done. There is also provision for reading an existing beam card, modifying it and rewriting it.

B-6. Implant Dosimetry Using the PC for Input-Output

Personnel: T. L. Gallagher, BCL
W. E. Powers, M.D., Radiology
E. Van Patten, BCL
W. F. Holmes, BCL
S. J. Smith, BCL

Support: FR 00161
FR 00215
G 22296
IBM Contract

A program that calculates radiation intensities from needle implants has been used for several years (see PR 2, B-10), first on the IBM 7072, then on the IBM 360/50. The input is a set of punched cards giving the type of needle and its coordinates measured from a stereo pair of X-ray films. The printed output shows radiation isodoses for five planes stacked one above the other, giving a three dimensional picture. The calculations themselves take only a few minutes. If a high speed X-ray developer unit is used, it is possible to photograph the needles, measure their coordinates, and calculate radiation intensities, while the patient is still under anesthesia. When the output indicates incorrect needle implantation, the needle may be reinserted. The procedure requires rapid access to a large computer over direct lines. The Programmed Console (see PR 2, A-1), using the RACS system in the IBM 360/50 provides this facility. A program has been written that calls the implant calculating program into execution in the IBM 360/50; displays questionnaires for the needle information; and sends the numbers, typed as answers to these questionnaires, to the IBM 360/50 as normal program input. Output is returned as a set of five stacked planes with radiation intensities on a 17 x 17 grid of points within each plane. Selected isodose curves may be displayed for any plane, and planes may be viewed in any desired order.

B-7. Optimization of External Radiation Beams for Therapy Planning

Personnel: T. L. Gallagher, BCL
W. E. Powers, M.D., Radiology

Support: FR 00215
Washington University
G 22296

A scheme has been developed for the maximization of the integral radiation dose in a specified tumor region, subject to a set of constraining conditions in the total treatment area. The mathematical expressions which describe the

effect of an external radiation beam impinging on a homogeneous medium are nonlinear. The attenuation of the radiation in body tissue decreases almost exponentially but is complicated by geometric factors and electron build-up phenomena. Since the dose at a particular point is proportional to the source strength, an expression can be written for the dose at a point in a medium resulting from a source of unit strength. A linear programming problem can then be formulated using the source strengths as the set of unknown variables. Since it is the effects of angles of beam incidence, port sizes, and wedge angles upon dose which are nonlinear, the levels of these parameters are selected by perturbation and a re-evaluation of the objective function through the linear programming algorithm is carried out for each perturbation. The angle of beam incidence is always perturbed first since this parameter is more easily adjusted in actual patient treatment. The port size is adjusted for a changing angle of incidence. The search toward optimality must proceed until both the angles of beam incidence and the wedge angles cease to cause an increase in the objective function. When equal maximum values of the objective function occur, the set of angles which changes least from its previous level is selected.

Optimum plans have been calculated for five anatomical regions, and the results compared with an initial configuration supplied by the therapist. The application of the procedure to a set of antrum cases demonstrates clearly that an equal weighting of initial relative source strengths can be grossly in error. Without violating the constraints, the integral dose in the tumor region was increased by factors of 1.4, 1.6, and 2.7 due to source strength adjustment alone. If a more reasonable selection of relative source strengths is made, for example, from the first linear programming solution, the percentage increase obtained by adjustment of the angles of incidence and wedge filter angles still increases the integral dose in the region of maximization by approximately 4 percent.

For those cases in which equal weighting of the initial relative source strengths is more appropriate, such as the selected plans for the bladder, larynx, and naso-pharynx, the improvements are significant but not dramatic. The average improvements for these cases were 11, 9, and 8 percent, respectively. These improvements are attributed to small adjustments of the original parameter levels. In its current state the procedure is considered a clinical research tool since it requires cooperative interaction between the therapist, a computer specialist, and the computer.

Paper presented:

T. L. Gallagher, "Optimization of External Radiation Beams for Therapy Planning", Presented at the Joint Meeting of the American Physical Society, Sociedad Mexicana de Fisica and Canadian Association of Physicists, Toronto, Canada, June 21-23, 1967.

Publication:

T. L. Gallagher, "Optimization of External Radiation Beams for Therapy Planning", Washington University, St. Louis, Missouri, 1967 (D.Sc. Dissertation).

C. Collaborative Data Processing

The collaborative mode of operation of the Programmed Console has been implemented during the past year through RACS (Remote Access Computing System), a time-sharing executive developed by Lockheed at Marietta, Georgia, and modified extensively by IBM and the staff of the Washington University Information Processing Center. As an interim measure RACS has been satisfactory, but long range goals include the use of the PC in the collaborative mode to manipulate large files and develop programs in languages other than FORTRAN. Since RACS is extremely limited in these regards we have begun to sketch the major specifications of a new system called WASP (Washington University Adjunct Systems Program). WASP is based on HASP (Houston Automatic Spooling with Priorities) developed by NASA in cooperation with IBM, and based on OS (Operating System/360). Because WASP is OS-based both the advanced filing capabilities and the variety of higher languages inherent in OS will be available to the user of a remote terminal served by WASP. Present plans call for the support of three kinds of remote terminals: IBM 2260's, LINC's, and Programmed Consoles.

C-1. PC - IBM 360 Communications

Personnel: E. Van Patten, BCL
D. A. Bridger, BCL
D. Velten, BCL
J. R. Cox, Jr., BCL
H. L. Mack, Jr., Information Processing Center

Support: FR 00161
FR 00215

Extensive changes to RACS (Remote Access Control System) for the IBM 360/50 were necessary to permit it to carry on an exchange of information with the PC. This IBM 360/50 resident system provides time-sharing among the various remote terminals and local jobs. It is limited, however, to accepting only FORTRAN jobs and calls to execute programs from the absolute library.

A set of control characters was chosen and the protocol for message identification and response was worked out to systematize communication between the two computers. Only 8-bit ASCII (American Standard Code for Information Interchange) characters are transmitted. The IBM 360/50 converts them to or from EBCDIC (Extended Binary Coded Decimal Interchange Code) and the PC to or from its own keyboard code. Provision is also made for sending pairs of octal digits as if they were ASCII characters to speed the transmission of large blocks of data and of PC programs.

C-2. PC Program Library in the IBM 360/50

Personnel: E. Van Patten, BCL
D. A. Bridger, BCL
H. L. Mack, Jr., Information Processing Center

Support: FR 00161

An allotment of disk space on the IBM system 360/50 is reserved for the storage of PC programs and data. Programs written for the two machines are brought into execution by loading a single card from the Datamaster. The particular operations to be performed are determined by the programmer's response to displays on the PC oscilloscope.

- 1) A PC program can be retrieved from the disk library file, sent to the PC and control turned over to the PC.
- 2) Programs which exist on LINC tape or on Datamaster cards may be transmitted to the IBM 360/50 to be stored on the file either as new entries, or to replace old ones.
- 3) Programs may be deleted from the library file.
- 4) An oscilloscope display may be obtained of a list of program names and the dates on which they were filed.

The file at present will accomodate 26 PC programs. There is a header at the beginning of the file which contains the names of the programs, their locations in the file, their lengths, and the dates filed.

C-3. High Speed Data Phone Interface for the IBM 360/50

Personnel: D. Velten, BCL
D. A. Bridger, BCL
V. W. Gerth, Jr., BCL
J. R. Cox, Jr., BCL

Support: FR 00161
FR 00215

The Programmed Console gains access to the IBM 360/50 through an IBM 2701 Data Adapter Unit. An IBM Transmission Adapter, capable of handling 1200 baud data rates, has not yet been delivered and consequently a high-speed adapter was designed at BCL. The Adapter consists of an IBM Parallel Data Adapter (PDA) and a hardware telephone interface. The interface contains a 10-bit shift register for serial-parallel conversion, control logic, and level converters. Data transfer is serial by bit over the leased voice-grade phone line and serial by byte (8 bits) between the interface and the PDA. The format is a leading start bit, a 7-bit ASCII code, a parity bit, and a trailing stop bit.

C-4. Data Switching System

Personnel: V. W. Gerth, Jr., BCL
C. E. Mitchell, BCL

Support: FR 00161

A flexible switching system has been developed to provide data communication between several locations in the hospital complex, the Information Processing Center, and BCL. Bell System data lines, BCL internal data distribution lines, and analog lines from the Acute Cardiac Care Unit all terminate at a patch panel at BCL. Data connection boxes have been installed in various labs at BCL and each of these can be transmitted between any LINC, PC and the IBM 360/50. There are currently two full duplex data lines to the Information Processing Center, one to the Compton Physics building, and one to the Mallinckrodt Institute of Radiology.

C-5. Long Distance Data Transmission Experiments

Personnel: V. W. Gerth, Jr., BCL
G. C. Johns, Computer Systems Laboratory

Support: FR 00161

The Programmed Console was demonstrated at the Radiological Society of North America's annual convention in Chicago, Illinois (see Introduction to Section B). In connection with this demonstration a voice grade, full-duplex data line was leased from A.T.&T. between the data switching center at BCL and Chicago, Illinois. During the time the line was not being used for demonstrations, tests were run to get information concerning error rates. The line was tested by connecting a LINC to a PC (both at BCL) by means of a data line going through Chicago. The data channel between St. Louis and Chicago was carried over an A.T.&T. microwave link and used conventional phone lines only within the cities.

A LINC program transmitted quasi-random blocks of data to the PC which then retransmitted the data to the LINC. The LINC then checked and categorized errors into word errors, bit errors, checksum errors, and complete communication failures. The error rate experienced was no greater than that on the data lines between BCL and the Information Processing Center three miles distant. The error rate increased markedly between 7 and 9 a.m. and between 4 and 6 p.m., in agreement with previous experience.

We conclude that the communication protocol and error detecting schemes now in use are applicable to long distance data transmission over leased lines.

C-6. Acoustic Coupler Testing Programs

Personnel: D. Gurwitz, BCL
V. W. Gerth, Jr., BCL

Support: FR 00161

The acoustic coupler is a standard device for transmitting data between computers via dial telephone lines. To test the coupler, programs were written to transmit data between the IBM 1050 terminal and the Programmed Console, and between the IBM 360/50 and the PC. Error rates are acceptable for data rates of 134.4 baud.

C-7. PC Editor

Personnel: M. D. McDonald, BCL

Support: FR 00161

The PC Editor program is designed to enter information into the PC via its keyboard, a line at a time with up to 40 characters per line. Any line already entered may be viewed, deleted, or changed. When satisfactory the line may be transmitted over phone lines and any number of additional lines may be entered in a similar manner. The PC Editor was written to allow PC programs to be transmitted from the PC to the LINC in assembly language and then when converted to machine language to be retransmitted to the PC for execution.

D. Applications of Computers to Cardiology

Grouped together in the following section are several reports of applications of computers to cardiology, especially ECG rhythm monitoring and fetal electrocardiography. Much of this work has been aided substantially by scientific collaboration and financial support from other departments in the University. Our colleagues and the sources of support are noted within each report.

D-1. ECG Rhythm Monitoring

Personnel: G. C. Oliver, Jr., M.D., Medicine
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J. R. Cox, Jr., BCL
H. A. Fozzard, M.D., University of Chicago

Support: FR 00161
Washington University

Work on the automatic classification of cardiac rhythms through computer monitoring of the electrocardiogram has a dual objective. First, a running summary of the distribution of an individual patient's rhythms should aid the evaluation of drugs for the control of rhythm and cardiac functions. Second, rapid automatic classification of cardiac rhythms, giving current information on the patient's status, would contribute to his improved care since it would release scarce, skilled personnel for other urgent and more variable tasks. Both of these objectives will be realized as a result of the recent award to the Washington University School of Medicine of a grant (HE 10695) for the installation and operation of a nine bed acute cardiac research unit at Barnes Hospital.

A set of transformations to produce successively more compact string-like representations of the ECG is an approach to rhythm classification that lends itself well to continuous on-line processing. Initial development of the AZTEC transformation and a first attempt at the Primitive transformation were carried out on the LINC (see PR 2, A-6). Starting in the fall of 1966, these programs were transferred to the PC and since then all new programming has been done on the PC. The noise classification and QRS recognition algorithms of the Primitive transformation have since been developed to a satisfactory state. Segments of AZTEC of 200 ms duration are placed in one of three categories: quiet, low noise, and high noise. Quiet signals are expected to be completely analyzed, low noise signals are searched only for QRS complexes, and high noise signals are not further

analyzed. The basic QRS recognition algorithm, which operates on both low noise and quiet data, searches for large slopes which form an upright or inverted V-shaped signal whose height and width are within certain limits. The search is terminated at this point for low noise data while for quiet data the search continues on both sides of the V looking for sloping segments which may be added to the basic V to form the total QRS.

Extensive investigation of a wide variety of ECG waveforms has shown that while the present AZTEC gives sufficient detail on the larger P and T waves for low heart rates, the characterization is probably inadequate for lower amplitude P waves and rhythms where the P and T waves are superimposed. We are at present investigating three not necessarily mutually exclusive approaches to this problem. One approach is to use a low-pass filter on quiet, non-QRS sections of the sampled waveform and then form an AZTEC string with much reduced aperture to get more waveform detail while retaining the data reduction ratio present in the original AZTEC. A second approach is to represent the P and T waves as a linear combination of the outputs of a set of analog orthogonal filters. The third approach is to form an average QRST waveform from selected complexes and to subtract this average waveform from the current QRST interval which is under investigation. This last technique is the most promising but may be costly in terms of computer space and time. Thus at the present time the Primitive transformation consists of a string of code words characterizing variable length intervals as QRS or non-QRS along with their noise classification. QRS characters have an additional code word describing the shape of the QRS in terms of its major sloping components.

Work has proceeded on some of the measurements needed at the Cycle level. These include QRS waveshape categorization as normal or abnormal, instantaneous and average R-R interval deviation, and average heart rate. In order to evaluate the performance of these measurements, informational displays have been developed for the storage oscilloscope, including a plot of average heart rate and detection of ventricular premature contractions.

D-2. AZTEC, A Preprocessing Program Used for Real-Time ECG Analysis

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G. C. Oliver, Jr., M.D., Medicine
H. A. Fozzard, M.D., University of Chicago

Support: FR 00161
Washington University

A preprocessing program developed for real-time monitoring of the electrocardiogram by digital computer has proved useful for rhythm analysis (see D-1). The program suppresses low amplitude signals, reduces the data rate by a factor

of about 10, and codes the result in a form convenient for analysis. A concise description of the general algorithm is given below in a form that is easy to understand, but not readily implemented.

The AZTEC transformation may be described as follows:

let v_i be the i^{th} sample following an initial sample v_0 . Let v_{\max} and v_{\min} be the maximum and minimum values respectively of the set $\{v_i\}_0^m$ where i ranges from 0 to m . If $v_{\max} - v_{\min} \leq K$ for the set $\{v_i\}_0^{n-1}$ and $v_{\max} - v_{\min} > K$ for the set $\{v_i\}_0^n$ then the set $\{v_i\}_0^{n-1}$ is said to form an AZTEC "line", L . The line, L , is completely specified by its value, $v(L) = \frac{1}{2}(v_{\max} + v_{\min})$, and its duration $\tau(L) = n$ times the sampling interval. Let v_n now be the new v_0 and repeat the process. This much of the transformation is called a zero-order linear interpolator with aperture $K/2$. It has the property that, if L contains the sample v_i , then $|v(L) - v_i| \leq K/2$.

Let L_i be the i^{th} AZTEC line following a line, L_0 . The line, L_i , is said to be a "plateau" if $\tau(L_i) > T$. We call L_i an "extrema" if $\{v(L_{i+1}) - v(L_i)\} \{v(L_i) - v(L_{i-1})\} < 0$. The line, L_i , is a "bound" if L_i is a plateau or an extrema. A set of AZTEC lines $\{L_i\}_1^{m-1}$ is said to be a "slope", S , if no L_i is a bound and L_0 and L_m are bounds. The slope, S , is completely specified by its value, $v(S) = v(L_m) - v(L_0)$, and its duration, $\tau(S) = \sum_{i=1}^{m-1} \tau(L_i)$. The complete AZTEC transformation then consists of an ordered set of bounds and slopes.

Figure 1 shows a flow chart that leads easily to an implementation. Here the ordered set of bounds and slopes that form the AZTEC transformation develops as a string of characters, A_n , which may be stored consecutively in memory. Note that an upper limit on the duration of slopes and lines, T_{\max} , has been added to prevent overflow of the duration portion of an AZTEC character.

Figure 2 shows an ECG sampled at 500 eleven-bit samples per second (top) and the resulting AZTEC representation (bottom) as reproduced by a digital plotter. The AZTEC parameters are $K = 408$, $T = 4$, and $T_{\max} = 778$. The horizontal line at the upper left indicates 100 ms and the vertical line indicates one-eighth of full scale, in this case 400 μ volts.

Publication:

J. R. Cox et. al., "AZTEC, a Preprocessing Program Used for Real-Time ECG Analysis", submitted for publication.

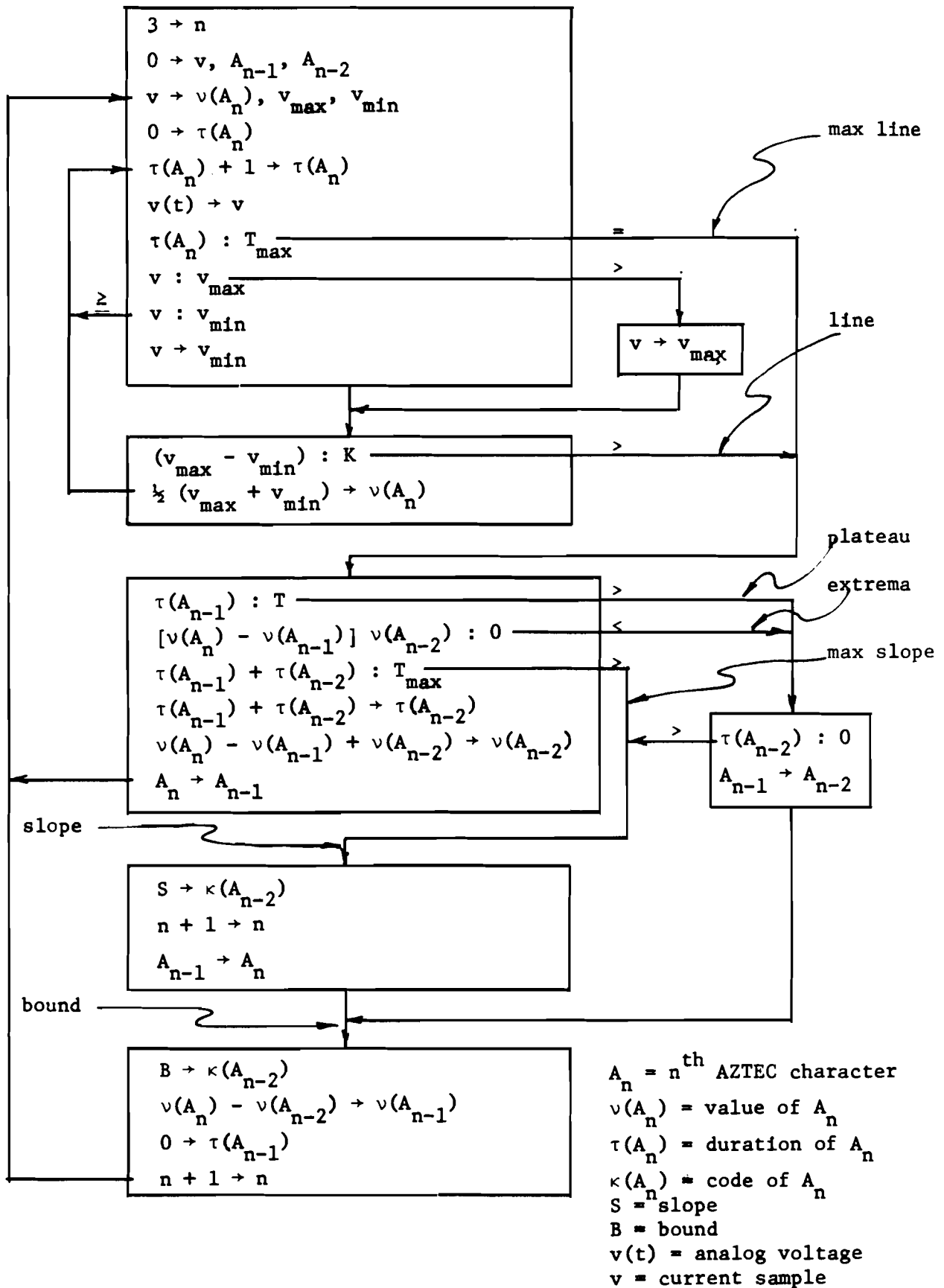


FIGURE 1 A flow chart of the AZTEC transformation. Input is the analog voltage $v(t)$ and output is the string of AZTEC characters, A_n .

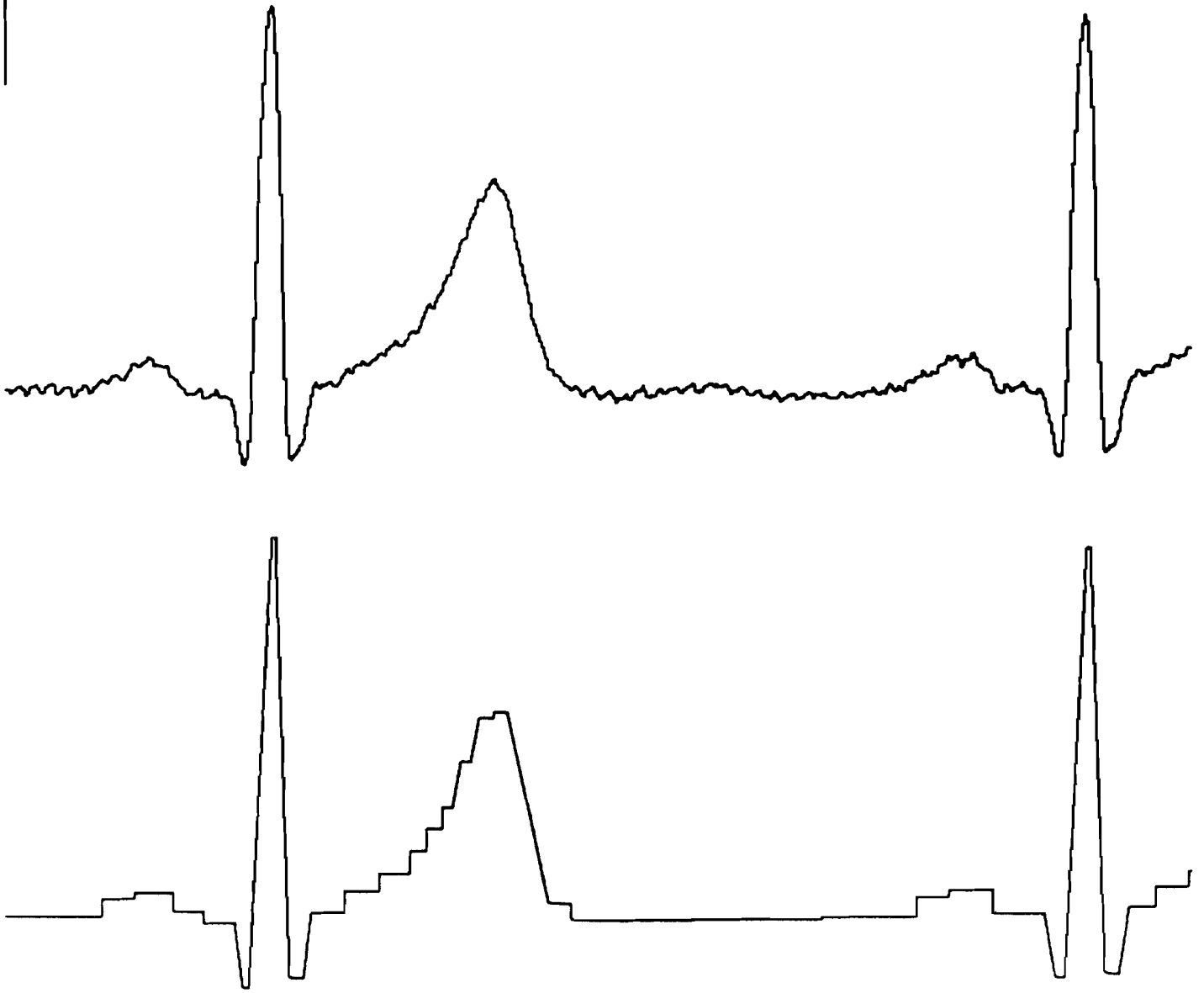


FIGURE 2 Sampled electrocardiogram and its AZTEC transformation as reproduced by an incremental plotter.

D-3. AZTEC Display and Plot Program

Personnel: F. M. Nolle, BCL

Support: FR 00161

This program was written for the PC to allow manipulation of the AZTEC transformation parameters with a convenient oscilloscope display and optional plotting of results for a permanent record. The program allows an analog channel to be monitored for sections of interest. When such a section is observed, the last 3000₈ samples may be frozen and selectable segments of the sampled waveform and corresponding AZTEC waveform are displayed. Keyboard options are used to vary the scale, baseline, and trace separation, to filter, to change the AZTEC parameters, and to plot the result along with vertical and horizontal calibration.

D-4. Detection and Enhancement of the Fetal Electrocardiogram

Personnel: D. H. Glaeser, BCL
M. R. Behrer, M.D., Pediatrics
J. R. Cox, Jr., BCL
R. B. Woolf, M.D., Obstetrics
J. M. Barnes, A.B., Pediatrics
F. L. Francis, BCL

Support: FR 00161
HE 09528
Washington University

During the past year, the development of data acquisition equipment and procedures has been completed and data from an average of 10 patients per week is being routinely recorded. Two abdominal leads and one standard limb lead are all simultaneously recorded. Two stages of processing are used which remove the maternal electrocardiograms from the abdominal leads and then arithmetically average consecutive sequences of 32 beats, storing these averages on LINC tape. Approximately 2000 such averages have been accumulated thus far. Average numerical values are being obtained for important parameters such as P wave amplitude and duration, P-R interval, and QRS amplitude and duration. T waves have not appeared with sufficient regularity to include these in our measurements. Inasmuch as our patient categories include both normal pregnancies and those in which one or more complications may be present, trends in correlations between these complications and FECG morphologic changes may emerge as our accumulation of data continues.

One difficulty which has arisen consistently in the averaged FECG's is moderate to serious distortion of lower frequency waves due to our choice of data bandwidth. Unfortunately, other considerations, low-frequency baseline variations in particular, preclude any change in the offending cutoff frequency. To overcome this difficulty, we have experimented with "inverse" digital filtering of the averaged FECG's. An "inverse" filter (with respect to a given filter) is one whose complex transfer function is the reciprocal of that of the given filter. The purpose of the inverse filter is to amplify frequencies attenuated by the given filter and vice versa. Preliminary results with simulated FECG's indicate that some restoration of low frequency waves is possible. Further work is required to determine whether this enables us to quantify more accurately the fetal P wave.

D-5. Optimum Estimation Techniques for the Fetal Electrocardiogram

Personnel: L. M. Medgyesi-Mitschang, Grad. Student, Electrical Engineering
J. R. Cox, Jr., BCL

Support: FR 00161
Washington University

Algorithms for the estimation of signals in noise have been developed using an extension of the work of Hellstrom and Woodward.¹ The estimates so obtained maximize the posterior probability density and may prove useful in the enhancement of the fetal electrocardiogram as well as of other biological signals. Generalizations of previous work include the removal of the requirement for white noise, the inclusion of a priori information about the signal's arrival time, and the extension of results to optimal processing of multiple observations.

1. C. W. Hellstrom, "Statistical Theory of Signal Detection", Pergamon Press, New York, 1960.

P. M. Woodward, "Probability and Information Theory, With Applications to Radar", McGraw-Hill, New York, 1953.

Publication:

L. Medgyesi-Mitschang, "Estimation of Signals in Noise with Almost Periodic Arrival Times", Washington University, St. Louis, Missouri, 1967 (D.Sc. Dissertation).

D-6. Experimental Investigation of the Conduction Pathways for the Fetal Electrocardiogram

Personnel: M. R. Behrer, M.D., Pediatrics
D. H. Glaeser, BCL

Support: FR 00161
HE 09528
Washington University

Continuing the research of the previous year (see PR 2, A-7) a series of ten experiments has been performed using pregnant ewes as the experimental preparation. These experiments were designed to test the hypothesis that the nasopharynx is the principal conducting pathway from the fetal heart to the uterine walls. Electrocardiograms were recorded a) on the abdomen prior to surgery, b) on the abdominal fascia, c) on the exposed surface of the exposed uterus, d) in the amniotic fluid, e) directly on the undelivered fetus by means of subcutaneous fetal limb electrodes sewn in place during temporary exposure, and f) on the delivered lamb. In addition, c), d), and e) were repeated after the head of the fetus had been delivered through an incision in the uterus which was then closed around the neck of the fetus. A number of conclusions may be drawn from these experiments:

1. The electrocardiogram of the fetus as recorded from the abdomen does not clearly resemble any of the standard leads, but the greatest similarity occurred for Lead III.

2. No significant reduction of signal amplitude or change in shape in d), e), and f) above occurs when the head has been delivered from the uterus.

3. Signal loss appears to occur from the uterine surface to the abdominal fascia rather than across the uterine muscle.

D-7. Infant Vectorcardiograms

Personnel: M. R. Behrer, M.D., Pediatrics
D. M. Swan, BCL

Support: Washington University
FR 00161

Quantification of the infant vectorcardiogram (VCG) is incomplete because the VCG changes steadily during the first few years of life. Extensive data will be required to accurately describe these changes and to differentiate between normal and abnormal vectorcardiograms. To help

collect these data a LINC program has been written to average 16 beats recorded from any standard 3-lead system and to generate both planar and stereoscopic views of the VCG. The duration of the QRS complex and the maximum and instantaneous vectors can be calculated and printed. Finally, three planar views may be plotted for a permanent record.

D-8. A Model for the Generation of the Human Electrocardiogram

Personnel: W. E. Long, Grad. Student, Electrical Engineering
J. R. Cox, Jr., BCL
H. D. Ambos, BCL

Support: Washington University
FR 00161

A system for simulating the transmission to the surface of the body of the electrical signs of the depolarization of the heart has been designed and constructed (see PR 2, C-8). The system consists of a plastic scale model of the two ventricles with 162 separate conducting surfaces spread over both the inner and outer surfaces of the ventricular walls and both surfaces of the septum. Each conducting section is connected by means of a separate wire to a patch panel. By connecting together the various elemental areas a variety of dipoles both in size and orientation may be simulated. These dipoles are driven by thirty-two separate and balanced sample-and-hold circuits. An interface with the LINC makes it possible to drive each of the thirty-two separate dipoles independently with waveforms stored in the LINC memory. Thus the external electrical effects of the depolarization of the ventricles can be simulated with speed, relative ease, and moderate accuracy.

With this simulated heart placed in a plastic torso filled with distilled water, sufficient current will flow to produce electrical signals like the electrocardiogram. Initial tests show that the major characteristics of the electrocardiogram are reproduced in the model. Much work remains to be done in shaping the depolarization wave and in the analysis of the effects of abnormal conditions in the myocardium such as that produced by an infarction.

D-9. On Line Computer Monitoring of Thoracic Impedance for Estimation of Cardiac Output

Personnel: S. P. Londe, M.D., Surgery
J. C. Morris, M.D., Surgery
F. M. Nolle, BCL
M. E. Dodge, B.S., Medical Student

Support: HE 08594
FR 00161
Washington University

A method for continuous monitoring of the cardiac output which would not require access to the blood stream would be of great value in determining the status of critically ill patients. It has been demonstrated that changes in cardiac output produce changes in the thoracic impedance waveform, but a strict mathematical relationship remains to be developed.

An on-line program which gives the weighted average of the thoracic impedance waveform related to the cardiac cycle (see PR 2, C-6) has been expanded to allow magnetic tape storage and hard copy via the CALCOMP plotter.

Canine cardiac outputs were determined by a dye-dilution technique with simultaneous recording of the thoracic impedance waveform and phonocardiogram. Circumferential cervical and lower thoracic band electrodes were used throughout and were found to give reproducible waveforms. Data plots of the cardiac thoracic impedance waveform were compared with the calculated cardiac outputs, but inherent variability in both techniques will necessitate a large number of experimental determinations with a significant spread of outputs for adequate statistical comparison.

D-10. Cardiac Output by the Dye-Dilution Technique

Personnel: G. C. Oliver, Jr., M.D., Medicine
F. M. Nolle, BCL
H. D. Ambos, BCL

Support: FR 00161
Washington University

A program has been written for the LINC for the rapid calculation of cardiac output and mean circulation time. Dye curves and calibration waveforms are transmitted to the LINC from the cardiac catheterization laboratory over leased telephone lines. The waveform is sampled every 125 ms, and by means of revolving storage the last 64 seconds of the signal are continuously displayed. The waveform can be frozen at any time by keyboard control. The time of the dye injection and of the onset of the curve are manually identified by cursors. A section of the downslope of the curve is likewise selected for exponential curve fitting. Exponential curves are generated using an iterative technique, and the exponential curve showing best fit (as determined by minimum area error) is displayed. Cursors are used to identify sections of the calibration curve corresponding to known dye concentrations. Data such as the patient name, amount of dye injected, and calibration concentrations used are entered from the keyboard in response to questions. Teletype outputs include the patient name, cardiac output, mean circulation time, curve area, and exponential decay constant. A filing system using the patient name has been developed which allows curves to be stored on or recalled from LINC tape. Approximately twelve cardiac outputs have been calculated, both by conventional means and by the above program, with excellent correlation.

E. Cochlear Models

Several reports describing research on cochlear models are presented in this section. The experiments here have been carried out in the Research Department of the Central Institute for the Deaf while most of the computational work has been done at BCL.

E-1. Model of the Hydromechanical Action of the Cochlea

Personnel: A. M. Engebretson, BCL
J. R. Cox, Jr., BCL
D. H. Eldredge, M.D., Central Institute for the Deaf

Support: FR 00161
NB 03856

The only direct observations of the motion of the basilar membrane have been made by Békésy. His observations have significantly influenced present cochlear model theory, since he saw for the first time that a traveling wave propagates along the basilar membrane when sound enters the ear. Békésy observed the motion of the basilar membrane through openings cut in the apex of the cochlea. Due to experimental limitations, his measurements of displacement and phase of the basilar membrane were taken for relatively low frequencies and apical positions along the cochlea. Because of the apparent difficulty of this experiment, no one has reproduced or added to these measurements.

Three well known cochlear models have been proposed by Zwislocki,¹ Fletcher,² and Peterson-Bogert.³ These models differ primarily in the parameter values used to describe the cochlear partition. Zwislocki has chosen parameter values which make his model a dispersive one. The position of the maximum of the traveling wave is determined by loss in the cochlear partition. Fletcher and Peterson-Bogert have chosen parameter values which result in a resonant model. The position of the maximum of the traveling wave is determined by the mass of compliance of the cochlear partition. Since both a dispersive and a resonant model seem to fit Békésy's experimental data, we have the problem of choosing between them.

There are other interesting problems relating to models of the cochlea. For example, a digital computer simulation of the traveling wave solution obtained from a dispersive model, when displayed in slow motion on an oscilloscope, does not look like the traveling waves that Békésy saw in the cochlea. Further, we cannot explain the discrepancy between the sharply tuned auditory nerve fibers of Kiang⁴ and the broadly

tuned envelopes observed by Békésy. It may be that present models ignore some important mechanical properties of the cochlea; possibly membrane displacement is not the significant aspect of membrane motion, or perhaps a sharpening mechanism exists between membrane motion and neural excitation.

We now see two ways in which to improve our understanding of cochlear hydromechanics. One approach is to study more thoroughly present models of the cochlea in order to choose between the dispersive model and the resonant model. We are attempting to use cochlear microphonic voltage (CM) as a second source of experimental data with which to test the models. However, this has required the development of a model relating CM to membrane displacement (see E-2).

The second approach is to develop a more exact mathematical formulation of the physics of the cochlea (see E-4). In this way the effect of simplifying assumptions used in the previously mentioned models can be studied. In addition, we hope to obtain a more direct relationship between parameters of the model and physical parameters of the cochlea.

1. J. Zwislocki, "Analysis of Some Auditory Characteristics", Handbook of Mathematical Psychology, Volume III, John Wiley & Sons, 1965.
2. H. Fletcher, "On the Dynamics of the Cochlea", Journal of the Acoustical Society of America, Volume 23, 1951.
3. L. C. Peterson and B. P. Bogert, "A Dynamical Theory of the Cochlea", Journal of the Acoustical Society of America, Volume 22, 1950.
4. N. Y-S. Kiang, et.al., "Discharge Patterns of Single Fibers in the Cat's Auditory Nerve", M.I.T. Monograph No. 35, M.I.T. Press, 1965.

E-2. Nonlinear Model of CM

Personnel: A. M. Engebretson, BCL
D. H. Eldredge, Central Institute for the Deaf

Support: FR 00161
NB 03856

When sound enters the ear, various components of voltage can be measured between the perilymph in scala vestibuli and scala tympani. Two of these components, summing potential (SP) and cochlear microphonic voltage (CM), are believed to originate in the hair cells as a result of cochlear partition vibration. At low sound pressures little if any SP is present and the CM is linearly related to the input sound pressure. At higher sound pressures (about 50 db SPL) the CM waveforms become obviously distorted and in some cases SP becomes prominent. For these sound pressures tones interfere with each other producing harmonic and combination frequency components in the CM. In addition the fundamental component for each tone is reduced from the value obtained when each tone is presented separately.

Summating potential which is observed as a baseline shift of the CM during the duration of a tone is a very complex phenomenon. The phenomenon is altered by drugs, anoxia, excess pressure applied across the cochlear partition, DC voltage applied between scala vestibula and tympani, injury to the middle ear, malfunctioning stimulus and recording equipment, and other undefined variables. The most frequently observed SP occurs at high levels concurrent with asymmetric distortion of the CM waveforms. These observations tend to confirm the theory that SP is simply a distortion product of the CM. At higher frequencies of stimulation, although the SP remains the same, the CM appears to be less distorted and more symmetric. However, a low pass filtering of the CM voltage can account for such differences at higher frequencies. Whitfield and Ross¹ have suggested that the gross electrodes used in these experiments introduce a low pass filter artifact into the CM measurements. In addition, the cochlea acts as a low pass filter for distortion products that might exist in the traveling wave.

The absence of a good intuitive understanding or a simple mathematical analysis of the behavior of such nonlinear systems prompted the construction of the nonlinear model shown in Figure 3. The linear mixer (summing network) represents the basilar membrane which drives the hair cells. The nonlinear diode network represents the hair cells which probably produce a peak limited CM at high sound pressures. The low-pass filter at the output represents the filter artifact that has been proposed by Whitfield and Ross. Figures 4 and 5 show the striking similarities between CM voltage from the guinea pig cochlea and the waveforms from the model. We are encouraged by the fact that such a simple nonlinear model for the hair cells exhibits so many properties of CM, including SP and interference. We are now adding this model of the hair cell to our cochlear model in order to study the behavior of the distributed system.

1. I. C. Whitfield and H. F. Ross, "Cochlear-Microphonic and Summating Potentials and the Outputs of Individual Hair-Cell Generators", Journal of the Acoustical Society of America, Volume 38, 1965.

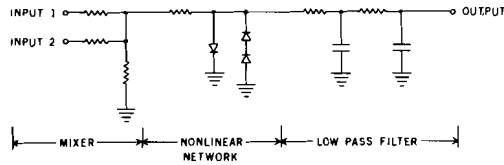


FIGURE 3 Circuit diagram of the electronic nonlinear model used to produce the waveforms shown in Fig. 4b and Fig. 5b. The mixer section of the model merely adds linearly the two input signals.

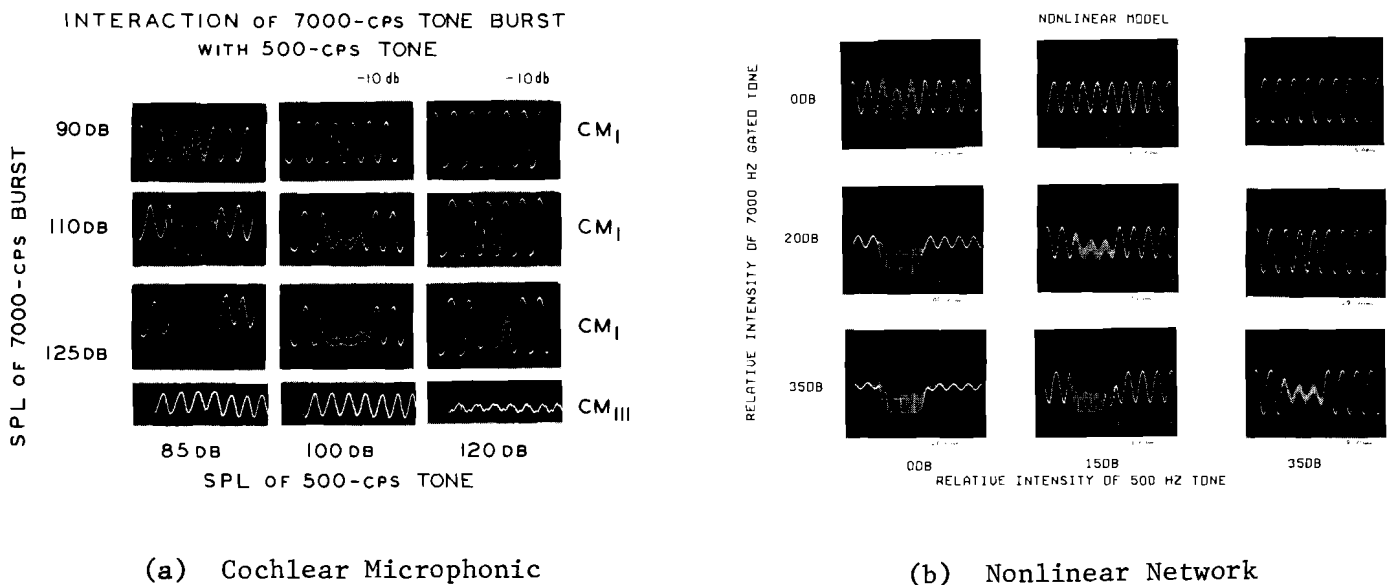
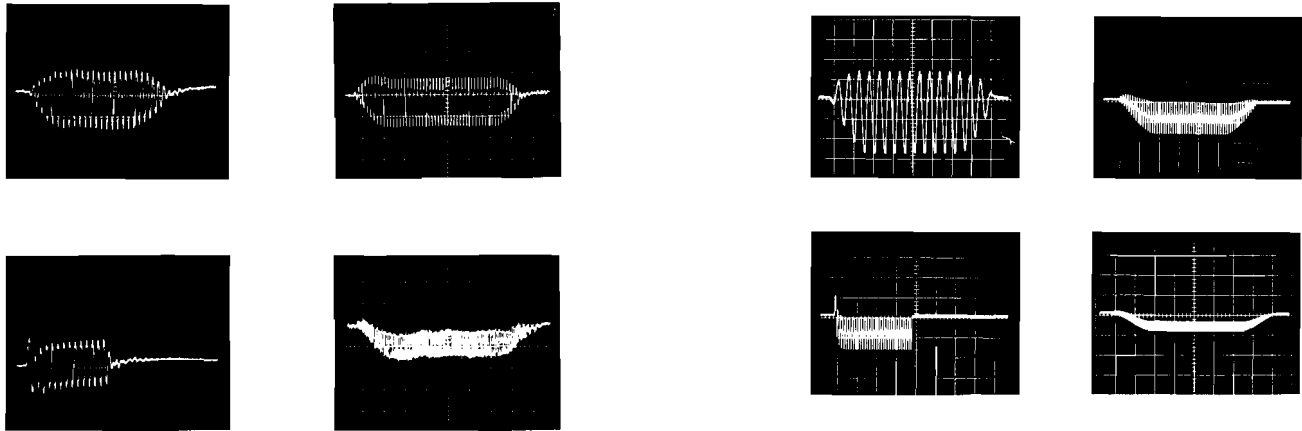


FIGURE 4 The waveforms observed in the cochlea (a) and in the nonlinear network (b) are shown for a 7000 CPS gated tone added to a 500 CPS continuous tone. As the intensity of the 500 CPS tone is increased the waveform becomes more distorted. Increasing the intensity of the 7000 CPS gated tone decreases both amplitude and distortion of the 500 CPS tone.



(a) Cochlear Microphonic

(b) Nonlinear Network

FIGURE 5 Typical responses of cochlear microphonic voltage and the nonlinear network to gated tones for various turn-on times and frequencies. The low pass filter at the output of the nonlinear network produces the transient at the beginning of the gated tone. The asymmetry of the nonlinear network produces the baseline shift during the duration of the tone which is similar to summing potential observed in the cochlea. The sawtooth nature of the network waveforms is also a consequence of the low pass filter.

E-3. Interference in the Cochlea

Personnel: A. M. Engebretson, BCL
D. H. Eldredge, M.D., Central Institute for the Deaf

Support: FR 00161
NB 03856

A particularly striking aspect of the cochlear microphonic voltage (CM) is the way in which one tone interferes with another. For loud sounds, which produce nonlinear CM, the addition of a second loud sound tends to linearize the first. This effect is seen in the input-output curves of the fundamental component of the first tone shown in Figure 6(a). The linearization effect is a phenomenon which probably occurs in most nonlinear systems. For example, the curves of Figure 6(b) were obtained from a simple resistor-diode voltage divider network (Fig. 3). The nonlinear transfer function for the network is shown in the insert of Figure 6(b).

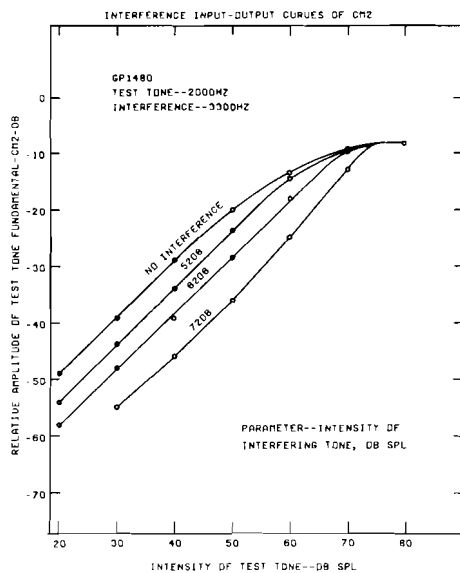
Linearization can be shown mathematically by approximating the non-linear transfer function by a polynomial with coefficients a_1, a_2, a_3, \dots and by assuming an input signal of the form, $A \cos \omega_A t + B \cos \omega_B t$. The expression which results for the fundamental component ω_A , is:

$$F_{\omega_A}(A, B) = a_1 A + (3/4)a_3 A(A^2 + 2B^2) + (5/8)a_5 A(A^4 + 6A^2 B^2 + 3B^4) + (35/64)a_7 A(A^6 + 12A^4 B^2 + 18A^2 B^4 + 4B^6) + \dots$$

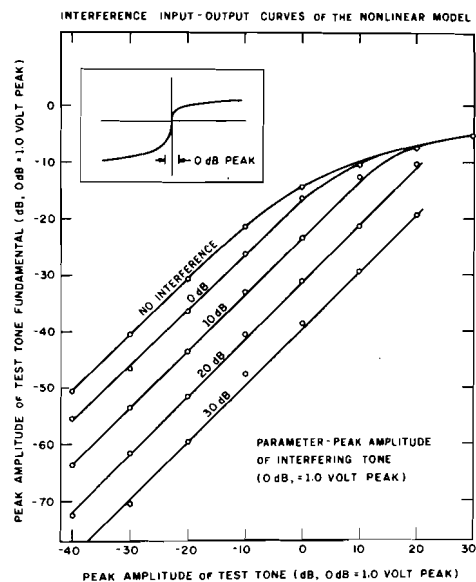
One can see from this equation that if the peak amplitude of the second tone (B) is much greater than the peak amplitude of the first tone (A), the input-output function is linear with respect to A. Increasing B increases the linear range of A. One also can see from the equation that for A much larger than B, the input-output curve is the same as for A alone. These observations from the equation correspond to the general trend of the experimental data of Figure 6.

Paper presented:

A. M. Engebretson, D. H. Eldredge, "A Model of the Nonlinear Behavior of Cochlear Microphonic and Summating Potential", Presented at the 73rd meeting of the Acoustical Society of America, New York, April 19-22, 1967.



(a) Cochlea



(b) Nonlinear Network

FIGURE 6 Interference input-output curves for the cochlea (a) and the nonlinear network (b). A wave analyzer with a 10 CPS narrow band filter was used to measure the magnitude of the fundamental component of the distorted waveforms.

E-4. Lumped Constant Approximation to Fluid Motion in the Cochlea

Personnel: J. R. Cox, Jr., BCL

Support: FR 00161

Models of the cochlea have been derived by others which take account of the mass reactance of the fluid moving longitudinally in the cochlear duct (Zwislocki) and the fluid moving normally to the basilar membrane (Fletcher). During the past year we have developed an approximate solution to the partial differential equation for fluid motion in the cochlear duct which simultaneously includes both of these mass reactances. From these results it is easy to see that the mass of the membrane itself is small by comparison with the effective mass of the surrounding fluid. This result casts doubt on the assumption that the mass reactance associated with the motion of the membrane can be neglected.

This lumped constant approximation to the fluid motion has been utilized in the development of a transmission line model of the mechanics of the cochlea. Effects of the compliant coupling between adjacent sections of the membrane are also included. The resulting fourth order partial differential equation with nonconstant coefficients has not been solved.

F. Other Laboratory Applications of Computers

Computer applications which are not described in previous sections and which involve a strong coupling to the laboratory environment are reported in this section. A few supporting programming activities are also described. Again much of the work depends upon collaboration from our colleagues. Their names and any associated financial support are listed at the beginning of each report.

F-1. Transmission of Data from a Microspectrophotometer

Personnel: J. M. Enoch, Ph.D., Ophthalmology
A. L. Bodicky, BCL
J. R. Cox, Jr., BCL
R. E. Hitchens, BCL
M. D. Lien, BCL

Support: FR 00161
NB 02168

Measurement of the transmission of monochromatic light of varying wavelengths through retinal tissue yields information on the mechanics of color sensitivity of the eye. A requirement for extensive processing of the data produced by the microspectrophotometer used for this work has led to the design (see PR 2, C-4) and construction of a data transmission system. This system consists of two data sets and an interface unit. The wavelength of light emitted by the source within the microspectrophotometer is transmitted digitally to the interface unit from a 10-bit shift position encoder. An analog-to-digital converter is used to code the analog voltage which represents the intensity of light passing through the retinal tissue in the microspectrophotometer. Two 12-bit toggle switch sets are available on the unit for transmitting other information in coded form. All information is then converted to serial digital form by the interface unit. With the aid of the two data sets, the serial output from the interface unit will be transmitted over a voice grade phone line to a LINC at BCL for processing.

F-2. Data Terminal Box Generator of Pseudo-Random Numbers

Personnel: D. H. Glaeser, BCL
J. R. Cox, Jr., BCL
S. M. Rhode, BCL

Support: FR 00161

A frequent application of both digital and analog computers is the simulation of the performance of a physical system or a mathematical model subjected to some form of random environment. A source of random numbers or a random voltage is required to effect the simulation. Many physical systems are inherently random in their behavior, e.g., "noise diodes", photomultiplier tubes coated with radioactive paint, etc. Use of these devices has the serious disadvantage of an inability to duplicate exactly a random sequence. To eliminate this shortcoming, mathematical techniques have been developed to generate sequences of pseudo-random numbers. The two most popular of these are 1) the multiplicative congruence method, and 2) the additive method. Each of these methods results in a periodic sequence of numbers which exhibit desirable random properties over fractions of a period. The first of these methods is quite slow when programmed on a LINC, due to the long multiplication time of the machine. The second method suffers from inadequate knowledge of the dependence of the statistics of the sequence on parameters of the generator.

Since about 1956, a great deal of attention has been given to sequences of binary digits generated by linear recurrence, modulo 2.^{1,2,3} In addition, Tausworthe⁴ described the properties of random numbers generated by selecting contiguous bits from these sequences and appropriately weighting them. Inasmuch as a simple implementation of linear recurrences exists in a shift register with modulo 2 feedback, this method, when incorporated into a LINC data terminal box, appears very attractive. Analysis has shown that the distribution of m -bit numbers generated by an r -bit shift register ($m \leq r$) is approximately uniform, while the autocorrelation coefficient of the sequence of numbers so generated will approximate that of sampled white noise.

Certain values of r (the number of stages in the shift register) present the advantage that if $p = 2^r - 1$ is a Mersenne prime, all sequences generated by irreducible polynomials of degree r will have length p . We have constructed such a generator with $r = 31$ ($p = 2,147,483,647$). From this, a periodic sequence of 12-bit pseudo-random numbers having the statistical properties described above can be obtained. An advantage of the linear recurrence technique of generation is that the exact sequence may be changed by changing the elements of the linear feedback network, while the period and statistical properties are unchanged. Thus each allowed feedback configuration may be considered to generate one sample function from a random process.

We are presently testing the distribution of the numbers generated by the 31-bit shift register. One of the six different feedback configurations may be selected by front panel switches. Numbers may be requested at intervals of duration not less than 10 microseconds, which is faster than any proposed application of the generator will require.

We expect to employ the generator to test recent mathematical results (see D-5) in estimation theory as applied to fetal electrocardiography. Optimum processing techniques will be compared empirically to simpler methods of signal enhancement such as simple averaging.

1. S. Golomb, "Sequences with Randomness Properties", Final Progress Report, Glenn L. Martin Company, June, 1965.
2. T. Birdsall and M. Restenbatt, "Introduction to Linear Shift-Register Generated Sequences", Technical Report No. 90, University of Michigan Research Institute, October, 1958.
3. R. Hampton, "A Hybrid Analog-Digital Pseudo-Random Noise Generator", Simulation, Volume 4, March, 1965.
4. R. Tausworthe, "Random Numbers Generated by Linear Recurrence, Modulo Two", Mathematics of Computation, Volume 19, 1965.

F-3. Evoked Response Display System

Personnel: S. Goldring, M.D., Neurosurgery
P. E. Stohr, M.D., Neurosurgery
R. L. Hill, BCL
H. Agress, Jr., Neurosurgery

Support: FR 00161
NB 06947
NB-HE 06833

This display system provides audio-visual contact between the neurosurgeon and a LINC computer at a remote location. Evoked responses from the surface of the brain are amplified and transmitted over a co-axial cable to a LINC computer where a predetermined number of samples are stored in the computer's memory. This is repeated for a group of responses from the same electrode location and the group is averaged. The resultant response is displayed on the LINC output oscilloscope, and closed circuit television enables the surgeon to view the response on a monitor in the operating room. The LINC operator may view the surgery procedure on a monitor located at the computer site, and a two-way voice communication channel is provided between the surgeon and the LINC operator. A system is being designed to amplify signals from a probe containing eight electrodes in a grid array and to multiplex these signals onto a cable for transmission to the LINC. The LINC program is being rewritten to accommodate the eight multiplexed signals.

F-4. Teaching Program for Diagnostic Radiology

Personnel: M. D. McDonald, BCL
K. C. Tsien, Temple University

Support: FR 00161

This PC program is designed to lead a student through a detailed study of an X-ray of the abdomen in order to determine whether or not there is a possible malignancy in the colon.

After some preliminaries, the student responds yes or no to a series of questions designed to determine whether:

- 1) the entire colon is filled
- 2) some portion of the colon is displaced
- 3) the caliber of the colon increases steadily from sigmoid to cecum
- 4) the margins are smooth and slightly bulging between plicae
- 5) the barium column is homogeneous

At the termination of the question sequence in each of the five major sections, one or more conclusions suggested by the responses given are displayed. Repeated use of the program may provide useful practice for the student.

F-5. Diagnostic Isotope Studies

Personnel: E. J. Potchen, M.D., Nuclear Medicine
P. E. Stohr, M.D., Neurosurgery
R. P. Eaton, M.D., Metabolism
S. J. Birge, M.D., Metabolism
J. S. Clifton, Radiology
R. L. Hill, BCL

Support: FR 00161
FR 00215
AT (11-1)-1653
Washington University

Currently three categories of investigative techniques using radioisotopes employ computer analysis of results. These are:

- 1) Metabolic studies requiring model building techniques
- 2) Kinetic studies and flow analysis
- 3) Image processing with rectilinear scanners

Ultimately, analysis of data from multiple sample automatic counters will also be included.

By courtesy of Dr. Mones Berman a copy of the NIH SAAM 23 compartmental analysis simulation and model building program has been obtained and adapted to operate on the IBM 360/50. Using this program models have been constructed for the investigation of fatty acid metabolism, of calcium metabolism and absorption, and of magnesium metabolism and absorption.

A general purpose digital data acquisition system has been developed and installed, based on a Kennedy incremental tape drive (500 bps, 556 bpi). This system is capable of programmed scanning of one to six sources, of 10 BCD digits each, in any sequence, and of recording their output on a 7 track magnetic tape in IBM compatible format.

This system is used in combination with:

- 1) Stationary multiple probe arrays for kinetic studies using short half life isotopes.
- 2) A rectilinear scanner, equipped with additional positional and control logic and nucleonic circuitry for image processing and development of scanning techniques using simultaneous injection of two or more short lived isotopes (see PR 2, C-11).

Paper presented:

E. J. Potchen and J. S. Clifton, "The Problem of Organ Delineation in a Changing Blood Background", Presented at the 14th Annual Meeting of The Society for Nuclear Medicine, Seattle, Washington, June, 1967.

J. S. Clifton, E. J. Potchen, "Digital Data Recording and Image Enhancement Techniques in Rectilinear Scanning", Presented at the 14th Annual Meeting of The Society of Nuclear Medicine, Seattle, Washington, June, 1967.

F-6. Plotting Subroutines

Personnel: A. M. Engebretson, BCL
D. J. Manson, BCL

Support: FR 00161

Several subroutines, useful in the operation of an incremental plotter (CALCOMP Model 565), have been assembled into two packages, one for the LINC and one for the PC. These subroutines simplify the writing of specialized programs for plotting data and characters on the LINC and PC. Each package consists of a linear interpolation subroutine which connects two points with a straight line, a character plot subroutine, and a pen control subroutine. A character table is included for each machine which prints all characters that can be entered from the keyboard. The character tables, which can be interchanged between packages, are shown in Figure 7.

0123456789: p-+| #ABCDEF6HIJKL

MNOPQRSTUVWXYZ=u, .θ[_]

()*+, - . / 0123456789: ; < = > ? @ ABCDEF6

HIJKLMNPQRSTUVWXYZ[\] ^ _ ! " # \$ % & ' ,

` abcdefghi jklmnopqrstuvwxyz { | } ~

FIGURE 7. Characters Generated by Subroutines for an Incremental Plotter. The LINC character set is at the top and the PC character set is below.

F-7. DBLFLT Subroutines

Personnel: M. D. McDonald, BCL

Support: FR 00161

DBLFLT, a set of double-precision floating-point subroutines for the LINC (see PR 2, A-14) have been described in BCL Technical Report No. 2. Also described are I and O, general purpose decimal input and output routines for use with DBLFLT, and several arithmetic subroutines. The Report includes annotated listings of DBLFLT, I, and O.

Publication:

M.D. McDonald, "DBLFLT: Double Precision Floating Point Subroutines", Biomedical Computer Laboratory Technical Report No. 2.

F-8. Fast Printer Installation and Subroutine Programming

Personnel: F. M. Nolle, BCL

Support: FR 00161

A Motorola TP-4000 four line per second printer has been installed as a LINC output device. The interface design uses DEC Flip Chips installed in a data terminal frame PIU. A general purpose print subroutine has been written which frees the user of timing consideration. The subroutine stores 6-bit character codes in a revolving string. The printer is started when at least one full line is in the character string and is stopped at the end of the last full line. Magnetic tape interrupts are sensed and the interrupted instruction is then restarted.

F-9. Dynamics of Pulmonary Blood Flow During Cyclic Lung Inflation

Personnel: L. J. Thomas, M.D., Anesthesiology
A. Roos, M.D., Anesthesiology and Physiology

Support: FR 00161
HE 00082

The pulmonary vascular response to cyclic lung inflation is under study in excised cat lungs. Vascular inflow and outflow pressures are kept constant while the time course of blood flow is observed during sinusoidal

inflation over a wide range of frequencies and tidal pressures. Inflation is achieved by 1) increasing airway pressure with constant pleural and perfusion pressures ("positive pressure inflation"), and 2) lowering pleural pressure with constant airway and perfusion pressures ("negative pressure inflation"). Pressures and volume inflow are continuously recorded on an oscillograph and on magnetic tape for later processing by a digital computer (LINC) to allow analysis (including Fourier) and X-Y plotting.

The following results apply to the first harmonics. 1) During "positive pressure inflation", blood flow is approximately 180° out of phase with inflation pressure at all frequencies (0.06 to 0.8 Hz) and tidal volumes tested, indicating a resistive coupling between blood flow and lung inflation. 2) During "negative pressure inflation" blood flow at low frequencies is either 180° out of phase (large lung volume), or in phase (small lung volume) with lung volume; the shift approaches 90° (flow leading) at higher frequencies, suggesting largely capacitive coupling.

G. Information Processing Research

The following projects involve research in information processing. The work is directed toward the development and evaluation of new computational methods in support of biomedical research. Most of the work made extensive use of the facilities of the Washington University Information Processing Center.

G-1. Information Storage and Retrieval

Personnel: R. A. Dammkoehler, BCL
M. N. Bhide, BCL

Support: FR 00215

Research directed toward the development and evaluation of computer-based systems for the storage and retrieval of biomedical information was continued in this period. The main objectives of this effort were:

Acquisition and analysis of machine-readable text corpora suitable for experimentation with adaptive retrieval algorithms.

Establishment of an experimental users group to participate in evaluation studies.

Design and construction of an interactive retrieval system and monitoring programs in support of the experimental trials outlined in our original proposal.

Development and evaluation of associative and adaptive retrieval models based on higher order term associations and document-term discrimination criteria.

In the pursuit of the objectives listed above, a third document collection (in addition to the two experimental corpora taken from the cerebrovascular literature) was assembled. Four hundred and fifty abstracts of articles from current literature on thrombosis, fibrinolysis and blood clotting were selected on the basis of their relevance to the interests of an eight-member research team working in that area. The abstracts were keypunched and the data analyzed using frequency distribution, concordance and content analysis routines (see PR 2, B-6). On the basis of statistics derived from a factor analysis (varimax rotation) of the distribution of nominatives in the corpus, one hundred multi-term factors were selected as indexing terms. This procedure, in contrast to simple term occurrence schemes, appears to be equivalent to concept indexing and yields results similar to those obtained by manual indexing methods. The individual abstracts are indexed with reference to the presence or absence of the multi-term group within the body of the text.

The preprocessing of abstracts and the automatic selection of index terms enable us to produce a document collection, or sublibrary of materials, which may be thought of as a nearly homogeneous sample of the literature. No attempt is made to partition the collection into categories, and in fact, the indexing terms are deliberately chosen in such a way as to maximize document-term and term-term interaction. This of course implies that there is no underlying simple structure of term-term relationships, a result verified by our earlier investigations with the cerebrovascular literature.

A major commitment was made to the design and development of an interactive retrieval system to be used in support of experimentation with adaptive retrieval algorithms. This system, now operational, allows a remote user to initiate a retrieval request from an IBM 2260 display terminal and, following a short initial computation, to view the abstracts of documents ranked in order of their numerical relevance to his original query. Computations are performed on a centrally-located IBM 360/50 operating in a multi-programmed (partitioned) environment. A self-contained filing system and console command monitor allows the user to page forward and backward through his results, and to modify the search criteria and restart at any time.

Although our experience with the operational system has been limited, some interesting results have been obtained. The model of greatest sophistication differentially weights index terms as a function of the user's evaluation of the relevance of previously retrieved abstracts. The optimal weights are determined by maximizing a linear objective function relating the inverse cost of retrieval with respect to particular terms, subject to numerical constraints established by the previous application of the retrieval algorithm. Subsequent use of the new weights produces a revised retrieval ordering with documents similar in content to those previously judged relevant having the highest numerical relevance scores. Mathematically this reduces to a dynamic programming problem requiring the intermediate solution of a linear programming problem at each of n decision points. The process is terminated when the linear programming solution does not produce a re-ordering of the remaining documents.

Publications:

R. A. Dammkoehler, "Information Storage and Retrieval", Handbook of Computer Applications in Radiology, Radiotherapy, and Nuclear Medicine, Chapter 7, C. C. Thomas, Springfield, Ill. (In preparation).

R. A. Dammkoehler, "Direct Input of Textual Information", Chapter 5, Ibid.

G-2. Biomedical Data Processing Research

Personnel: J. M. Vanderplas, BCL
J. P. Miller, BCL

Support: FR 00215
G 22296

The two computer programs which were reported previously, one to compute Bayesian posterior probabilities, the other to compute prime implicants of disjunctive Boolean functions, have been explored and extended further. Their applications and ramifications for biomedical data processing have also been extended and explored.

An interesting and, potentially, extremely valuable theorem of Boolean algebra was explored in connection with one of the difficulties reported in the previous period (see PR 2, B-12). The attempt to reduce the 21-variable function reported then resulted in 270 prime implicants and 26 unique minterms. Application of the theorem shown below made clear just why the function could not be reduced further.

The theorem is a generalization of the basic theorem which states,

$$xy + x\bar{y} = x$$

and the generalization states, "wherever m elements are linked by the meet operation (intersection) with each of the possible non-zero combinations of the remaining $2^{(n-m)}$ elements taken $(n-m)$ at a time, then the join (union) of all such terms is equal to the meet of the original m elements."¹

It follows from the above theorem that if a function in n variables is to be reduced to a function of m variables, then the meet of m variables must occur $2^{(n-m)}$ times in the original function so that all of the possible $n-m$ elements may be present in the function.

It will be recalled that, in connection with the representation of biomedical variables, e.g., symptoms, that each term of the function is a single case (i.e., a patient) and that the function is the join of the patients, each having a meet of symptoms. Thus, in order to reduce the function of n variables to prime implicant form in $m < n$ variables, there must be $2^{(n-m)}$ cases, or patients in the sample.

The above theorem has implications for the necessary conditions under which reduction may be carried out on a given set of symptoms. For the sample utilized previously, with the number of cases equal to 437, the value of $(n-m)$ would be a maximum of 8, since with $(n-m) = 9$ the number of cases would need to be 512. Therefore, the maximum reduction of the function would be to a set of prime implicants with $(21-8) = 13$ variables. This fact accounts nicely for the large number of prime applicants generated by the computer program and also for the large number of irreducible minterms.

Further applications of the Boolean-Bayesian programs have been explored during the present report period. In addition to the possibility of reducing complex symptom configurations to simple form, it is possible to apply the Boolean methods to the reformulation of certain biomedical and psychological test and measurement instruments. Two such instruments, the MMPI and the Allport-Vernon-Lindzey Study of Values, are currently being investigated

from this point of view. Both of these instruments yield profile "scores" on a number of "variables" whose measurement status depends upon assumptions of interval status, continuity, and normality of distribution of the "scales". These assumptions may be questioned, of course. The Boolean method requires only the assumption of mutually exclusive classes.

Two possibilities have presented themselves thus far: one possibility is to expand the MMPI items into a 500 variable function and the Allport-Vernon into a 45 variable function, reduce the functions to prime implicant form and classify the protocols according to the derived categories. The other possibility is to make use of the "scales" of the instruments and rewrite the "profile" as a minterm in 12 or 6 variables, respectively, using the median or normal extremes as cutting points.

The first possibility would require an enormous number of cases, as indicated by the previously mentioned theorem, to effect any reasonably small derived function; the second possibility would require assumptions of discontinuity of the scales previously assumed to be continuous.

The results of these investigations into the possibility of treating test data as categories rather than as assumed continuous variables have rather extensive implications for the development of logical procedures for medical and psychological tests. Many such tests (e.g., patch tests, history items, genetic classes, etc.) are actually categories, and it is very difficult to treat them either as homogeneous with continuous variables or to force them into discrete variable form. The Boolean methods implemented here will provide a means for circumventing some of these difficulties.

1. H.G. Flegg, Boolean Algebra and its Application, Chapter 6, Wiley and Sons, New York, 1964.

Publication:

J. M. Vanderplas, "A Method for Determining Probabilities for Correct Use of Bayes' Theorem in Medical Diagnosis", Computers and Biomedical Research, Volume 1, November, 1967 (In press).

G-3. Re-Design of General Inquirer System

Personnel: J. P. Miller, BCL
G. Psathas, Ph.D., Social Science Institute

Support: FR 00215
G 22296
MH 08664
MH 12889

The General Inquirer computer system for the 7094-1401 computers was designed originally for the content analysis of a wide variety of textual

materials. An analysis of the results of the extensive use of the original program written by Phillip Stone of Harvard University and a later version by our group at Washington University for the 1401-1311 indicated the need for revision in order to take advantage of recent improvements in computer hardware and software.

The General Inquirer system is built around a dictionary constructed according to the users' investigative theory. To allow the investigator to express his dictionary more easily the special language Dictionary Definition Language (DDL) was designed. This language makes the dictionary self-documenting and allows for the painless specification of conditional tagging statements. Specifications were constructed so that Ingerman's "Syntax Oriented Translator" could be used to translate DDL statements into usable code. Additional projects, intended to facilitate user-system communications, involved the design of on-line file creation and editing routines. Preliminary specification for a retrieval language have also been developed.

Other technical improvements were the construction of an algorithm for the removal of post-fixes and the extension of the source document to a 128 character set. Preliminary specifications were also constructed so that the post-processing routines might be executed in either a batch processing or a time-sharing interactive mode.

Publication:

J. Philip Miller and George Psathas, "A 1401-1311 Tagging Program for the General Inquirer", submitted for publication.

G-4. A Linear Model for Description of Psychotherapy Interaction

Personnel: J. P. Miller, BCL

Support: FR 00215
G 22296

The General Inquirer is a system of content analysis which makes possible the reduction of the verbalizations of both patient and therapist in a psychotherapy interview to frequencies of occurrence of particular relevant themes or tags. A simple descriptive model of this interaction has been developed in which the frequency of occurrences of tags in a particular utterance is related to both the frequency of tags in the previous speaker's utterance and the frequency in the same speaker's previous utterance.

This linear model was tested by a canonical correlation between the two sets of variables. Since the number of variables under question became inordinately large, a stepwise canonical correlational procedure was developed which excludes variables on a varimax-like criterion, thus reducing the number of variables in the equations without significantly lowering the degree of the relationship.

Paper presented:

J. Philip Miller, "A Procedure for Stepwise Canonical Correlational Analysis",
submitted for presentation at the fall 1967 Meeting of the Psychometric
Society.

H. Medical Data Processing

The following research projects are primarily numerical or statistical in nature and often make use of existing computational techniques. The work was carried out by laboratory staff members using the facilities of the Washington University Information Processing Center.

The investigator responsible for the project is listed first. Bio-medical Computer Laboratory staff members collaborating with this investigator are listed on succeeding lines.

H-1. Computation of X-ray Data of Malate Dehydrogenases

Personnel: L. J. Banaszak, Ph.D., Physiology and Biophysics
G. S. Whitlow, Jr., BCL

Support: GB 5888
GM 13925

The computational facilities have been used during the last year as part of a research program studying the structure of heart muscle malate dehydrogenases. The computations consist of ordinary processing of single crystal x-ray data. This includes scaling of x-ray diffraction data from different films, merging of heavy atom derivative data, calculation and correction for a random temperature variation, and the calculation of difference Patterson projections. The latter is being used to survey potential heavy atom derivatives and to attempt to locate the heavy atoms in the unit cell of the crystal.

H-2. Homogeneity Control in a Shock Treatment Experiment

Personnel: H. R. Butcher, Jr., M.D., Surgery
G. S. Whitlow, Jr., BCL

Support: HE 10389

An experiment was arranged to test different methods of hemorrhagic shock treatment, using live rats. Six test groups of rats were bled to induce shock. The groups were then treated respectively according to six different methods. To insure homogeneity among the groups of animals, a program was written for the IBM 360/50 to compute means and standard deviations for the parameters of weight, blood pressure, hematocrit, serum sodium, serum potassium, and serum protein concentrations. The distributions

parameters were obtained for each subject: 1) earphone-generated sound pressure level (db); 2) ear canal diameter (mm); 3) head band force (gm); 4) earphone location (cm); 5) visually determined acoustic leak (cm); 6) acoustic transmission loss (db). The measurements of item 1) were obtained by three replications at each of the eight frequencies ranging from 125 to 4000 Hz. All other items were measured only once.

The IBM 360/50 was used to obtain the following statistical analyses:

1) Correlation coefficient between replications of sound pressure level measurement yielding an estimate of repeatability of this measure.

2) Correlation matrix (13 x 13) for the eight criterion variables and five covariates.

3) Analyses of variances of the sound pressure level data separately for each of the eight frequencies. The sources of variations tested by F test were age, sex, and age-sex interaction. In addition, variations between subjects but within groups were tested using the between-replications component as the error term.

H-5. Synthesis of Eco-System Response

Personnel: D. M. Gates, Ph.D., Center for the Biology of Natural Systems
L.E. Papian, M.S., Center for the Biology of Natural Systems
G. S. Whitlow, Jr., BCL

Support: ES 00139

The Center for the Biology of Natural Systems has developed a method by which any leaf (or needle) in any combination of environmental conditions can be represented. This is done with an energy budget equation which describes energy exchange by radiation, convection, and transpiration between the organism and the environment, described by parameters such as air temperature, relative humidity, wind speed, solar radiation, and thermal radiation from surrounding surfaces and the atmosphere. The IBM 360/50 was used to solve this equation and develop tables for all given environmental parameters. Graphic representations of portions of these tables were obtained by feeding the tabular data obtained from the IBM 360/50 into a LINC which in turn drove an incremental plotter.

H-6. Detectability of Tonal Signals at the Absolute Threshold

Personnel: I. J. Hirsh, Ph.D., Central Institute for the Deaf
C. S. Watson, Ph.D., Central Institute for the Deaf
G. S. Whitlow, Jr., BCL

Support: NB 03856

A useful approach to the study of the sensitivity of the human ear to brief tonal signals is to apply methods developed in the context of

the theory of signal detectability. Frequencies have been studied from 125 to 4000 Hz with listeners tested in both binaural and monaural conditions. In these tests, psychometric functions (input-output functions for the auditory system) were established in one experiment for each of twelve listeners, for each frequency, and under each of the two listening conditions, binaural and monaural. Thus, 144 functions were obtained, each by a least-squares fit to the experimental data. A program developed at BCL enabled the rapid calculation of slope and intercept for each such function, and each was, in fact, repeated four times to examine the effects of four different constraints on the data.

H-7. Computation of Self-Noise in the External and Middle Ear

Personnel: A. F. Niemoeller, Sc.D., Central Institute for the Deaf
G. S. Whitlow, Jr., BCL

Support: NB 03856

An electrical analog of the external and middle ear is being used to determine the spectral density of the velocity of the stapes due to random molecular motion in the lossy elements of the external and middle ear including the radiation impedance of the pinna. Noise velocities and pressures at various points in the analog ear have been computed with the IBM 360/50. In particular, the pressure on and velocity of the stapes due to this noise have been computed. In addition, a computer program has been written to compute spectrum levels of the sound pressure at the entrance to the ear canal which would produce the computed levels at the stapes due to random molecular motion. The computed spectrum levels at the entrance to the ear canal will then be compared with spectrum levels of minimum audible noise fields (monaural listening in a diffuse noise field) which have been published by Sivian and White.¹ In this manner, it should be determined within the accuracy of the analog whether the self noise of the external and middle ear in any way limits the hearing acuity of the normal listener.

1. L. J. Sivian and S. D. White, "On minimum audible sound fields", Journal of the Acoustical Society of America, Volume 4, 1933.

H-8. Computation of Fluorometric Enhancement Titrations of Antibody

Personnel: C. W. Parker, M.D., Medicine
G. S. Whitlow, Jr., BCL

Support: AI 04646
AI 09881
AI 00219

A spectrofluorometric method for the study of antibody-hapten interactions has been developed in the Department of Medicine. The technique utilizes increases in fluorescence of ϵ -5-dimethylaminonaphthalene-1-sulfonamido-lysine (ϵ -DNS-lysine) in the presence of rabbit anti-DNS antibody. Antibody-bound ϵ -DNS-lysine undergoes a thirtyfold increase in fluorescence quantum yield as well as a blue shift in the emission maximum. The fluorometric technique is valuable in the characterization of the antibody combining site and in the assessment of antibody heterogeneity, affinity, and concentration. The computer program was devised to assist in the calculation of the fluorescence data. The program takes as input data the fluorescence values of the saline blank, the temperature of the blank, the fluorescence enhancement factor, and a series of points at which the raw fluorescence value is measured for increasing proportions of the ϵ -DNS-lysine. The program then calculates, among other things, the amount of bound antibody present at each point, the association constant for each point, and the heterogeneity index. Finally the program averages the association constants, and lists the absolute values for free hapten and bound hapten at each point. While these operations are relatively simple in principle they are extremely time-consuming when performed manually.

Paper presented:

C. W. Parker and C. K. Osterland, "Hydrophobic Binding Sites on Myeloma Proteins and Macroglobulins", Presented at the 24th Annual Meeting of the American Federation for Clinical Research, Chicago, Illinois, November 3, 1966.

Publications:

C. W. Parker, "Fluorescence Enhancement in the Study of Antibody Hapten Reactions", Proceedings of the 50th Annual Meeting of the Federation of American Societies for Experimental Biology, 1966 (Abstract).

C. W. Parker, "Spectrofluorometric Methods", Handbook of Experimental Immunology, Blackwells, Scientific Publications, Oxford (In press).

H-9. Acetylcholinesterase Activity and Electronic Structure

Personnel: R. L. Schnaare, Ph.D., St. Louis College of Pharmacy
G. S. Whitlow, Jr., BCL

Support: St. Louis College of Pharmacy
G 22296

An understanding of the mechanism of action of existing drugs and the design of new ones would be aided by an understanding of the relationships between the electronic structure of drugs and their pharmacological activity.

In the present project, electronic structure is calculated theoretically by the LCAO-MO method employing the Huckel approximations with neglect of overlap. A program was written for the IBM 7072 which consisted of an eigenvalue-eigenvector calculation with subroutines to calculate parameters corresponding to electronic properties of the compound. This program has been used to calculate the electronic structure of a series of alkyl-substituted ammonium ions. The program is at present being adapted for the IBM 360/50 to take advantage of the greater quantity of high speed core storage.

H-10. Preliminary Study of Platelet Levels and Hemorrhage

Personnel: T. J. Vietti, M.D., Pediatrics
G. S. Whitlow, Jr., BCL
R. S. Ganesan, BCL

Support: AC 00108

Although a reduction in platelet count is usually associated with hemorrhage, the exact relationship is unknown. One difficulty is the high variability in platelet counts in both normal and diseased patients. The normal patient may have a platelet count varying from 150,000 to 350,000 per cubic mm. To investigate the relationship between platelet count and hemorrhage, charts of suitable patients treated by the Hematology Clinic of the St. Louis Children's Hospital were reviewed, with the periods of time at which the platelet counts were 30,000/cu. mm or less tabulated carefully with respect to degree and site of hemorrhage, fever, infection, and other factors. Some specific questions for which this investigation is designed are: whether the presence of fever and/or infection enhances hemorrhage; whether the duration at a given level of thrombocytopenia plays any part in predisposing a patient to hemorrhage; and what critical levels of platelet count are associated with what degrees of hemorrhage. The computation of the accumulated data is presently in progress.

H-11. Investigation of Lead Intoxication in Children

Personnel: T. J. Vietti, M.D., Pediatrics
G. S. Whitlow, Jr., BCL
R. S. Ganesan, BCL

Support: AC 00108

Two avenues of investigation into the problem of lead intoxication are being pursued. The first deals with the analysis of hospital records of children diagnosed as lead intoxication cases, to attempt to find general

trends. It was found that general analysis of such field data is quite complex, as no definite statistical or mathematical model could be found to fit the data. What was needed were certain "umbra penumbra" methods in the style of Tukey. The library subroutines for these methods were obtained from the Health Science Computing Facility at UCLA.

The second area of investigation was to compare the merits of DTPA and calcium versenate as chelating agents in the treatment of lead intoxication. These two agents were applied experimentally in varying combinations on patients. The preliminary results tend to indicate that DTPA may be superior to calcium versenate in chelating lead, although its effect could not be conclusively studied with the present experimental design.

VI. TRAINING ACTIVITIES

During the year BCL engaged in the following training activities:

Biostatistics Course July - September 1966

The course was taught by George S. Whitlow, Jr., and dealt with elementary applications of statistics to medical research. Part of the financial support for the course came from the Department of Otolaryngology. Attending the course were:

| | |
|--------------------------|--|
| Munawar Ahmad, M.D. | Otolaryngology, Homer G. Phillips Hospital |
| Bruce Berryhill, M.D. | Otolaryngology |
| Richmond Brownson, M.D. | Otolaryngology |
| Thomas Calcaterra, M.D. | Otolaryngology |
| Sam. E. Kinney, M.D. | Otolaryngology |
| Robert Maltz, M.D. | Otolaryngology |
| Hernando Rodriguez, M.D. | Otolaryngology, Homer G. Phillips Hospital |
| Roy Sessions, M.D. | Otolaryngology |

Elementary Electronics Course for Technicians October 1966 - February 1967

The course was taught by Donald H. Glaeser and dealt with basic vacuum tube and transistor circuits including amplifiers, oscillators, voltage regulators, and digital logic elements. Attending the course were:

| | |
|-------------------------|-----------------------------|
| Dieter Ambos | BCL |
| Andrew L. Bodicky, B.S. | BCL |
| Charles Buerke | BCL |
| Fred L. Francis | BCL |
| James Haller | Computer Systems Laboratory |
| Kenneth Lewis | Computer Systems Laboratory |
| Larry Lewis | Computer Systems Laboratory |
| Steve M. Rhode | BCL |
| Dale Richardson | Computer Systems Laboratory |
| James Spence | Computer Systems Laboratory |

Basic Course in Statistics for Programmers February - March 1967

The course was taught by Ramasami Ganesan and included fundamental concepts of probability, estimation and tests of hypotheses, and problems of large data files. The course was given in cooperation with the Committee on Professional Activities of the Blind, directed by Dr. T. D. Sterling of the Department of Applied Mathematics and Computer Sciences, Washington University. Attending the course were:

Guy Clawson
Paul Lauer
Carl Muudschenk
Sandra Price, B.S.

Dick Robbins
John Schuck, A.B.
Dave Schwartzkopf, B.S.
Russell Thompson, A.B.
Bettina Yancey

Course in LINC and PC Programming February - April 1967

The course was taught by Michael D. McDonald and was held primarily for the personnel of BCL and the Computer Research Laboratory. The subject matter included binary arithmetic and coding for the two computers in both machine language and assembly language. Attending the course were:

| | |
|----------------------------|-------------------------------|
| Dieter Ambos | BCL |
| Leonard J. Banaszak, Ph.D. | Physiology |
| Andrew L. Bodicky, B.S. | BCL |
| Charles Buerke | BCL |
| John Clifton, Ph.D. | Radiology |
| Fred L. Francis | BCL |
| Ramasami Ganesan, M.S. | BCL |
| Rexford Hill, M.S. | BCL |
| Monte Lien, B.S. | BCL |
| Donald J. Manson, Ph.D. | Physics, St. Louis University |
| Fred Moses, B.S. | Computer Systems Laboratory |
| Steve M. Rhode | BCL |
| Dale Richardson | Computer Systems Laboratory |
| James Spence | Computer Systems Laboratory |

Course in LINC Programming April - May 1967

The course was taught by Michael D. McDonald and included binary arithmetic and coding in both machine language and assembly language. Attending the course were:

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|-------------------------|-----------------------------|
| Thomas Brugger, M.D. | Psychiatry |
| William Glenn, A.B. | Medical Student |
| Susan Graesser, B.S. | Computer Systems Laboratory |
| Martha McCrate, B.S. | Biostatistics |
| James Satterfield, M.D. | Psychiatry |
| Andy Yunice, M.S. | Veterans Hospital |

Course in FORTRAN IV Programming May 1967

The course was taught by Elizabeth Van Patten and G. S. Whitlow, Jr. Exercises using a remote terminal for program preparation were included. Attending the course were:

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|-------------------------|--------------------------------|
| Andrew L. Bodicky, B.S. | BCL |
| A. Maynard Engebretson | BCL |
| William Glenn, A.B. | Medical School |
| Susan Graesser, B.S. | Computer Systems Laboratory |
| Joan Jackson, B.S. | Central Institute for the Deaf |
| Martha McCrate, B.S. | Biostatistics |

Programmed Console Demonstration Film

A silent color film showing the use of the Programmed Console as an aid to radiation treatment planning was produced in the spring of 1967 under the direction of Michael D. McDonald. The film shows the details of the operation of the major PC programs in the radiation treatment planning project: Enter Doses (see B-5), Enter Patient Contour (see B-2), Superimpose Beams (see B-1), and Implant Dosimetry Using the PC for Input-Output (see B-6). Support for this training film came from Washington University.

VII. PUBLICATIONS

Publications and papers presented during the period covered by this report are listed below.

R. Burstein, "The use of Norethindione-Mestranol in the Immediate Post-Partum Period", Presented to the American College of Obstetricians and Gynecologists, Houston, Texas, October 24, 1966.

J. S. Clifton and E. J. Potchen, "Digital Data Recording and Image Enhancement Techniques in Rectilinear Scanning", Presented at the 14th Annual Meeting of the Society for Nuclear Medicine, Seattle, Washington, June, 1967.

G. B. Cook, "A Comparison of Simple and Multiple Primary Cancers", Cancer, Volume 19, July, 1966.

J. R. Cox, Jr., H. A. Fozzard, F. M. Nolle, and G. C. Oliver, Jr., "AZTEC, a Preprocessing Program Used for Real-Time ECG Analysis", submitted for publication.

R. A. Dammkoehler, "Direct Input of Textual Information", Chapter 5, Handbook of Computer Application in Radiology, Radiotherapy, and Nuclear Medicine, Charles C. Thomas Publisher, Springfield, Illinois (In preparation).

R. A. Dammkoehler, "Information Storage and Retrieval", Chapter 7, Ibid.

A. M. Engebretson and D. H. Eldredge, "A Model of the Nonlinear Behavior of Cochlear Microphonic and Summating Potential", Presented at the 73rd Annual Meeting of the Acoustical Society of America, New York, April 19-22, 1967.

T. L. Gallagher, "Optimization of External Radiation Beams for Therapy Planning", Washington University, St. Louis, Missouri, 1967 (D.Sc. Dissertation).

T. L. Gallagher and W. E. Powers, "Programmed Console - An Aid to Radiation Treatment Planning", Presented at the 8th Medical Symposium sponsored by the International Business Machines Corporation, Poughkeepsie, New York, April 3-6, 1967 (To be published by IBM).

T. L. Gallagher, "Small Computers for Radiation Therapy and as a Communicative Device", Presented at the National Conference on Computer Applications in Radiology, Columbia, Missouri, April 10-12, 1967.

T. L. Gallagher, "Use of Communicating Devices for Radiation Therapy Planning; Autonomous and Collaborative Modes of the Programmed Console and its Aid to the Therapist in Treatment Planning", Presented at the Conference on the Use of Computers in Radiology, Chicago, Illinois, October 20-23, 1966.

T. L. Gallagher, "Optimization of External Radiation Beams for Therapy Planning", Presented at the Joint Meeting of the American Physical Society, Sociedad Mexicana de Fisica and Canadian Association of Physicists, Toronto, Canada, June 21-23, 1967.

M. D. McDonald, "DBLFLT: Double Precision Floating Point Subroutines", Biomedical Computer Laboratory Technical Report No. 2, May 31, 1967.

L. Medgyesi-Mitschang, "Estimation of Signals in Noise with Almost Periodic Arrival Times", Washington University, St. Louis, Missouri, 1967 (D.Sc. Dissertation).

J. Philip Miller, "A Procedure for Stepwise Canonical Correlational Analysis", submitted for presentation at the fall 1967 Meeting of the Psychometric Society.

J. Philip Miller and George Psathas, "A 1401-1311 Tagging Program for the General Inquirer", submitted for publication.

C. W. Parker, "Fluorescence Enhancement in the Study of Antibody Hapten Reactions", Proceedings of the 50th Annual Meeting of the Federation of American Societies for Experimental Biology, 1966 (Abstract).

C. W. Parker, "Spectrofluorometric Methods", Handbook of Experimental Immunology, Blackwells, Scientific Publications, Oxford (In press).

C. W. Parker and C. K. Osterland, "Hydrophobic Binding Sites on Myeloma Proteins and Macroglobulins", Presented at the 24th Annual Meeting of the American Federation for Clinical Research, Chicago, Illinois, November 3, 1966.

E. J. Potchen and J. S. Clifton, "The Problem of Organ Delineation in a Changing Blood Background", Presented at the 14th Annual Meeting of the Society for Nuclear Medicine, Seattle, Washington, June, 1967.

W. E. Powers, T. L. Gallagher, V. W. Gerth, Jr., W. F. Holmes, J. R. Cox, Jr., "Programmed Console for Radiation Therapy Planning", Presented at the 1966 Annual Meeting of the American Association of Physicists in Medicine, Chicago, Illinois, December 3, 1966.

W. E. Powers, T. L. Gallagher, V. W. Gerth, Jr., W. F. Holmes, J. R. Cox, Jr., "Programmed Console for Radiation Therapy Planning", submitted to Radiology.

J. M. Vanderplas, "A Method for Determining Probabilities for Correct Use of Bayes' Theorem in Medical Diagnosis", Computers and Biomedical Research, Volume 1, November, 1967 (In press).