1965

Progress Report No. 1

Biomedical Computer Laboratory

PROGRESS REPORT

No. 1

August 15, 1965

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

BIOMEDICAL COMPUTER LABORATORY

WASHINGTON UNIVERSITY SCHOOL OF MEDICINE

PROGRESS REPORT NO. 1

15 April 1964 - 30 June 1965

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I. INTRODUCTION

The first progress report from the Biomedical Computer Laboratory summarizes work done during the period from the formation of the laboratory until June 30, 1965. Funds for the development of the laboratory were made available by the Division of Research Facilities and Resources of the National Institutes of Health on January 1, 1964. During the first quarter of that year, planning and renovation of space was carried out and on April 15, 1964 the original staff members of the laboratory moved into their new quarters at 700 S. Euclid Avenue. Thus this report represents work carried out over a period of slightly more than a year. Succeeding reports will cover exactly one year from July 1 to June 30.

This report contains sections on the Sources of Support, Personnel, Physical Resources, Research Projects, Training Activities and Publications. Research projects are divided into three subsections grouped according to three facets of the laboratory's activities. The first facet, laboratory applications of digital computer techniques, involves close interaction of digital equipment, the experimenter and the experimental apparatus. Often the LINC (Laboratory INstrument Computer) is used. A second facet, computational applications of computer techniques, utilizes conventional data processing equipment at the Washington University Computational Center (IBM 7072) to solve problems that are often statistical or mathematical in nature. The third facet of the laboratory's activities is collaboration with other laboratories, departments or institutions. This collaboration takes the form of consultation or design help by staff members of the Biomedical Computer Laboratory provided to other investigators outside the laboratory.

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-00161-01	Biomedical Computer Laboratory Facility
FR-00215-01	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:

AI-06154-01	Epidemiology and Streptococci Infections
CA-06800-03	Cancer Evaluation of Cancer Chemotherapy Agents
CA-08023-01	Cancer Clinical Research Center
CA-09741-06	Biometry of Colonic and Rectal Neoplasms
FR-00149-01	LINC Computer Evaluation
FR-05389-01	General Research Support
GM-07176-06	Cellular Differentiation Induced by Environment
GM-08117-05	Enzyme Structure and Mechanism
GM-09830-03	Cellular Regulation of Protein Synthesis
GM-10642-03	Nucleic Acid Metabolism in Differentiating Tissues
HE-06084-03	Physiology of Upper Respiratory Tract Airway and Pulmonary Function
HE-08507-01	Pressure, Flow, and Impedance Relationships in the Dog
HE-09528-01	The Study of the Fetal Electrocardiogram Utilizing the LINC Computer
MH-03804-02	Effects of Anxiety on Verbal Perceptual Learning

MH-05806-04	Behavioral Correlates of Neurophysiological Variables
MH-10293-02	Cortical D.C. Correlates of Behavior
NB-03856-03	Auditory Communication and its Disorders
NB-04513-02	Coordinated Basic and Clinical Brain Research Program
NB-04774-02	Factors Affecting Intraocular Pressure
5T5-GM-8-09	Student Research Training Grant
5T1-GM-807-04	Epidemiological Training Program
5T1-NB-5240-06	Student Research Training Grant

Two National Science Foundation grants, a National Space Agency grant and a U.S. Army grant helped to support portions of several projects:

NASA NSG-581	Multipurpose Disciplinary Research Support Grant
NSF G-22296	Expansion of Computing Center
NSF GE-7994	Undergraduate Research Participation
U.S.Army DA-49-193-MD-2491	Laboratory and Epidemiology Research on Hemolitic Streptococci

Finally, portions of many projects were supported by non-Federal funds from:

American Cancer Society
Ellis-Fischel State Cancer Hospital
Helen Hay Whitney Fellowship
Mallinckrodt Institute of Radiology
Saint Louis Heart Association
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. National Institutes of Health support is listed by grant number only. All other support is listed by granting agency or institution.

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.

Research Associates

William E. Ball, Sc.D. *
Richard A. Dammkoehler, M.S. *
James Vanderplas, Ph.D. *
George S. Whitlow, Jr., B.S.

Research Assistants

A. Maynard Engebretson, M.S.
V. William Gerth, Jr., M.S., since September 15, 1964
Donald H. Glaeser, M.S.
Daniel J. Landiss, B.S., since June 15, 1964 *
Michael D. McDonald, B.S.
Floyd M. Nolle, B.S.

Programmers

David Bridger, B.A. *
Sharon R. Davisson, B.A.
Richard M. Hesse, M.S., since June 28, 1965
Lynda McLaurin, since December 28, 1964 *
J. Philip Miller, B.S.
David Sholtz, B.A. *
Irving C. Tang, D.Sc. *
Bruce Walz, B.S. *

Engineering Assistants

Harry Agress, Jr., since June 14, 1965
Harry R. Grodsky, B.S., since June 1, 1965

Electronics Technicians

S. Philip Berger, since Feb. 1, 1965 *
Fred L. Francis
Richard E. Hitchens, since Feb. 27, 1965 *
Robert T. Kimack
Charles E. Mitchell, since July 13, 1964

Secretaries

Wanda J. Meek
Sharon L. Passero, since Sept. 1, 1964 *

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

ADVISORY COMMITTEE

The Liaison Committee for the Computer Sciences under the chairmanship of Dr. R. M. Krause served the Biomedical Computer Laboratory in an advisory capacity since it was appointed by Dean M. K. King on October 23, 1964.

Harvey R. Butcher, M.D., Surgery
Donald H. Eldredge, M.D., Central Institute for the Deaf
Herman N. Eisen, M.D., Microbiology
Richard M. Krause, M.D., Preventive Medicine
Wm. W. Sleator, Jr., Ph.D., Physiology
M. M. Ter-Pogossian, Ph.D., Radiology

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

M. Remsen Behrer, M.D., Pediatrics
R. I. Berns, B.S., Computation Center
C. H. Boll, Ph.D., Applied Mathematics and Computer Science
Estelle Brodman, Ph.D., Medical Library
William R. Brown, B.S., Radiology
L. E. Bubb, Computation Center
Max Burger, M.D., Biochemistry
Robert Burstein, M.D., OB/GYN
Vincent F. Castelucci, B.A., B. S., Neurology
Sam L. Clark, M.D., Anatomy
Wesley A. Clark, B.A., Computer Research Laboratory
J. M. Cooper, B.S., Computation Center
Burl M. Dillard, M.D., Surgery
Jay Enoch, Ph.D., Ophthalmology
Harry Fozzard, M.D., Internal Medicine
Marvin J. Friedenberg, M.D., Radiology
T. L. Gallagher, M.S., Computation Center
Robert Goldstein, Ph.D., Otolaryngology

Washington University (Cont'd.)

R. L. Hamblin, Ph.D., Sociology
L. Harth, B.A., Pediatrics
John Heiss, Ph.D., Molecular Biology
William Holmes, Ph.D., Computation Center
John W. Josse, M.D., Microbiology
M. Kawasaki, M.D., Otolaryngology
David E. Kennell, M.D., Microbiology
David M. Kipnis, M.D., Internal Medicine
Michael Koenig, M.S., Computer Research Laboratory
Richard M. Krause, M.D., Preventive Medicine
L. L'Abate, Ph.D., Medical Psychology
J. Levine, M.D., Preventive Medicine
J. P. Locksmith, M.D., Radiology
W. H. McAlister, M.D., Radiology
Robert A. Moses, M.D., Opthalmology
J. R. Nelson, M.D., Internal Medicine
James M. Nusrala, B.A., Neurology
J. H. Ogura, M.D., Otolaryngology
James L. O'Leary, M.D., Neurology
Se ero M. Ornstein, A.B., Computer Research Laboratory
Roy R. Peterson, M.D., Anatomy
William E. Powers, M.D., Radiology
Albert Rhoton, M.D., Neurosurgery
James H. Satterfield, M.D., Psychiatry
Walter P. Schauman, B.S., Electrical Engineering
Aleene K. Schneider, B.A., Radiology
Kenneth D. Serkes, M.D., Surgery
Alfred I. Sherman, M.D., OB/GYN
K. E. Shumate, B.S., Computation Center
William Sleator, Jr., Ph.D., Physiology
L. H. Snow, B.S., Computation Center
K. Togawa, M.D., Otolaryngology
Donald F. Wann, Sc.D., Electrical Engineering
Ralph B. Woolf, M.D., OB/GYN
Roy R. Wright, M.D., Neurology
Robert Wurtz, Ph.D., Neurology and Physiology

Central Institute for the Deaf

Merrill K. Bauer, B.S.
Hallowell Davis, M.D., Sc.D.
Donald H. Eldredge, M.D.
Truman Mast, M.D.
James D. Miller, Ph.D.
Arthur F. Niemoeller, Sc.D.
Peter B. Weston, M.A.

Ellis-Fischel State Cancer Hospital

Galen B. Cook, M.D.
A. McChesney Evans, M.D.
Miriam G. Hoag
John S. Spratt, Jr., M.D.

St. Louis University

Howard M. Yanof, Ph.D., Physiology

STUDENTS

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

Graduate Students

Bernard D. Aims, M.S.
Milton H. Hieken, B.S.
Louis Medgyesi-Mitschang, M.S.
Albert F. Ruehl, M.S.
Kenneth R. Thompson, M.S.

Medical Students

Frank Letcher
George McDonald
David Polage
Stephen VanMeter

CHANGES IN PERSONNEL

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

Robert T. Kimack, Senior Electronics Technician, on June 5, 1964.

Bernard D. Aims, Graduate Student, completed the requirements for the degree of Master of Science in Electrical Engineering on August 15, 1964.

Bruce Walz, Programmer, on September 15, 1964.

Philip S. Berger, Electronics Technician, on May 21, 1965.

Sharon R. Davisson, Programmer, on May 31, 1965.

Lynda McLaurin, Programming Assistant, on May 31, 1965.

Irving Tang, Programmer, on June 15, 1965.

The personnel contributing to each of the research projects reported in Section V are listed there. Personnel not employed by the Biomedical Computer Laboratory are listed along with their academic degrees and departments. Unless otherwise indicated all personnel are members of the staff of Washington University.

IV. PHYSICAL RESOURCES

On April 15, 1965 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 now available for laboratory applications of digital computers includes the LINC (Laboratory INstrument Computer). This small stored-program computer has been designed specifically for use in the biology laboratory where there is a requirement for strong coupling between the computer, the investigator and other experimental equipment. At the present time there are six LINCs in the Washington University Medical community. Two of them are at the School of Medicine and one at Central Institute for the Deaf. The remaining three LINCs belong to our sister laboratory, the Computer Research Laboratory, but are available to the staff of BCL. Other facilities include a well-stocked electronics shop, a large inventory of electronic and computer test equipment, a variety of digital system modules and tape recorders, both digital and analog.

On August 1, 1964, the laboratory space was increased by an additional 983 square feet on the second floor of the building just south of the original space. Facilities for computational applications are housed in this space and are presently limited to an IBM 1050 teleprocessing system connected to the IBM 7072 at the Washington University Computation Center. Plans call for the installation of a satellite computer communicating directly with the Computation Center in the fall of 1965. Another increase in space planned for late 1965 will provide ample office space for programmers and students interested in computational applications.

V. RESEARCH PROJECTS

A. Laboratory Applications

The following research projects were carried out primarily through the efforts of the laboratory staff members, but often with the collaboration of investigators from other departments. In this section we emphasize laboratory applications in which close coupling between computer, experimenter and experimental apparatus is required. In each case the staff member most directly involved is listed first, with other personnel in alphabetical order.

1. An Adjustment Procedure for Digital-Analog Converters

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

Support: FR-00161-01

The adjustment of digital-analog converters has in the past been carried out by informal techniques often neither efficient nor rigorously accurate. A theoretical treatment of this problem has been developed. The procedure studied requires that inputs to the converter of 2^n-1, 2^n and 2^n+1 be applied cyclically. The n^{th} trimming resistor is then adjusted so that the three output voltages are equally spaced. One iteration starting with the least significant bit is sufficient. The procedure is quite general and can be applied to any binary digital-analog converter of the ladder or summing-point variety. No absolute voltage measurements are necessary. A publication of this work is in preparation.

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2. Cochlear Model

Personnel: A. M. Engebretson, BCL
J. R. Cox, Jr., BCL

Support: FR-00161-01

Several theories or models of the mechanical action of the cochlea have been investigated. The best models seem to be those of L. C. Peterson and B. P. Bogert (J. Acous. Soc. Am., 23: 369-381, 1950), H. Fletcher (Speech and Hearing in Communication, Ch. 14, 1964, D. Van Nostrand Co., Inc.) and J. Zwislocki (Analysis of Some Auditory Characteristics, Technical Rep., Laboratory of Sensory Communication, Syracuse University, 4c-24c, 1963). In each of these models, the cochlea is considered a

one-dimensional system. The resulting differential equations of motion are identical in form. The models differ in method of solution, the numerical values chosen for physical parameters and certain simplifying approximations that are made. Zwislocki's model is most useful because he uses simplifying approximations that result in a differential equation which can be solved analytically using the WKB approximation method.

A program was written for LINC which solves the differential equations exactly. The program uses double-precision floating-point arithmetic subroutines (see V-A-17). Agreement between the approximate solution and the computer solution indicates that the WKB approximation is very good and therefore useful as an initial check of the model.

Zwislocki's model was adapted for the guinea pig cochlea and compared with cochlear microphonic data (see V-A-4). The model can be made to agree in a gross way with experimental data.

Several programs have been written which plot and display different aspects of the solution to the cochlear model. One plots an isometric view of the solution as a function of distance from the stapes and of time. The resulting plot demonstrates how the traveling wave propagates along the cochlear partition.

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3. Impedance Measurements of the Cochlear Partition

Personnel: A. M. Engebretson, BCL

Support: FR-00161-01

A difficulty encountered in checking cochlear models (see V-A-2) is that some of the parameter values which are required for the model are not known. One parameter which must be adjusted is the resistance of the cochlear partition. This resistance determines how fast traveling wave energy is dissipated along the cochlea and consequently the position of maximum vibration of the cochlear partition. A second parameter is compliance of the cochlear partition. Available measures of compliance are either static measurements or those obtained by using test hairs. Neither measure may be appropriate to the cochlear model.

Any dynamic measurement of the partition impedance made on a whole cochlea will be confounded by the traveling wave propagating along the partition and in the adjacent fluid. Work aimed at measuring the impedance of isolated segments of the cochlear partition has begun.

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4. Measurements of Cochlear Microphonics in Guinea Pig Cochleas

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

Support: FR-00161-01
NB-03856-03

When the cochlear partition vibrates, a small voltage is generated between the fluid in scala vestibuli and scala tympani. This voltage, called the cochlear microphonic (CM), seems to be proportional to the displacement of the cochlear partition.

By using a differential-electrode recording technique, the vibration pattern of the cochlear partition can be inferred from CM measurements at several positions along the cochlea of an experimental animal. In 1952 Tasaki, Davis and Legouix (J. Acous. Soc. Am., 24: 502-519, 1952), reported on CM measurements taken from guinea pig cochleas. To verify and add to their results frequency response measurements were repeated with redesigned and improved equipment. The data agree with the exception of Turn I measurements for high frequencies. It is believed that the differences are due to an improvement in the high frequency characteristics of the recording equipment.

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5. DATAMEC Sampling Programs

Personnel: V. W. Gerth, Jr., BCL
J. R. Cox, Jr., BCL

Support: FR-00161-01

Continuous sampling of analog signals over a long period of time is difficult for LINC because of the small memory size. To overcome this problem, sampling programs have been written which utilize a DATAMEC D2020 digital tape unit to store the digital representations of the samples. Sampling may be carried on continuously, limited only by the total amount of data that can be stored on one tape. Certain sampling rates are more convenient than others but the range of sampling rates available is sufficient to satisfy most requirements. The highest rate is 25 kc with 6 bits of precision and no record gaps. At 2.2 kc the full 8 bits of precision of the sample is retained and record gaps are included without loss of data. Intermediate rates sacrifice either precision or record gaps. Rates slower than 2.2 kc are easily obtained with no sacrifice.

An advantage in using the DATAMEC for storage is that processing on a larger machine is easily achieved by transferring tapes.

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6. Digital Data Line Transmission Experiments

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

Support: FR-00161-01

In order to supply background information in support of future projects, a study was made of digital data transmission facilities available as a service of the Southwestern Bell Telephone Company. A data line terminated at both ends in type 202D Data Sets was installed between the Biomedical Computer Laboratory and the Digital and Information Systems Laboratory on the Washington University main campus. Measurements confirmed the line specifications. A number of experiments were performed using LINC as an automatic error checking device to evaluate methods of serial data transfer. It was demonstrated that under certain conditions reliable transmission could be achieved at a data rate of 1800 bit/sec., well in excess of the specified 1200 bit/sec.

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7. Isodose Contour Plotting Programs

Personnel: V. W. Gerth, Jr., BCL
Harry Agress, Jr., BCL
D. J. Landiss, BCL
William E. Powers, M.D., Radiology
Aleene Schneider, B.A., Radiology

Support: FR-00161-01

To reduce the time required to plot isodose contours for radiation therapy (see Section V-B-7), programs are in preparation for LINC and PC (Programmed Console) which will automate the task. PC is a small digital computer designed to serve as a remote console for large computers (see Section V-C-3). The contour plots produced by both machines will be presented as oscilloscope displays within seconds after the input data is available from the IBM 7072. Since the IBM 7072 and the LINC or PC will be geographically separated by a few miles, the data will be transferred by telephone lines.

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8. Precise Digital-Analog Conversion Experiments

Personnel: V. W. Gerth, Jr., BCL
R. E. Hitchens, BCL
D. J. Landiss, BCL

Support: FR-00161-01

An evaluation of the digital-analog conversion modules produced by Digital Equipment Corporation was conducted. The TYPE 1561 digital-analog module was evaluated to determine if alignment to a 12-bit accuracy could be achieved. An automatic test fixture was constructed which makes possible rapid alignment using a procedure reported elsewhere (see V-A-1). Digital-analog modules of the new Flip-Chip line (Type A601) were evaluated and found to be particularly convenient since no alignment is required. To test further the Flip-Chip digital-analog modules, a LINC Data Terminal plug-in-unit with two of the Flip-Chip 12 bit digital-analog converters is being constructed.

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9. Artifacts in Self-Triggered Backward Averages

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

Support: FR-00161-01

When averages of spontaneous, asynchronous activity are desired, a technique known as "backward averaging" is utilized. This scheme permits storage of part of the on-going activity until a decision can be made as to whether or not this activity contains a signal to be incorporated into an average. The method is similar to that reported by Hon (E. H. Hon and S. T. Lee, Medical Elec. and Biol. Engr., 2: 71, 1964). One way of detecting the presence of a signal is by comparison of the activity to a constant threshold. If noise is superimposed on the signal, threshold crossings during one noise phase are considerably more probable than during the opposite phase. The effect of this is to produce an average containing an artifact whose polarity depends on the most probable noise phase and whose amplitude depends on the signal-to-noise ratio.

A computer simulation of this situation permitting variations of many of the parameters involved has been written for LINC. Computer generated noise with amplitude and bandwidth control is added to a known signal and averaged. Qualitative results have been obtained and a publication is in preparation.

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10. Construction of Quantizing Encoder

Personnel: D. H. Glaeser, BCL

Support: FR-00161-01

There has often arisen an application for an encoder (analog-digital converter) which has an encoding rate greater than that permitted by the internal encoder of the LINC. In addition, the need for greater precision in the encoding process than that permitted by LINC has been demonstrated. To this end we have constructed an eight-bit version of a quantizing encoder. The logic and electronic components have been checked and are operational. Following completion of final tests the encoder will be installed in the electrophysiological laboratories of Central Institute for the Deaf for use in the measurement of cochlear microphonics (see V-A-4). Another version will be built having greater precision for use in the data acquisition laboratory of the fetal-electrocardiogram project (see V-A-12).

Publication:

J. R. Cox, Jr. and D. H. Glaeser, "A quantizing encoder", IEEE Trans. on Elec. Computers, EC-13: 250-254, 1964.

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11. Design of an Esophogeal Electrode for Infant Electrocardiography

Personnel: D. H. Glaeser, BCL
F. L. Francis, BCL
S. VanMeter, Medical Student

Support: FR-00161-01

To permit correlation of the fetal electrocardiogram as measured on the maternal abdomen with the standard esophogeal leads in the newborn infant, a small esophogeal electrode was designed and is now in use. This consists of a No. 8 Fr. catheter through which has been passed Microdot 60-3905 miniature coaxial cable. The tip is a silver plated machined copper cylinder which is crimped onto the catheter. The distal end of the catheter is sealed with acrylic cement to make the entire device liquid tight for sterilization.

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12. Detection and Enhancement of the Fetal Electrocardiogram

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

Support: FR-00161-01
HE-09528-01 (equipment support since 4/15/65)

Arrangements have been made with the Department of Obstetrics and Gynecology and a laboratory established in the OB/GYN clinic to process patients reporting for their regular checkup. Two rooms were set aside, one housing data acquisition equipment and the second providing bed space for the patient during the recording session. Part of the equipment used is similar to a three-channel polygraph. A magnetic tape recorder is used to retain all data for any desired future reference. This laboratory permits a LINC to be used on-line. With appropriate input, the computer continually processes input data, and, after a delay of about 500 milliseconds, produces an analog output consisting of that portion of the abdominal signal of the mother not attributable to the maternal ECG. In many cases, the morphology of the fetal signal may be investigated in this record. Some of this data has been processed off-line by a digital filtering program to determine the degree of improvement in signal-to-noise which results from matched filtering techniques.

We have continued our data acquisition during this period with a great deal of emphasis placed on an investigation of optimum electrode placement. Eighteen patients were included in a study to determine the optimum location of abdominal electrodes to maximize the fetal electrocardiogram and minimize the interference from all other sources, primarily the maternal electrocardiogram and respiratory interference.

Each electrode location was evaluated through the use of four indicators of fetal signal quality. These are: 1) The average peak-to-peak maternal ECG. 2) The average peak-to-peak fetal ECG. 3) The ratio of fetal ECG to random noise in the record. 4) The ratio of fetal ECG to low frequency (respiratory) shifts of the baseline.

On the basis of Items 2) and 4), the best electrode pair is in the midline from umbilicus to pubis. The minimum maternal ECG occurred in a midline electrode pair with the upper electrode situated halfway between pubis and umbilicus and the lower electrode at the pubis. The largest (FECG to random-noise) ratio occurred in

a pair with one electrode in the left upper and the other in the right lower quadrants on a line through the umbilicus. In all cases the ground electrode was located on the flank.

The backward averaging program which is used to process the abdominal data has been improved to contain 512 points in the average, with a one millsecond interval between points. Each average point is now accumulated in double precision to permit incorporation of an analog-digital converter in the system having greater precision than that which is an integral part of LINC. Since the ratio of maternal ECG to fetal ECG in the abdominal record is quite large, the precision of encoding of fetal activity has largely been limited to 5 bits or less. The external 10-bit encoder (see V-A-10) will alleviate this problem. A Data Terminal plug-in-unit to provide interface with this encoder is being built.

Plans are being made to automate many of the operations now manually performed by one or more operators. Much of this equipment presently in the experimental laboratory will be incorporated into this system which should be completed at the end of the summer of 1965.

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13. Dropout Tests of Magnetic Tape and Magnetic Tape Recorders

Personnel: D. H. Glaeser, BCL
F. L. Francis, BCL

Support: FR-00161-01

The problem of recording digital data on analog magnetic tape recorders for the purpose of automatic data coding and retrieval has been under study. Since a signal dropout, whether caused by tape or tape transport, could easily cause the code written to be improperly read, extensive tests of 1/4 inch tape and the Precision Instruments Model 6100 tape recorder have been run. Some testing of an Ampex FR 1300 tape recorder and 1/2 inch tape were also made to provide results for comparison with the PI 6100. The PI 6100 did not give satisfactory performance on these tests, while the FR 1300 did.

Dropouts clearly attributable to tape for several rolls of tape are tabulated below. Each entry corresponds to one 1800 ft. roll of 1/4 inch tape. Each tape was run 5 times in the course of the test. Four total channels of electronics were used such that the total number of dropouts for any tape is given by 20 times the average shown in the table.

Ampex 748 Roll 1	0.4/channel
Ampex 748 Roll 2	0.8/channel
Audio Devices B56Wb-2	0.8/channel
3M (Scotch) 203	0.8/channel
3M (Scotch) 499	0.6/channel
3M (Scotch) 599	3.0/channel
3M (Scotch) 861	1.6/channel

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14. Data Gathering Techniques for Electrophoretic Patterns

Personnel: Harry R. Grodsky, BCL
Harry Agress, Jr., BCL
Robert Burstein, M.D., OB/GYN
J. R. Cox, Jr., BCL

Support: FR-00161-01

The work with electrophoretic patterns described elsewhere (see V-B-19) uses a Beckman Model RB Analytrol to plot a curve of the density of the serum sample versus distance. The curve is continuous and appears as five humps; four globulins and albumin. At present each hump is integrated by hand and compared to the total area on a percentage basis.

Because of the large number of patterns involved in this study, work has begun on an interface and programs to allow the LINC to obtain the normalized areas directly from the Analytrol. The curve is now plotted by a pen which is driven by a servo motor. Since no voltage proportional to the pen deflection is available within the device a single-turn precision potentiometer will be connected to the servo motor. A voltage derived from potentiometer will be sampled by LINC. A program has been written which will locate the five humps and perform the necessary integration.

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15. Radiation Mapping Program

Personnel: M. Koenig, BCL, CRL
J. R. Cox, Jr., BCL
Albert Rhoton, M.D., Neurology

Support: FR-00161-01

Work is underway to use the LINC to record and analyze the radiation emitted by an organ of a patient who has ingested a substance containing a radioactive isotope. As the scintillation probe

is swept slowly across the area of the organ, it detects radiation with energies ranging from primary radiation to scattered and background radiation. The LINC will classify the pulse height produced by each incoming particle into one of 64 energy levels and increment the appropriate location in memory. At periodic intervals, contents of the memory will be transferred to magnetic tape. At the end of a complete scan, the tape will contain information on how many particles were detected in each of the 64 energy levels at each point of the scan. Contrast enhancement, dual-tracer studies, contour mapping and other processing techniques will be investigated to aid in the diagnosis of tumors of the brain, liver, and thyroid.

The instrument presently in use at Barnard Hospital is a Picker X-Ray Corporation's Magnascanner having outputs in form of photographic film and a dot array on Teledeltos paper. Gathering more complete data along with the proposed processing techniques should materially improve the resolution of the system.

Detailed plans for modification of the Magnascanner, for construction of an interface with LINC and for the preparation of a program are essentially complete.

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16. The Tektronix 564 Storage Oscilloscope as a LINC Output Device

Personnel: D. J. Landiss, BCL

Support: FR-00161-01

A Tektronix 564 storage oscilloscope was modified to accept both deflection and control signals from the LINC, so that the display can be written, stored, and finally erased, all under direct computer control. The modification required the installation of four relays and a switch inside the scope. Later, two more scopes were modified but only three relays were installed because experience indicated that independent control of both halves of the screen was unnecessary.

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17. DECAL (Desk Calculator)

Personnel: M. D. McDonald, BCL

Support: FR-00161-01

DECAL (Desk Calculator) is a program which allows the user to manipulate mixed integer-fraction decimal numbers, (input via the LINC keyboard) to perform sundry operations of them, and to print

results via the Teletype and/or store results in tables for future use. For use by DECAL, a set of double-precision floating point routines were written.

Using DECAL one may add, subtract, multiply, divide, exponentiate and take square root or natural logarithm; the results of any series of operations may be automatically accumulated.

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18. GUIDE System

Personnel: M. D. McDonald, BCL
S. R. Davisson, BCL

Support: FR-00161-01

The GUIDE System is a collection of routines which provide for the control of a file of binary programs. Binary programs may be entered into or removed from the file, or executed by name; also, the system (GUIDE and LAP4) may be copied from one tape to another, either tape may be rewound, and the LAP4 system may be initiated or restored. Furthermore, an index of the programs contained in the file is kept and may be viewed on the scope.

A number of convenience programs were also written and entered into the GUIDE file to form a basic set of utility programs. Among the convenience programs are the following: Keyboard Teletype, to allow typing on the Teletype from the LINC keyboard; Manuscript Print and Quick Manuscript Print, for producing teletyped hard-copy of manuscripts; Loader for Octal and Decimal Integers, Display Potentiometer Settings, Oscilloscope Surrogate, to sample the analog inputs at specified rates and display the sampled waveform; Octal Listing; Binary-to-Manuscript Disassembler; Index Print, to obtain hard-copy of GUIDE or MS file indices; Compare, to compare blocks on tape and indicate discrepancies.

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19. LAP4 (LINC Assembly Program 4)

Personnel: M. D. McDonald, BCL
S. R. Davisson, BCL

Support: FR-00161-01

Extensive additions and revisions were made to the LINC Assembly Program 3 (LAP3) resulting in LAP4 which, in conjunction with GUIDE, was issued as "A LINC Utility System". The following modifications are most noteworthy:

Errors were corrected in the Remove, Insert, and Convert Meta Commands. Convert and Convert Manuscripts were modified to implement the detection of undefined and multiply-defined tags. The Display Meta was completely rewritten, removing control of the MS display from the knobs and placing it on the keyboard. The Copy Meta was also rewritten in order to allow the use of upper memory if LAP4 is being run on a double memory machine. In addition, three new Meta Commands were written - Start LAP, Start GUIDE, and Manuscript Control, the latter allowing the filing and retrieval of LAP Manuscripts by name.

Publication:

M. D. McDonald, S. R. Davisson and J. R. Cox, Jr., "A LINC Utility system", BCL Report, March 1965.

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20. Calibration of LINC Analog Preamplifiers

Personnel: C. E. Mitchell, BCL
J. R. Cox, Jr., BCL

Support: FR-00161-01

To simplify the task of calibrating the analog channels of the LINC an external probe and a calibrator program have been developed. The probe is used to supply a square wave which switches from zero volts to plus or minus one-half volt. The polarity of the square wave is selected by means of a switch located on the probe body. If the analog preamplifiers are set correctly the one-half volt square wave will be converted to -0 and $+(100)_8$ for positive polarity or -0 and $-(100)_8$ for negative polarity. The analog probe is operated from the calibrator output of a Tektronix oscilloscope.

The calibrator program (ANACAL) automatically examines all eight analog channels for a square wave input. If a signal is present the program selects that channel and displays the signal along with its octal equivalent. By observing the LINC scope, adjustment of the offset and gain controls on the preamplifiers can be accomplished easily.

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21. Redesign of the Analog Preamplifiers

Personnel: C. E. Mitchell, BCL
D. H. Glaeser, BCL

Support: FR-00161-01

The LINC analog preamplifiers were redesigned to improve stability and operating characteristics. Problems inherent in the original printed circuit cards made calibration difficult because of drift and interaction of gain and offset controls. The redesigned card has the following advantages:

1. No interaction of the offset and gain controls.

2. Backlash was eliminated from the potentiometers by substitution of a new type.

3. The circuit no longer requires selection of transistors or resistors.

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22. Detection of Cardiac Arrhythmias

Personnel: F. M. Nolle, BCL
J. R. Cox, Jr., BCL
H. A. Fozzard, M.D., Internal Medicine

Support: FR-00161-01

Following acute myocardial infarction, cardiac arrhythmias occur in 13 to 41 percent of the cases with a corresponding mortality rate of 15 to 60 percent (see Coronary Care Units, Specialized Intensive Care Units for Acute Myocardial Infarction Patients, PHS Bulletin 0-748-407, U.S. Govt. Printing Office, 1965). The development of a system for long-term heart-rate monitoring in order to detect these arrhythmias seems desirable for two reasons: First, quick detection may make possible more prompt treatment of serious arrhythmias and second, a study of frequency of occurrence of minor arrhythmias preceeding a major arrhythmia may indicate some method for predicting the occurrence of major arrhythmias.

Preliminary work has been done using the LINC computer to measure and record intervals between successive R waves in the electrocardiogram using a simple criterion which recognizes the triangular shape of the R wave. Recognition of large instantaneous R-R interval deviations from an average interval and of average intervals greater or less than some fixed limits will give an indication of some arrhythmias but cannot hope to classify them.

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23. Digital-Controlled Audio Stimulus Generator

Personnel: F. M. Nolle, BCL
D. H. Eldredge, M.D., Central Institute for the Deaf

Support: FR-00161-01
NB-03856-03

The digital-controlled audio stimulus generator produces a trapezoidally modulated audio signal for research on the auditory system. The signal is the output of a digital-analog multiplier where the audio signal gain is varied by an eight-bit digital approximation to the desired modulating envelope. The digital version of the trapezoidal envelope is derived from a binary up-down counter.

The up-down counter and associated control circuitry are constructed from Digital Equipment Corporation system modules. The digital-analog multiplier uses amplifier and analog switch modules which are compatible with the DEC modules. The plug-in modules occupy one 5-1/4 inch by 19 inch rack-mounting bay with a front panel containing manual controls. Power supplies may be located remote from the unit and have additional capabilities to supply other equipment.

The manual controls allow independent variation of the envelope rise, plateau, and fall times from 1/2 millisecond to several seconds. The rising phase of the envelope is synchronized to a zero-crossing of the input audio signal and may be triggered internally or externally. The on-off ratio is at least 80 db for frequencies up to 8 kcps and is down to 72 db at 20 kcps. The frequency response is flat from zero to above 50 kcps. Harmonic distortion is less than 0.1 percent. Low-frequency switching transients are at least 60 db below the full-scale output.

Two of the audio stimulus generators have been built at the Central Institute for the Deaf. One of these was placed in operation in November 1964 in the Neurophysiological Laboratory of Dr. D. H. Eldredge, replacing a prototype which had been used since January 1964. The other generator was placed in operation in March 1965 in the Clinical Laboratory of Dr. H. Davis. Particular attention has been directed toward elimination of low-frequency switching transients and no adjustments have been necessary since the generators were placed in operation. A publication is in preparation describing the design and operation of the stimulus generator.

24. Transistor Analog Switching

Personnel: F. M. Nolle, BCL

Support: FR-00161-01

Transients which occur when transistor switches are changing states may cause problems in digital-analog output devices. Two common types of transients are due to switch driving waveform feedthrough and non-coincident switching state changes. The digital-controlled audio stimulus generator (see V-A-23) uses a large number of transistor shunt switches in the digital-analog multiplier. The 2N1305 transistors which are used in these shunt switches have relatively slow turn-off times so that some undesirable transients of about 0.5 microsecond duration are introduced into the system. A large number of faster transistors have been tested as replacements for the 2N1305 transistors but none of them have been found to meet all of the specifications on saturation resistance, offset voltage, leakage current, and driving waveform feedthrough. A series-shunt switching arrangement using 2N1305 transistors is considerably faster than the shunt switches and shows promise for replacing them.

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V. RESEARCH PROJECTS

B. Computational Applications

The following research projects are primarily computational in nature. The work was carried out by laboratory staff members using the IBM 7072 digital computer at the Washington University Computational Center and often the IBM 1050 Teleprocessing System located at the Biomedical Computer Laboratory. The listing of personnel on these projects is arranged in the same way as in Section V-A.

1. Symbolic Information Processing

Personnel: W. E. Ball, BCL
R. I. Berns, B.S., Computation Center
R. A. Dammkoehler, BCL
T. L. Gallagher, M.S., Computation Center
L. H. Snow, B.S., Computation Center

Support: FR-00215-01

An important phase of the research effort supported by FR-00215-01 is an attempt to develop computer-based systems which perform symbolic rather than numerical computations. Through the use of list processing languages it is possible to write programs which substantially reduce the effort required in the formulation of analytical methods basic to quantitative analysis. Furthermore, because the symbolic manipulation is performed internally, the resultant expression can be converted to a machine language program to be used in subsequent numerical evaluations. If this concept is proven practicable, an investigator can make use of a complex computational system without learning the language conventions of FORTRAN or the details of numerical analysis techniques.

The immediate objective of this work is to develop a computer-programming system that will make it possible to manipulate and solve mathematical problems without the necessity of doing detailed programming. Eventually this system is to fit into a general mathematical model-building program. Thus the system must be constructed with general symbol-handling capabilities and a flexible, easily used, form for input.

The initial work was concerned with the symbolic solution of non-linear differential equations. This particular area was picked as a starting point since most time-dependent physical systems are

described by such equations. Symbolic solutions were required to allow the possibility of symbolic parameters in the equations.

The mathematical analysis of the symbolic equation-solving problem has indicated two potential methods of approach:

Method A: Based on a truncated power-series expansion, this method makes it possible to obtain an excellent measure of the error in the final solution.

Method B: Based on a truncated Chebyshev series expansion, this method gives a solution with a given accuracy over a much wider interval than Method A. However, the determination of the actual error for any given problem is more difficult for Method B.

The general programming system is currently divided into five phases:

Phase 1: Reads the problem definition and compiles an appropriate set of internal control statements to control the remainder of the system operation. This phase of the work has been finished for a slightly restricted set of problem types.

Phase 2: Establishes solutions to equations by symbolic series expansion. At present solution Method A is used, but some work has been done on the evaluation of Method B as an improved replacement for A.

Phase 3: Does the actual work of solving for the individual symbolic coefficients in the expansions established by Phase 2. This phase is essentially complete.

Phase 4: Combines the algebraic solution obtained from Phases 2 and 3 (if such solutions were required) with any other algebraic conditions present in the problem definition, and then determines the symbolic parameter values based on additional conditions (such as experimentally measured variable values). This is a problem in non-linear regression, and as such has been solved, but has not yet been incorporated into the programming system.

Phase 5: Produces final output. Work on this phase has not yet begun.

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2. Analysis of Naso-Pulmonary Function

Personnel: R. A. Dammkoehler, BCL
M. Kawasaki, M.D., Otolaryngology
J. R. Nelson, M.D., Otolaryngology
J. H. Ogura, M.D., Otolaryngology
K. Togawa, M.D., Otolaryngology

Support: FR-00215-01
HE-06084-03
NSF G-22296
NASA NSG-581

A continuing series of experiments conducted by J. H. Ogura, M.D., has yielded data relating changes in pulmonary function and surgical reconstruction of the nasal passageway. The mechanism by which such changes are interrelated is as yet unknown. In attempting to isolate the cause and effect of changes in pulmonary function, measured as compliance and resistance, the investigators have challenged the validity of existing models of pulmonary function and are presently engaged in studies which will test a new hypothesis, leading to the derivation of more adequate descriptions of this complex phenomena.

In research to be carried out with both animals and clinical patients complete physiological monitoring and automatic recording of pulmonary function will be performed under controlled laboratory conditions. Computer analysis of multichannel recordings (intra-esophaegal pressure, flow, volume, etc.) will isolate the components of resistance and compliance, which theoretically account for changes in pulmonary function.

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3. Familial Aggregation of Group A Streptococci

Personnel: R. A. Dammkoehler, BCL
R. M. Krause, M.D., Preventive Medicine
J. Levine, M.D., Preventive Medicine
J. M. Cooper, B.S., Computation Center

Support: AI-06154-01
5T1-GM-807-04
U.S.Army DA-49-193-MD-2491

In support of a project initiated by R. M. Krause, M.D., modifications to our generalized cross-classification program were required. The opportunity to work on a typical epidemiologic study also provided additional insight into the nature and course of such an investigation. As a result we now have the rationale for the

development of a more useful program and language which will assist medical researchers in data screening and hypothesis formulation.

Clinical data was obtained by Dr. Krause on several hundred subjects exposed to streptococcal infection during a midwinter epidemic. This data was subjected to a factor analysis and rotation as part of our classification experiments. Studies of the rotated factors indicated the presence of several distinct sub-groups within the sample population, corresponding to the familial aggregation patterns suspected by the investigator and confirmed by conventional contingency analysis.

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4. Numerical Taxonomy

Personnel: R. A. Dammkoehler, BCL
C. H. Boll, Ph.D., Applied Mathematics and Computer Science
J. H. Satterfield, M.D., Psychiatry
K. E. Shumate, B.S., Computation Center

Support: FR-00215-01
NSF G-22296

The use of mathematical techniques for the classification of psychiatric patients on the basis of common symptoms and clinical observation was continued by the research staff. Several alternative methods were applied in the analysis of 100 cases, characterized by 235 attributes. Through an iterative process, requiring repeated computer runs, procedures for eliminating redundant attributes were developed and tested empirically. As yet no rigorous method for such condensation has been found.

A comparison of the classification methods proposed by Sokal and Tanimoto was made, and substantial agreement between the derived patient classes and clinical impression was observed. However, both methods are highly sensitive to the presence of redundant or spurious attributes, limiting their value in all but the most carefully planned and controlled clinical experiments.

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5. Numerical Techniques in Information Processing

Personnel: R. A. Dammkoehler, BCL
J. M. Vanderplas, BCL
D. A. Bridger, BCL
J. P. Miller, BCL
D. Sholtz, BCL

Support: FR-00215-01
NSF G-22296

A series of experiments has been initiated in order to determine the extent to which mathematical classification techniques can be used in the indexing, retrieval and dissemination of medical publications. A collection of documents describing current research in the cerebrovascular field, was provided by J. O'Leary, Professor and Chairman of the Department of Neurology and will serve as the experimental literature domain for the initial investigations. Of primary interest are those techniques proposed by Borko and Bernick, Maron and Kuhn, Jones and Guiliano, Baker, Briner, Hilman, Sokal, and Tanimoto.

During the first twelve month period a number of programs necessary to the research activity were developed and used in a preliminary analysis of the document collection. Those of special interest are: 1) Free form input to a selective dissemination system (IBM version II), 2) an SDI-compatible concordance and KWIC indexing and editing system, 3) a generalized document analysis system which produces an n-dimensional index term vector for each document, 4) programs for computing mutually exclusive, and posterior probabilities, 5) a system to compute prime implicants of disjunctive normal Boolean functions which can be used to simplify term-term relationships.

In the first experiment 437 abstracts were prepared and analyzed, producing a concordance and frequency measures on all non-trival words. The 100 most common nominatives were selected as index terms, in accordance with the methodology reported by Borko and Bernick. Document-term frequency vectors were then obtained, correlations computed, and the resulting matrix was factor analyzed and a simple structure (Varimax) rotation performed. These rotated factors were used to compute document scores, and the documents, thus classified, examined for similarity. Next the factors were analyzed in an attempt to relate them to classification categories. In a second experiment, a similar procedure was followed, but document-term vectors were formed on the basis of simple occurrence rather than frequency.

The results obtained thus far can be summarized as follows:

(1) Factors derived on the basis of simple term occurrence are more meaningful than frequency based factors.

(2) Simple occurrence, when used as a basis for deriving term related factors, produces a more meaningful classification of documents than frequency dependent factors.

(3) Neither technique can be used to affect a classification which is more than 50% correct when applied to medical publication data. (Compared to 80% reported by Borko in an analysis of articles from the computer field.)

In a third experiment, the 409 articles used by Borko, Bernick, Maron and Kuhn, were analyzed and a frequency distribution of all non-trivial words prepared. The distribution was compared to that obtained from the cerebrovascular articles, but no significant difference could be observed. However, it was noted that the 100 most frequent words used in the cerebrovascular literature account for only 33% of the variance explained by the first twenty principal factors. A letter to Harold Borko requesting the comparable statistic for his experiment has been sent (but not answered). Similarly, comparison of the derived term list with a manually constructed term list obtained from MEDLARS indicates that word frequency is not a reasonable criterion for selecting index terms in medical areas.

In a fourth experiment, recently initiated by Professor Vanderplas, the same data will be subjected to an analysis patterned after that proposed by Maron and Kuhn. As they used a manually prepared list of index terms, we shall use the MEDLARS list rather than the derived frequency terms.

Publications:

W. E. Ball, "The SLIP system for information processing", Proceedings of the 19th Semi-Annual Guide Meeting, October 1964.

R. A. Dammkoehler, "Numerical techniques in information processing", Proceedings of the 20th Semi-Annual Guide Meeting, May 1965. (In press.)

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6. Statistical Analysis and Programming

Personnel: R. A. Dammkoehler, BCL
L. L'Abate, Ph.D., Medical Psychology
R. L. Hamblin, Ph.D., Sociology
J. W. Josse, M.D., Microbiology

Support: FR-00215-01
GM-10642-03
MH-03804-02
NSF G-22296

Several new statistical methodologies were evaluated in a series of experiments initiated by the principal investigator. In general, this work may be separated into two major classes: a) Parameter estimation and b) Multivariate analysis. In particular, the problems of immediate concern are those relating to parameter estimation in non-linear, time dependent models describing biological phenomena and the effects of experimental error on both parametric and non-parametric statistical analyses.

The research plan followed in studies of methods of non-linear parameter estimation is similar to those proposed by Quenoiulle and Tukey, which requires the analysis of K samples (without replacement) of m sets of observations from a collection of n sample values. This method was applied successfully to a series of enzyme kinetic models proposed by J. Josse in conjunction with his work on nucleic acid metabolism.

Studies of the effects of experimental error on various multivariate analyses were conducted by R. L. Hamblin. The procedure adopted in the first of a continuing series of experiments called for the generation of artificial data from a known model and the addition of normally-distributed random error terms to the predictor values. The data thus generated is then subjected to analysis and the propagation of the error studied as a function of sample size and normal random error variance. Techniques now under investigation include: multiple regression (stepwise forward and stepwise condensation), factor analysis, canonical correlation, and several non-parametric methods. Our objectives are : 1) to establish error tolerance values for automatic data recording devices, 2) to determine the reliability of computational algorithms commonly used in statistical programs, 3) to gain experience in the interpretation of analytical data obtained from fixed models containing error terms of known distribution, and 4) to study the effects of interdependent predictor variables on conventional methods of statistical analysis.

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7. Dose Rate Distributions from Intracavitary and Interstitial Radioactive Implants

Personnel: T. L. Gallagher, M.S., Computation Center
Wm. E. Powers, M.D., Radiology
A. Schneider, B.A., Radiology
K. E. Shumate, B.S., Computation Center
I. C. Tang, D.Sc., BCL

Support: FR-00215-01
American Cancer Society, 42364-P
NSF G-22296

Modifications and extensions have been made to our existing computer program which calculates the dose rate distribution from linear sources at 1565 points in cubic volume, 10cm on a side, by approximating the Sievert integral by Gaussian quadrature. Absorption in the source shield and patient, scatter of radiation, and geometry corrections were taken into account in the original program.

Revisions of the original program for linear sources have been incorporated into the computer program RAIS (RadioActive Implanted Sources).

These revisions include:

a) Options for allowing variable spacing in all three coordinate directions.

b) Rotation of the dose rate distribution such that a coordinate direction is parallel to any specified linear source in the implant.

c) Rotation of coordinate axes (however, a right-handed system is maintained).

d) Provision for abbreviated output which may subsequently be transmitted to the user via an IBM 1050 data communications system.

e) Options to allow changes in the basic source, shield, and isotope libraries at execution time.

A program for dose rate distributions from point sources (RadioActive Point Implant Dosimetry, RAPID) has been obtained by revision of the original program. All options mentioned above have been incorporated into this program, with the exception of revision b.

Comparison with the existing available computer programs from other installations was made. Each program closely fits the sources and implant methods of the originating institution; however, RAIS is the most versatile of the programs.

Publications:

W. E. Powers, C. R. Bogardus, Jr., Wm. White, T. L. Gallagher, "Computer estimation of dosage of interstitial and intracavitary implants", Radiology (in press).

W. E. Powers, A. K. Schneider, K. E. Shumate, H. Fotenos, T. L. Gallagher, "Evaluation of methods of computer estimation of Interstitial and intracavitary dosimetry", Am. Jour. Roentgenology (in press).

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8. Roentgen Size of Normal Kidneys

Personnel: B. J. Walz, B.S., BCL
M. J. Friedenberg, M.D., Radiology
T. L. Gallagher, M.S., Computation Center
J. P. Locksmith, M.D., Radiology
W. H. McAlister, M.D., Radiology

Support: FR-00215-01
FR-05389-01
NSF G-22296

Analyses were performed on the roentgen size of normal kidneys for 1286 patients from a general hospital population without recognizable renal disease. The kidney size was measured on abdominal roentgenograms obtained during intravenous urography, expressed as a function of the patients body surface area, and correlated with age, sex, and race. From these data, idealized normal (gaussian) distribution curves were constructed which indicate the range in size of normal kidneys in the population studies and the difference in size between each kidney in an individual subject.

Three categories of patients emerged as different to a statistically significant degree (99 percent level), namely, children, adult males, and adult females.

Publication:

M. J. Friedenberg, B. J. Walz, W. H. McAlister, J. P. Locksmith, T. L. Gallagher, "Roentgen size of normal kidneys", Radiology, 84: 1022-1030, 1965.

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9. Comparison of Various Tenometers in the Measurement of Optic Pressure

Personnel: G. S. Whitlow, Jr., BCL
Donald R. Franz, BCL
Robert A. Moses, M.D., Opthalmology

Support: NB-04774-02
NSF G-22296

This project involved the evaluation of readings made by different technicians at different stations with different instruments and different methods of measuring optic pressure.

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10. Effectiveness of Therapy for Colon Cancer, Implementing an Analysis of Mortalities by the Method of Probits

Personnel: G. S. Whitlow, Jr., BCL
John S. Spratt, Jr., M.D., Ellis-Fischel State Cancer Hospital

Support: CA-09741-06
NSF G-22296

This project involves the study of approximately 1100 subjects with a firm diagnosis of colon cancer. Relative information for each subject has been coded, the code itself involving some 34 characteristics with an average of 8 attributes per characteristic. Life tables have been constructed for each attribute, and probits are being constructed for each attribute, and probits are being constructed for selected categories. Correlations will be attempted on these probits, together with their confidence belts, the primary purpose being to test the significance of post-operative survival as compared to various therapy treatment plans.

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11. FORTRAN to LINC Compiler

Personnel: G. S. Whitlow, Jr., BCL

Support: NSF G-22296
FR-05389-01

The first stages of compiler design have been completed to enable a compilation from standard FORTRAN II source statements into the LINC object code with LAP symbolic statements as an intermediate output.

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The purpose of this investigation was to provide a language to the medical researcher consisting of a rather simple set of rules (FORTRAN) to serve as an immediate aid in the writing of short programs for execution on the LINC.

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12. Implementation of a Statewide Cooperative Tumor Registry

Personnel: G. S. Whitlow, Jr., BCL
Burl M. Dillard, M.D., Surgery
D. R. Franz, BCL
Kenneth D. Serkes, M.D., Surgery

Support: NSF G-22296
FR-05389-01

The purpose of this study is to provide a general plan of implementation for a Missouri Cooperative Tumor Registry. Of primary consideration is the design of reporting forms for use by member institutions. The ultimate purpose of the study is to design a regionalized system for retrieval of information from the registry, this information to be used in conjunction with various research activities as well as for periodic dissemination of reports.

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13. Incidence of Multiple Primary Cancers per Man-Year of Follow-up

Personnel: G. S. Whitlow, Jr., BCL
Galen B. Cook, M.D., Ellis-Fischel State Cancer Hospital
Miriam G. Hoag, Ellis-Fischel State Cancer Hospital
John S. Spratt, Jr., M.D., Ellis-Fischel State Cancer Hospital

Support: CA-08023-01
CA-09741-06
FR-00215-01

This project involves the examination of data from the Ellis-Fischel State Cancer Hospital in order to determine:

a) If cancers are of the nature of an accidental fluctuation.

b) If the incidence of multiple cancer is dependent on the presence of previous neoplasms.

c) If the incidence of multiple cancer is dependent on age.

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14. Information Retrieval of X-ray Diagnosis and Pathology Data

Personnel: Donald R. Franz, BCL
William R. Brown, B.S., Radiology
Marvin J. Friedenberg, M.D., Radiology
David Sholtz, BCL

Support: NSF G-22296
Mallinckrodt Institute of Radiology

The Mallinckrodt Institute of Radiology conducts over 70,000 X-ray examinations annually. It is extremely important to follow up the diagnoses to see if they were correct, and to get this information back to the physicians concerned so that improvements can be made in the accuracy of diagnosis. A mechanized system was set up to perform the billing functions and at the same time prepare input to a master file of X-ray diagnoses. The mechanized billing system also profides monthly summaries of X-ray activities useful in workload planning, budgeting, etc.

An important output of the mechanized system is a monthly list of diagnoses made, grouped by physician, showing both confirmed diagnoses and erroneous diagnoses as determined by pathology reports. A separate file of matched diagnosis and pathology records is maintained to facilitate retrieval of this information for research purposes.

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15. Lymphoma-Leukemia Cancer Case Study

Personnel: G. S. Whitlow, Jr., BCL
D. R. Franz, BCL
A. McChesney Evans, M.D., Ellis-Fischel State Cancer Hospital

Support: NSF G-22296
CA-06800-03
Ellis-Fischel State Cancer Hospital

This project involves a study of all leukemia and lymphoma cases over the past 30 years at the Missouri State Cancer Hospital. Cases are identified by county of residence, year of symptom onset, and stage of disease. Analyses include mean survival time for each tumor type, correlation of delay from symptom onset to first therapy with survival, correlation of sociologic factors, geographic factors, and weather factors with incidence of cancer cases.

Publications:

A. McChesney Evans, "Lymphoma: an analysis of 460 cases from the Ellis-Fischel State Cancer Hospital", Annals of Internal Medicine, 62: 1094, 1965.

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16. Mechanization of Serial Records in the Medical School Library

Personnel: Donald R. Franz, BCL
Estelle Brodman, Ph.D., Medical Library
David Sholtz, BCL

Support: NSF G-22296
FR-05389-01
Washington University School of Medicine

A master tape file created to contain all the serial holdings is run monthly through a computer program which creates a receipt card for each issue of each journal that is to be received in the next month. Also, incoming receipt cards update the holdings statements, and provide bind messages for completed volumes. Receipt cards remaining at the library at the end of a month serve as claim notices for issues not received. Monthly lists provide complete information on each title, with updated holdings statements. A list of titles, alphabetically by subject, is also provided. Daily lists of incoming journals are created mechanically from the receipt cards. Between monthly update runs, a weekly cumulative list in alphabetic order is created from the sorted receipt cards. The Kardex file has been eliminated.

This system has been in operation at Washington University, and several dozen other universities and organizations have obtained copies of the system. Some are implementing the system directly, while others are utilizing parts of it.

The Medical Library has presented several symposiums on machine methods in libraries, and has produced a 16mm sound film of the operation of the system.

Publication:

E. Moore and E. Brodman, Letter to the editor, Bulletin of the Medical Library Assoc., 53: 99-100, 1965.

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17. Plasma Cell Grain Counts

Personnel: G. S. Whitlow, Jr., BCL
Sam L. Clark, Jr., M.D., Anatomy
D. R. Franz, BCL

Support: NSF G-22296
FR-05389-01
GM-07176-06

Plasma cells were incubated in a solution of radioactive protein for various time lengths, then fixed, cut, and treated

with photographic emulsion and developed. Size of the cell nucleous, Golgi apparatus and endoplasmic reticulum were obtained from enlargements. Silver grains were counted as a measure of radioactivity.

Data were analyzed for the effects of incubation time on Golgi grains per unit weight, and endoplasmic reticulum grains per unit weight.

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18. Relationship Between Race and Sex with the Number of Vertebrae Present in Human Cadavers

Personnel: G. S. Whitlow, Jr., BCL
D. R. Franz, BCL
Roy R. Peterson, M.D., Anatomy

Support: NSF G-22296
FR-05389-01

An evaluation was performed of the number of vertebrae in samples of cadavers to determine if there was a relation to race, sex, or their interaction.

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19. Serum Electrophoretic Patterns in Pregnancy

Personnel: G. S. Whitlow, Jr., BCL
Robert Burstein, M.D., OB/GYN
D. R. Franz, BCL

Support: NSF G-22296
FR-00215-01

This research is directed toward early detection of problems in pregnancy so that appropriate therapy can be instituted at the earliestpossible time. Physiologic rejection of the pregnancy by the mother has been previously demonstrated. If there is an immune reaction by the maternal host, antibodies are formed and their presence should be detected. Since all pregnancies are not aborted, there must be some alteration in the immune response. Study of the alteration in the serum globulin components might indicate evidence of antibody production.

Data gathered to date has been used to establish bands of normal values throughout pregnancies for each component. Work on data-gathering techniques is reported elsewhere (see V-A-14).

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20. Study of Insulin Response of Diabetics and Non-Diabetics Under Various Stimuli

Personnel: D. R. Franz, BCL
David M. Kipnis, M.D., Internal Medicine
G. S. Whitlow, Jr., BCL

Support: NSF G-22296
FR-05389-01

This study is in its initial stages and consists of four groups of subjects under various glucose and orinase tolerance tests. Blood glucose, plasma insulin and NEFA are measured versus time, giving different response curves for each group of subjects. The four groups under consideration are normal-weight non-diabetics, obese non-diabetics, normal-weight diabetics, and obese diabetics.

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21. Tritium and Carbon 14 Data Analysis and Plot

Personnel: G. S. Whitlow, Jr., BCL
D. R. Franz, BCL
David E. Kennell, M.D., Microbiology

Support: NSF G-22296
GM-09830-03

Originally, the method of obtaining plots of tritium and carbon 14 had about a week's delay from time of data collection to time of obtaining a plot. Plots were caluculated and drawn manually by technicians. Since results of one experiment were needed to set up the next experiment, a minimum delay time was required.

A program was created to read the data from punched cards, make all calculations, and plot the graphs. Computing time for this program is less than 2 minutes. After the program was put into operation, a researcher on a different project found that with a small modification the program solved her needs also.

Publication:

D. Kennell and A. Kotoulus, "Chemical fractionation of nucleic acids and protein and estimation of their radioactivity using filters", (submitted).

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22. Union List of Serials for Libraries

Personnel: D. R. Franz, BCL
David Sholtz, BCL

Support: NSF G-22296

This project, studied in conjunction with the Higher Education Coordination Council, involved the creation of a union list of serials for libraries in the Missouri-Illinois area, with the capability of yearly updating. The union list will carry over 14,000 different titles. Each participating library will be able to obtain listings of its holdings. Each title is coded to show all the libraries holding the publication on the master list. Copies of the master list will be available to all libraries.

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V. RESEARCH PROJECTS

C. Collaborations with Other Organizations

The following research projects have been carried on for the most part in other laboratories, departments, or institutions. Responsibility for the research lies outside the Biomedical Computer Laboratory. However, portions of these projects involve collaboration with or supervision by staff members of our laboratory. In some cases the research has been supported by funds from our laboratory. To make clear the goal of the research the complete project is outlined. Special mention of the collaborative efforts is made where they deal with only a portion of the project.

The investigator responsible for these projects is listed first. Biomedical Computer Laboratory staff members are listed only if their efforts are of a continuing nature. The outside organization through which major support is derived is listed along with the source of that support.

1. A Digital Sine Wave Oscillator

Personnel: Bernard D. Aims, M.S., Graduate Student
J. R. Cox, Jr., BCL

Department: Electrical Engineering

Support: Washington University School of Applied Science and Engineering

An audio oscillator that generates sinusoidal waveforms using digital techniques has been constructed. The frequency can be controlled by a digital computer which makes the device potentially useful in frequency response experiments, particularly in the area of physiological research. The amplitude of output voltage is not a function of frequency. Second harmonic distortion can be reduced below 0.30 percent of the fundamental; all other distortion components are significantly less. Because the digital oscillator is inherently very stable, it can be used to generate extremely low frequency sinusoids.

Publication:

B. D. Aims, "A digital sine wave oscillator", M. S. Thesis, Washington Univ. (1965).

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2. Averaging Techniques for Extracting Acoustic Signals from Noise

Personnel: M. K. Bauer, B.S., Central Institute for the Deaf
J. R. Cox, Jr., BCL
A. M. Engebretson, BCL
J. D. Miller, Ph.D., Central Institute for the Deaf
A. F. Niemoeller, Sc.D., Central Institute for the Deaf
P. B. Weston, M.A., Central Institute for the Deaf

Institution: Central Institute for the Deaf

Support: NB-03856-03
FR-00161-01

It is often necessary to measure signals at levels near and below the threshold of human and animal hearing. In the past such measurements were made indirectly by assuming that the signal attenuators and sources were linear. It would be more desirable to measure such signals directly. Since these low-level signals are often of a repetitive nature, averaging techniques can be used to extract the signal from the noise. A LINC program and a special data-terminal plug-in module is used in two ways. For low frequencies, the waveform is sampled and averaged continuously, using the plug-in module to synchronize the computer eliminating jitter in the time at which samples are taken. An external clock in the module can be restarted from a triggering signal generated by the signal source. For frequencies above the audible range techniques similar to those used in a sampling oscilloscope allow operation up to an effective rate of 500,000 samples per second.

Publication:

J. D. Miller, A. M. Engebretson and P. B. Weston, "Recording the waveform of periodic acoustic signals at levels near and below 0.0002 μbar, J. Acous. Soc. Amer., 36: 1591-1593, 1964.

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3. Design and Construction of a Programmed Console

Personnel: J. R. Cox, Jr., BCL
W. A. Clark, CRL

Department: Electrical Engineering

Support: Washington University School of Applied Science and Engineering

During the Spring Semester a course in computer design was offered to graduate students with Electrical Engineering or Computer Science backgrounds. During the last six weeks of this course the

students designed, assembled, and debugged a small, stored-program computer called the Programmed Console (PC). The most important characteristic of the PC is its ability to send and receive data over a communication channel (Bell System Data Set, Type 202D). The PC has a 4096-word by 12-bit memory with a cycle time of 2 microseconds. The central machine timing is controlled by a delay chain and currently has a cycle time of 3.5 microseconds. The circuitry for the PC consists of approximately 150 flip-chip modules loaned to the University by the Digital Equipment Corporation. The instruction repertoire is small but adequate and contains instructions for sending or receiving 1 word of data over the communications channel. The addressing scheme allows locations 1-255 to be addressable in a single instruction word. An option uses any location 1-255 for an indirect address. Additional options allow two word instructions for which the second word is either a 12-bit operand or a 12-bit address. I/O equipment includes the communication channel, a Tektronix 564 Storage Oscilloscope and an Invac keyboard.

The PC has a simple operating console and the order code contains instructions that forbid or permit console functions. These instructions are required because the PC must not attend to console functions whenever messages are being transmitted or received. Of course, there is a manual override switch on the console that allows the operator to have final control. Thus, the PC can serve as a self-contained computer, a satellite computer for a larger machine, or an intelligent remote console.

An additional console feature is the Load function. The initiation of this function sends a special signal to a central computer indicating that the PC is requesting basic routines. This function is implemented entirely with hardware. When received by the PC these basic routines allow the PC to begin functioning as a computer.

Information may be transmitted over the channel at a rate of 1000 bits per second. The word format consists of a leading '1' bit, 12 data bits and a final '0' bit. The leading and trailing guard bits are required so that a known transition will indicate the beginning of a word and make possible resynchronization. The Load function is implemented by turning off the data carrier for a fraction of a second.

The dataphone channel is currently arranged so that the PC communicates with a LINC. The LINC interface with the channel is completely programmed and the only hardware required is for level standardization. This arrangement, while awkward, is all that is necessary to provide the PC with a large program and data file.

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4. A Filtering Technique Useful in Recording Fetal Electrocardiograms

Personnel: M. H. Hieken, M.S., Graduate Student
J. R. Cox, Jr., BCL
D. H. Glaeser, BCL

Department: Electrical Engineering

Support: Washington University School of Applied Science and Engineering
FR-00161-01

In recording fetal electrocardiograms from leads located on the maternal abdomen, it is frequently true that the dynamic range of tape recorders is marginal for recording the unfiltered signals. In the detected signal, low frequency components (resulting from breathing, changes in electrode resistance, or other factors) are of considerable amplitude compared to components of greater interest, such as the fetal QRS complex. When the amplitude range of the tape recorder is set to accomodate the large amplitude low frequency signals, the high frequency signals are frequently in the noise level of the tape recorder's playback amplifier.

A magnetic tape recording technique has been devised which attenuates the low frequency components during the recording process and amplifies the low frequencies on playback. The special filters designed to perform the frequency-selective attenuating and amplifying are the exact inverse of one another, resulting in a reproduced signal free from phase distortion. With the special pre-recording and playback filters, a mean-square signal-to-noise ratio improvement slightly greater than 3 db can be realized relative to the recording system without the filters.

Since the special filters are easily synthesized from operational amplifiers and passive electrical components, the recording technique can be applied to any signal whose frequency components are separable. A publication of this work is in preparation.

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5. The Relationship between the Mammalian Cardiac Action Potential and Contraction Strength under Varying Physiological Conditions

Personnel: Frank S. Letcher, B.A., Medical Student
Wm. W. Sleator, Jr., Ph.D., Physiology

Department: Physiology

Support: 5T5-GM-8-09
FR-00161-01

An intracellular microelectrode is used to measure the transmembrane action potential of single cells in an *in vitro* mammalian cardiac muscle preparation. Contractions of the whole preparation are measured by a mechano-electronic transducer radio tube. Preparations are driven by an external stimulus and are generally guinea pig, rabbit, or human myocardium. The LINC is used to make on-line recordings on magnetic tape of the waveform outputs of the microelectrode and of the transducer. At the same time, the integral of the microelectrode output between two limits (set by LINC) is computed and stored. The maximum of the output of the transducer tube is also computed and stored by LINC. The apparatus for this experiment has been set up at BCL and programs are in operation.

Further application of LINC will involve processing the data to reveal physiologically significant relationships between given parts of the cardiac action potential and the contraction.

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6. Operating Characteristic Analysis

Personnel: J. D. Miller, Ph.D., Central Institute for the Deaf

Institution: Central Institute for the Deaf

Support: NB-03856-03

In the analysis of evaluative processes in speech communication it is helpful to compute the "receiver operating characteristic". A program is in operation that uses listener's predictions of the accuracy of speech communication events to compute measures of the correctness of the predictions. This work is carried on using the IBM 1050 located at BCL.

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7. Processing Audiometric Data

Personnel: J. D. Miller, Ph.D., Central Institute for the Deaf

Institution: Central Institute for the Deaf

Support: NB-03856-03

This program converts audiometric-threshold data from attenuator settings to sound pressures and then finds the means, and sums of squares of interest. This work is carried on using the IBM 1050 located at BCL.

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8. Infant Vectorcardiograms

Personnel: David L. Polage, Medical Student
M. R. Behrer, M.D., Pediatrics
D. H. Glaeser, BCL

Department: Pediatrics

Support: 5T5-GM-8-09
FR-00161-01

The goal of the project is to define the ranges of several parameters of infant vectorcardiograms using 50 - 100 normal infants. The values of these parameters are to be computed with programs now written for the LINC computer.

The parameters chosen were: 1) Angle and magnitude of instantaneous vectors every 10 milliseconds around the QRS loop; 2) angle and magnitude of the maximum vector of the QRS loop. Programs have been written to: 1) Average large number of individual complexes; 2) display the vectors on the screen; 3) display the calculated values.

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9. System Design of a Small Multisequence Computer

Personnel: K. R. Thompson, Graduate Student
J. R. Cox, Jr., BCL

Department: Electrical Engineering

Support: Washington University School of Applied Science and Engineering

A small multisequence computer was designed, but not built, for computations and controlling objects in real time. It has a word

length of 18 bits and a storage capacity of 4096 words with 6 interrupt channels (2 for tape and 4 for time interrupt). The computer can be interrupted in the middle of an instruction with no loss of efficiency. The problem of reading or writing on 2 tape channels interlaced with computing is given special attention.

Publication:

K. R. Thompson, "System design of a small multisequence computer", M.S. Thesis, Washington Univ., 1964.

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10. Image Scanning and Pictorial Data Processing

Personnel: D. F. Wann, Sc.D., Electrical Engineering
P. S. Berger, BCL
J. R. Cox, Jr., BCL
W. Schauman, B.S., Electrical Engineering

Department: Electrical Engineering

Support: FR-00161-01
NSF GE-7994

Investigation is underway of pictorial density measurements under direct control of a digital computer using a photodiode array in conjunction with an incremental plotter. The picture or photograph whose density is to be quantized will be locally illuminated with an optical fiber. A photodiode output will be sampled, converted to digital form, and stored in the LINC memory for further processing. The photodiode circuit has been designed and tested. Currently, the diode array is being attached to the incremental plotter and tests are under way to evaluate the system performance.

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11. Electrical Field Patterns Associated with Evoked Activity in Central Nervous System Structures

Personnel: R. R. Wright, M.D., Neurology
J. R. Cox, BCL
S. M. Ornstein, CRL

Department: Neurology

Support: FR-00149-01

A LINC program has been written for the purpose of studying the instantaneous electrical field patterns associated with evoked activity in central nervous system structures. The field under

study at the present time is related to an evoked response in the cortex of the cingulate gyrus. This electrical field is asymmetrical. The asymmetry appears chiefly related to the configuration of the cortex as a generator.

An average of 32 evoked responses are taken at each of a large number of recording positions in a given coronal plane of the cat brain. These positions form a grid of points whose instantaneous voltages (with respect to the stimulus) are stored on LINC tape. From these data the instantaneous electrical fields can be plotted and correlated with the corresponding section of the cat brain. The contour plotting program (see V-A-7) will be used for this purpose.

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12. Steady Potential Correlates of Intracranial Reinforcements

Personnel: Robert H. Wurtz, Ph.D., Neurology and Physiology

Department: Neurology

Support: FR-00149-01
MH-10293-02
NB-04513-02
5T1-NB-05240-06
FR-00161-01

Self-stimulation and escape behavior has been tested on rats with stimulating electrodes implanted in hypothalamus and mid-brain. After testing, recording electrodes were attached so that the D.C. potential could be recorded from the cortical surface using a reference electrode on nasal periosteum. Utilizing the LINC, 100 responses to stimulation were averaged, and a D.C. shift was identified. This shift appeared to be associated with the reinforcing effect of the stimulation since the stimulus intensity required for behavioral effects and D.C. shifts was similar and since stimulus points producing no motivational effects also produced no D.C. shifts.

The critical step in averaging D.C. potentials is the elimination of cumulative D.C. changes arising from movement of the animal or drift in the amplifiers. A technique worked out in collaboration with J. R. Cox subtracts a weighted average of the D.C. potential just prior to the averaging period from each sample taken during the averaging period.

Publication:

R. H. Wurtz, "Steady potential correlates of intracraneal reinforcement", (submitted).

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13. Studies of Synaptic Change in the Aplysia Visceral Ganglion with Contingent Reinforcement

Personnel: Robert H. Wurtz, Ph.D., Neurology and Physiology
Vincent F. Castellucci, B.A., B.S., Neurology
James M. Nusrala, B.A., Neurology

Department: Neurology

Support: FR-00149-01
MH-10293-02
NB-04513-02
5T1-NB-05240-06

A change in the functional connection between presynaptic terminal and postsynaptic neuron is assumed by most micro-physiological theories of learning. One variation of such theories predicts that if the postsynaptic neuron fires after a presynaptic terminal has been active, the connection between the pre- and postsynaptic neuron is facilitated while other inactive synaptic junctions are unchanged. In order to test this theory, LINC has been programmed to recognize a particular excitatory-post-synaptic potential (EPSP) and respond to the occurrence of this EPSP by either passing current and producing a spike potential ("reinforcement") or simply noting the frequency with which the EPSP is followed by a spontaneous spike ("non-reinforcement"). A second EPSP is also recognized and is used as a control; variations in the experiment may be made during the experiment by means of console switches. The LINC program contains sections for selecting EPSP's as standard for recognition, for testing recognition and performing the experiment, for displaying data, and for moving between program segments and setting up storage areas. In addition to complete control of the experiment, LINC stores all data on LINC tapes and prints on a Teletype (as the experiment is proceeding) the frequency of association between spikes and the EPSP's, and the EPSP and spike time-intervals.

The method of waveshape recognition used in identifying EPSP's was developed in collaboration with J. R. Cox who also carried out the logic design of an external clock for the data terminal box. Various subroutines and aid in programming has been provided by the BCL staff.

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14. Hydraulic Impedance to Blood Flow in the Dog

Personnel: H. M. Yanof, Ph.D., Physiology, St. Louis University School of Medicine
M. D. McDonald, BCL

Institution: St. Louis University Medical School

Support: HE-08507-01

The hydraulic impedance of the vascular bed of dog is measured by using pressure transducers and a special pump with known volume-velocity. By manipulating the state of the vascular bed with drugs, response data are obtained on analog tape. These data are transferred to digital form on LINC tape at BCL. A program is now being written for LINC to compute the input-impedance and phase velocity as a function of the driving frequency of the pump.

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15. Enzyme Molecule Interactions

Personnel: Wm. Holmes, Ph.D., Computation Center
R. I. Berns, B.S., Computation Center
M. Burger, M.D., Biochemistry

Department: Computation Center

Support: Saint Louis Heart Association
Helen Hay Whitney Fellowship
GM-08117-05
FR-00215-01

The interactions between four active sites on the same enzyme molecules were studied. There are a number of possible chemical mechanisms; however, they all lead to steady state rate equations of the form,

$$V = \frac{\sum_{i=1}^{4} a_i s^i}{1 + \sum_{i=1}^{4} a_i s^i}$$

where V is the rate of substrate reaction in the steady state, and s the initial substrate concentration. The constants a_i depend on the values of the rate constants and enzyme concentration. Each possible mechanism also imposes some general constraints on the range of the constants. Thus a systematic survey of the above equation may disclose qualitative features characteristic of a

particular mechanism. Such a survey is impractical for eight parameter equations, unless there is strong guidance in the choice of parameter sets. A preliminary survey using all combinations of five variations for five of the parameters revealed a number of interesting features, but also many nonessential curves. It was felt that a great increase in the efficiency of the survey would result if the experimenter could observe each curve when computed, and introduce new parameters, depending on the result. Since such on-line operation is too wasteful without a time sharing system, the survey will be continued on a PDP-5 Computer at the Engineering School. Constants may be set with the Teletype input and the computed curve displayed on the oscilloscope.

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16. Computer Analysis of Electron Spin Resonance Data

Personnel: T. L. Gallagher, M.S., Computation Center
L. E. Bubb, Computation Center
John Heiss, Ph.D., Molecular Biology

Department: Computation Center

Support: NSF G-22296
FR-00215-01

Computer programs have been written which calculate the least squares estimate of electron spin resonance (ESR) data by approximating the resonance with either one or two gaussian kernels. Instrument drift is removed by a quadratic approximating function, and partial transmission through the experimental sample is corrected by appropriate dispersion kernels.

The method of maximum neighborhood is used in fitting the resonances to the following forms:

For one resonance:

$$Y = B_1 + B_2 X + B_3 X^2 + B_4 (1 + V - 2B_5 V^2) \exp(-B_5 V^2)$$

Where X = channel number

$$V = X - B_6$$

For two resonances:

$$Y = B_1 + B_2 X + B_3 X^2 + B_4 (1 + V - 2B_5 V^2) \exp(-B_5 V^2) + B_6 (1 + R - 2B_7 R^2) \exp(-B_7 R^2)$$

$$X = \text{channel number}$$

$$V = X - B_8$$

$$R = X - B_9$$

all of the B values are allowed to vary independently to obtain the best fit.

Input consists of 5 digit values of relative ESR absorption signal arranged by ascending channel, 10 per card. The program allows for background correction and appropriate labeling of the experimental sample. Output consists of (1) a listing of the background and signal plus background as well as other input parameters; (2) the iteration parameters and coefficients of the functional fit for the method of maximum neighborhood; (3) a scaled plot of the signal curve and the fitted curve; and (4) a plot and punched cards of the residual. (Difference between the calculated and experimental values.)

Since the method of maximum neighborhood is an iteration technique, computation times are strongly dependent on initial estimates of the B values. It is expected that after some experience has been gained, the running times for a calculation will be no longer than 3 to 5 minutes on the IBM 7072.

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VI. TRAINING ACTIVITIES

During the year three short courses in programming the LINC have been offered. Staff members and students attending were:

May, 1964

Steve Corrie	Sophomore Medical Student
Wm. S. Coxe, M.D.	Neurosurgery
Francisca Lee	Sophomore Medical Student
Jay Liss	Sophomore Medical Student
David Polage *	Sophomore Medical Student
Michael Rumelt	Sophomore Medical Student
Joseph Ruwitch	Sophomore Medical Student
Henry G. Schwartz, M.D.	Neurosurgery
Bruce Walz	Sophomore Medical Student
Robert Wurtz, Ph.D. *	Neurology and Physiology

October, 1964

M. Remsen Behrer, M.D. *	Pediatrics
Judith Bennett	Computer Research Laboratory
Max M. Burger	Biochemistry
H. S. Farmer	Central Institute for the Deaf
V. W. Gerth, Jr. *	BCL
Loretta Glisman	Opthalmology
Louise Jager	Student, Washington University
Michael Koenig *	Computer Research Laboratory
G. R. Little *	Graduate Student
Louis Medgyesi-Mitschang	Graduate Student
A. F. Niemoeller, Sc.D. *	Central Institute for the Deaf
F. M. Nolle *	BCL
Albert F. Ruehl	Graduate Student
Aleene Schneider	Radiology
Wayne Schurter	Medical Psychiatry
James M. Vanderplas, Ph.D.	Computation Center
Roy R. Wright, M.D. *	Neurology

May, 1965

Merrill K. Bauer *	Central Institute for the Deaf
Thor Bruce, Jr.	Graduate Student
James H. Burgess	Physics
Vincent Castelucci *	Neurology
Margaret Clare *	Neurology
Robert Comotto	Neurology

Edward Eikman	Sophomore Medical Student
Donald Franz *	BCL
John Hered	Sophomore Medical Student
Masashi Kawasaki, M.D.	Otolaryngology
Frank Letcher *	Sophomore Medical Student
George B. McDonald *	Sophomore Medical Student
Albert Rhoton, M.D. *	Neurosurgery
Stephen Rothenberg	Central Institute for the Deaf
James A. Seddon, Jr.	Sophomore Medical Student
Stephen VanMeter *	Sophomore Medical Student
Howard M. Yanof, Ph.D. *	Physiology, St. Louis University

* These participants have used or are using the LINC actively in their own research. In most cases reports of this research will be found in Section V.

VII. PUBLICATIONS

Publications submitted or appearing during the period covered by this report, authored or supervised by BCL staff members, are listed below. Work on many of these publications was begun before the founding of the laboratory.

What can computers do that people cant?	In Report Proceedings Intl. Congress on Education of the Deaf & 41st Meeting of the Conv. of Am. Instructors of the Deaf, U.S. Govt. Printing Office, 1964.	J. R. Cox, Jr.
A quantizing encoder.	IEEE Trans. Electronic Computers, EC-13: 250-254, June 1964	J. R. Cox, Jr. D. H. Glaeser
Sampling and analog to digital conversion.	In Electronic & Computer-Assisted Studies of Bio-Medical Problems, ed. Schmitt & Caceres, Chas. C. Thomas, 187-206, 1964.	J. R. Cox, Jr.
The SLIP system for information processing.	In Proceedings of the 19th Semi-Annual Guide Meeting, October 1964	W. E. Ball
System design of a small multisequence computer. M.S. Thesis	Washington Univ.,1964	K. R. Thompson
A LINC utility system.	BCL Report, March 19, 1965.	M. D. McDonald S. R. Davisson J. R. Cox, Jr.
A digital sine wave oscillator, M.S. Thesis.	Washington Univ.,1965	B. D. Aims
Special-purpose computers in biomedical research.	In Computers in Biomedical Research, ed. Stacy & Waxman, Academic Press (in press).	J. R. Cox, Jr.
Numerical techniques in information processing.	In Proceedings of the 20th Semi-Annual Guide Meeting, May 1965 (in press).	R. A. Dammkoehler

Publications submitted or appearing during the period covered by this report authored by collaborators and reporting research to which Biomedical Computer Laboratory personnel made contributions are listed below:

Evoked responses to clicks recorded from the human scalp.	Annals N.Y. Academy of Science; Vol. 122, Art. 1, May 8, 1964	H. Davis A. Engebretson * E. Lowell T. Mast J. Satterfield N. Yoshie
Validation of evoked response audiometry (ERA) in deaf children.	(submitted)	H. Davis
Lymphoma: an analysis of 460 cases from the Ellis-Fischel State Cancer Hospital.	Annals of Internal Medicine, 62: 1094, 1965.	A. McChesney Evans
Roentgen size of normal kidneys.	Radiology, 84: 1022-1030, 1965	M. J. Friedenberg B. J. Walz * W. H. McAlister J. P. Locksmith T. L. Gallagher
Somatosensory cortex of man as revealed by computer processing of peripherally evoked cortical potentials.	Trans. American Neurolog. Assoc., 89: 108-111, 1964	S. Goldring D. L. Kelly, Jr. J. O'Leary
Averaged evoked somatosensory responses from exposed cortex.	Arch. Neurol., 13: 7-11, 1965	D. L. Kelly, Jr. S. Goldring J. O'Leary
Chemical fractionation of nucleic acids and protein and estimation of their radioactivity using filters.	(submitted)	D. Kennell A. Kotoulus
Recording the waveforms of periodic acoustic signals at levels near and below 0.0002 μbar.	J.Acous.Soc.Amer., 36: 1591-1593, 1964.	J. D. Miller A. M. Engebretson * P. B. Weston

* BCL staff member.

Letter to the editor.	Bulletin of the Medical Library Assoc., 53: 99-100, 1965	E. Moore E. Brodman
Computer estimation of dosage of interstitial and intracavitary implants.	Radiology (in press)	W. E. Powers C. R. Bogardus, Jr. Wm. White T. L. Gallagher
Evaluation of methods of computer estimation of interstitial and intracavitary dosimetry.	Am. Jour. Roentgenology (in press)	W. E. Powers A. K. Schneider K. E. Shumate H. Fotenos T. L. Gallagher
Steady potential correlates of intracraneal reinforcement.	(submitted)	R. H. Wurtz

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