Interface for rapid data transfer and evaluation

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INTRODUCTION

Minicomputers are quite useful for the acquisition and reduction of data from physical and biomedical research equipment. Minicomputers have become progressively less expensive and are now comparatively easily available for research investigators. At that point, the problem arises to interface minicomputers effectively to research equipment. This interfacing task became recently somewhat facilitated by specialized books and articles.1,2,3 Quite recently minicomputers were utilized for multiple ion detection in combined gas chromatography—mass spectrometry.4, 5 A computer centered instrument for simultaneous measurements of absorption and fluorescence was also described quite recently.6 Finally, a computer system for the acquisition and analysis of temperature jump data was described.7 Although a Biomation 802 transient recorder was used as fast analog-to-digital converter by the latter authors, they utilized a Digital Equipment Corporation PDP 11/20-8k and a teletypewriter ASR-33 as equipment connected to the output of the Biomation 802. In this paper we will describe the use of a Digital Equipment Corporation PDP 8/e-8k minicomputer as active processor between the Biomation 802 and a Hazeltine 2000 CRT terminal, which is also connected to a Hazeltine dual tape cassette.

Before the use of the minicomputer, we had produced data on paper tape in rather large quantities. The rolls of paper tape were then transferred to a large computer via an overnight carrier. Unfortunately, the large volume of long rolls of paper tape caused some operational problems at the main computer center. Furthermore, ten minutes were required for the production of paper tape with about 1,000 (8 bit) points per experiment from the Biomation 802. For our experiments, three minutes are required for thermal equilibration after a temperature jump and also for full attainment of a new equilibrium value after a pH jump. In other words, our Biomation 802 transient recorder is utilized on two types of chemical relaxation experiments: perturbation with the temperature jump apparatus and with the concentration jump apparatus (a pH-jump is a special case of a concentration jump).

The current arrangement allows us to conduct our experiments about ten times faster than before. We fill tape cassettes with data which are subsequently transferred through communication lines onto a large computer for thorough statistical analysis. This paper will describe the layout of the software and the details of the hardware configuration. No changes were made on the Biomation 802, allowing us to use a teletypewriter and the previously employed interface (Dijsican Model B203) as back-up for this computer system. However, we have not needed to use the back-up system since the minicomputer was first brought into operation in June of 1973. The equipment is used rather extensively in two research projects on the mechanism of action of enzymes.8,9

METHODS

The experimental arrangement centered around a Digital Equipment Corporation PDP 8/e-8k minicomputer, interfaced both to a Hazeltine 2000 CRT terminal with dual tape cassette unit, and to a Biomation 802 transient recorder. The latter is connected either to one of our temperature jump instruments9 or to our pH-jump apparatus.8 The details are best described by several figures.

A schematic of the temperature jump apparatus with detection of transmission changes is shown in Figure 1. A similar instrument is also available for detection of fluorescent changes, containing a half reflecting mirror between light source and cell (containing the chemical system). The mirror transmits excitation light and reflects fluorescence, emitted back from the cell. The temperature jump instruments are equipped with special AC-coupling circuits to improve the detection of small changes behind large (fast) transients.11 Three types of stopped flow instruments are available with the slowest one in considerable use: This is a pH-jump apparatus with detection of transmission changes and a time resolution of about 0.1 seconds.

The layout of the equipment around the PDP 8/e minicomputer is shown in Figure 2 without a 10 times wide band.
Figure 1—Schematics of a temperature jump apparatus with detection of transmission changes. The schematic shows abbreviated the current overall configuration of the apparatus. When a push button is pressed, a timing circuit is initiated, triggering first the oscilloscope deflection at A. After one centimeter of progression of the oscilloscope beam, a trigger pulse is generated at B, initiating the closing of the spark gap switch G. After about 0.5 millimeter further propagation of the oscilloscope beam, a trigger is generated at C, opening the grounding switch S in the detection circuit. The grounding switch is closed again at time D (or later). The extended grounding (from B to C) is used to prevent any processes to be shown on the oscilloscope screen, which are faster than the one currently under investigation and settings of the oscilloscope deflections, which are optimal for detection.

amplifier, which is located in front of the Biomation 802 and amplifies the signal derived from the temperature jump experiments. The data acquisition is controlled through interaction with displays on a Hazeltine 2000 CRT terminal. The controlling messages and the associated flow diagrams are shown in Figures 3, 4 and 5. More subroutines are actually used than shown in these three figures. A teletypewriter may also be connected and is essential for the initial loading of the binary program from a paper tape. (We encountered some problems in trying to use the Hazeltine cassette as alternate storage space for the programs: the problems are due to the fact that the interfacing Hazeltine terminal behaves inconsistently with respect to non-playable characters, when transmitted for recording onto the cassette.)

The geometric layout of the various integrated circuits on the interface board of the PDP 8/e are shown in Figure 6. Enough space is left to add additional control functions. The functional circuit diagram is distributed over Figures 7, 8 and 9, all of which are mounted on one DEC interface board M1709. The remote control of the Biomation 802 is not implemented yet. The instruction set of the interface is as follows (where xx stands for 63, the device code for the transient recorder):

6xx0: Interrupt off.

Turns off the interrupt flip-flop, i.e., clears it. This stops any interrupts due to data ready signals from the Biomation 802.

6xx1: Skip on flag.

The instruction following 6xx1 will be skipped if the next word from the Biomation 802 is available and such a signal has already come from the Biomation 802 to the interface board.

6xx2: Interrupt on.

Turns on the interrupt flip-flop, i.e., sets it to 1 and this way enables the Biomation equipment to interrupt normal execution of a program when next word is ready on the line.

Figure 2—Overall diagram of the computerized data acquisition system. The output of the amplifier in Figure 1 is connected to an isolation amplifier, producing also a ten times amplification for adaptation to the input characteristics of the Biomation 802 transient recorder. A Tektronix 602 storage oscilloscope is connected to the Biomation 802 to show the stored information. The transient recorder is directly connected to a PDP 8/e minicomputer with control information normally appearing on the Hazeltine 2000 CRT screen. Some minor editing is available before the data are transferred from the core of the PDP 8/e onto the Hazeltine tape cassette unit. From there, data are transferred onto the disk of a large CDC 6400 via telephone lines.
6xx3: Available for future expansion.
6xx4: Load the control register.
   This instruction will output the control bits which may do one of the following:
   (a) Effectively control execution of instruction 6xx5 (load)
   (b) Effectively control execution of instruction 6xx6 (read)
   (c) Start output from the Biomation 802. This will clear flag and pin 7 of the Biomation 802 will be grounded. (Ref: Biomation Manual—the user is required to ground pin 7 to start data transfer.)
   Accumulator is cleared at the end of the instruction.
6xx5: Load scales or control lines.
   Depending upon bit setting of instruction 6xx4, lower 6-7 bits of the accumulator are loaded into either the “voltage scale” buffer or “sweep time” buffer or “extra control lines” buffer register. Accumulator is cleared at the end of the instruction.
6xx6: Read scales or control lines.
   Depending upon instruction 6xx4 bit setting, “voltage scale”, “sweep time” or “control lines” are sensed and loaded into the accumulator. If more than one “read” control is turned on by 6xx4, the effect will be to “OR” the lines into the accumulator.

![Figure 3-Program Flow Chart of main program in the minicomputer and of short subroutines. The actual text of the control information from the minicomputer is directly shown. The five letters in the first print statement stand for:]

- R = Record data in core onto dual tape cassette
- D = Display data in core on the CRT terminal
- G = Go to Get new data from Biomation 802
- P = Punch data onto paper tape of tty
- E = End the program.

Starting point is at the beginning of core of the minicomputer, address 0000. The main program starts at Octal 0200. The data buffer starts at Octal 2000 and is Octal 2000 long. Location of the messages follows and the program ends at Octal 4400

![Figure 4-Flow Chart of subroutine SETCNT, responding to branch D. Sections of collected data may be presented on the screen without further editing capability]

The “voltage scale” and “sweep time” buffers drive corresponding scale lines high only if “voltage scale” and “sweep time” knobs are positioned “external” on the front panel of the Biomation 802.

“Extra control lines” (6 of them) give open collector output which can be pulled up to +15 volts (maximum current of 20 ma). Their main use will be for “relay” controls. (Note: When “sweep time” multiplier is neither x1 nor x2 then it is x4. Similarly when “voltage scale” multiplier is neither x1 nor x2 then it is x5.)

6xx6: Read scales or control lines.
   Depending upon instruction 6xx4 bit setting, “voltage scale”, “sweep time” or “control lines” are sensed and loaded into the accumulator. If more than one “read” control is turned on by 6xx4, the effect will be to “OR” the lines into the accumulator.

Control lines are [compare sections 5.5 to 5.7 of Biomation Manual] (i) Z Enhance (pin 6) goes to 1, when “sweep
which one can transfer data from the Biomation 802 into the PDP 8/e exist: (a) less than 500 μsec per word (b) greater than 2 msec per word.

If time taken to transfer data is not critical, range (b) is recommended.

RESULTS

Over the last few months, data were acquired with the described equipment on three different instruments, namely the temperature jump apparatus with detection of transmission changes (electron transfer experiments on cytochrome c), the temperature jump apparatus with fluorescence detection (binding of the fluorescing coenzyme NADH to liver alcohol dehydrogenase in the presence of inhibitors), and concentration jump experiments with detection of transmission changes at 633 millimicrons (detecting the various protonic forms of ferricytochrome c).

After users became familiarized with the various parts and their integrated action, they rapidly acquired mastery of the equipment and could perform soon experiments faster than before. Previously, the output of the Biomation 802 was transferred through an interface into a teletypewriter paper tape punch. As the teletypewriter produces only ten characters per second, ten minutes are required for the outputting of the data. With this new equipment, data are transferred out of the Biomation 802 and into the minicomputer within four seconds for a full set of 1024 “points”.

Although the subsequent transfer into the Hazeltine cassette unit takes a bit longer, a new experiment can in fact be conducted every three minutes, adequate for thermal equilibration in the thermostatted temperature jump cells and for almost all of the concentration jump experiments.

Although enough space is left on the PDP 8/e-8K, to write programs for the evaluation of the data, only the program

![Flow Chart of subroutine RECO, responding to branch R. Before the data are transferred from the core into the tape cassette, everything has to be set so that subsequent processing takes place smoothly and the data are properly identified by the “header card”, a line of up to 80 columns. Also some controls for the cassette are included in this program. The text as actually printed on the CRT screen is explicitly listed in the print statements. The printing “Position after ...” represents an abbreviation of the question: “How many files would you like to skip forward?”](image)

![Layout of integrated circuits on the interface board of the PDP 8/e; circled numbers refer to Biomation 802 pins](image)
Figure 7—Control circuit diagram for the interface board of the PDP 8/e

Figure 8—Load and read circuit diagram for the interface board of the PDP 8/e
Figure 9—Gating circuit diagram for the interface board of the PDP 8/e described in Figures 2, 3 and 4 was implemented. We decided on a small software package for the PDP-8/e, as a large library of data evaluation programs had previously been developed and was available in FORTRAN on the CDC 6400 of Northwestern University's Vogelback Computing Center. All programs are written for interactive processing, originally for use by teletypewriters. A program on the disk of the CDC 6400 provides for transfer of data from the Hazeltine dual tape cassette onto the disk of the CDC 6400 via ordinary communication lines. The data are then thoroughly evaluated in several stages, as schematically shown in Figure 10. Further details on the evaluation of data are presented in two Appendices. Appendix I describes the sequence of computer programs for the evaluation of data derived from pH-jump experiments (compare Reference 8), in Appendix II a sequence of computer programs is described for the evaluation of data from chemical relaxation experiments on a full enzyme catalyzed reaction cycle (compare Reference 9).

DISCUSSION

As was mentioned in the Introduction, an alternate computer based data acquisition and reduction system for chemical relaxation experiments is available. In that case, considerable software was developed and is kept in 8k of core of the minicomputer for further data reduction. This method is quite feasible if punched paper tape is the only medium of permanent storage of data. As we have higher speed equipment available, we prefer to keep our data initially on dual tape cassettes, subsequently for on-line evaluation on disk (of the CDC 6400 in Evanston) and matrices of primary and secondary data on seven track IBM magnetic tape (at high density). IBM punched cards of these data matrices can also easily be produced. To facilitate identification of individual data sets, every set contains a header- and a trailer-card, containing system specific information. The software is designed such that data sets are easily sorted out and interpreted.

Although the described equipment serves mainly for rapid data acquisition, the operating program may be further expanded, and still a considerable amount of central core is available for programming. However, it is doubtful that any non-linear least squares analyses could be conducted within the PDP 8/e without the addition of a disk with support system. A current disadvantage is the slow transfer rate of the data into the large CDC 6400. An increase in the transmission rate to the CDC 6400 would be highly desirable. Nevertheless, the current configuration is of considerable advantage and should be of interest to others, utilizing transient recording equipment.

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REFERENCES

APPENDIX I

Sequence of Computer Programs for the Evaluation of Data from the Cytochrome c-System

BIOI is a program stored on the Digital Equipment Corporation minicomputer PDP 8/e-8k and provides for the transfer of data from the Biomation 802 transient recorder to the Hazeltine dual tape cassette unit. Data sections may be displayed on the Hazeltine 2000 cathode ray tube and a heading to each set of data may be added from the key board.

PRETRAN is a program stored on disc of the Control Data Corporation 6400 computer in Evanston and called to transfer data from the Hazeltine dual tape cassette unit onto disc. Except for the control cards to obtain this program, all other systems operations are invisible to the user and built into the program via executive calls. The user only submits the name of the file, which he needs later on for further evaluation. This program also contains a subroutine to assist the user with difficulties, which he might have in obtaining data from the various instruments.

TRANSI is a program stored on disc of the CDC 6400 computer and called to reduce the data matrix to a size which can be easily handled by subsequent programs. As at least five data points from the Biomation 802 transient recorder are interdependent, due to the electronic rise time of the analog input circuitry, a minimum of five points ought to be averaged. Generally, ten to twenty points are averaged initially and the number of points averaged generally increases along the increasing data sequence at the option of the user. At this point, it is up to the user to distribute the points of the new data matrix reasonably well around the estimated relaxation time constants. If more numbers are supplied from disc than can be placed into a data matrix of fifty pairs, the remaining points are eliminated (this may occur when comparatively fast relaxation processes have been recorded on the Biomation 802; this should be generally avoided.) The abscissa of the data pair is computed from the time deflection and the number of data averaged. The ordinate is the average value of the data used for averaging and an error is also computed from the deviation of individual data points from the average.

DATAOPe is a program to analyze the input data matrix of not more than 50 pairs with a non-linear least squares subroutine, utilizing the Marquardt method. A constant plus a sum of exponentials is generally assumed as underlying equation. For n = 1, the data may be evaluated assuming up to three exponential terms. The program with n = 2 is an abbreviated one, assuming only one exponential term and a constant. In most of our evaluations, we are able to utilize this abbreviated program. The program produces three parameters per data set together with a standard error per parameter. The parameter in the exponent is equivalent to an apparent rate constant (or better: the inverse of a chemical relaxation time) while the remaining two parameters correspond to signal amplitudes (or better: equilibrium signal changes). As many data matrices are processed by this program, a new data matrix is produced, containing these parameters as a function of analytical conditions.

CYTOC2 is a program to evaluate the factors in the exponents from the previous program as a function of pH, resulting in "true" rate parameters. This program utilizes a non-linear least squares analysis program and offers a variety of models for the interpretation of the data.

SEQUEN2 evaluates the signal amplitudes of the parameters obtained from DATAOPe and according to models which correspond to protonic dissociations of protein forms. For pH jump experiments, no further evaluations are needed. However, for chemical relaxation experiments the protein concentration is varied initially at fixed pH. Another program (POWERSE) is then used before the pH dependence of the apparent parameters is evaluated by CYTOC2 and SEQUEN2.

POWERSE is a program utilizing a linear least squares analysis of a data matrix and useful for a variety of intermediate calculations. Standard errors of the parameters are also produced. Although the program allows for the utilization of a power series as input function, we rarely find the need to analyze our data beyond linear terms (original functions are frequently rearranged to give a linear expression).

REFERENCES

APPENDIX II

Sequence of Computer Programs for the Evaluation of Data from Liver Alcohol Dehydrogenase Experiments

Operation of the first four programs (namely BI01, PRETRAN, TRANSOL and DATA0Pn) is identical to those, described in Appendix I. The algorithm of Marquardt\textsuperscript{1} is thus used in DATA0Pn. Output from DATA0Pn is picked up by the following programs.

LADHn is a program specifically designed for liver alcohol dehydrogenase, with various versions available. Currently n = 2 is in use and n = 3 is in development. This program is used to analyze only the exponential parameters as a function of the analytical concentration of the components and of pH. No inhibitor is present. Equilibrium concentrations are computed from analytical concentrations with a specially developed subroutine\textsuperscript{2} which solves the fourth order equation effectively by numerical means. Such a high order equation has to be solved, as the enzyme concentration is at least equal to or larger than the smallest dissociation constant and/or comparable with the analytical concentration of other components.

POWERSE is an auxiliary program used for least squares analysis of data which can be described by a power series\textsuperscript{3} (eventually after rearrangement). Generally, the power series is not extended beyond the linear term.

SEQUEN\textsubscript{n} with n = 3 or n = 5, representing different versions. This program was designed for the analysis of experiments with liver alcohol dehydrogenase in the presence of imidazole. At this point, only the exponential factor is utilized in this program. A special subroutine\textsuperscript{4} was developed, as in the absence of ethanol a cubic equation has to be solved to compute the equilibrium concentrations from the analytical concentrations. The subroutine computes these concentrations numerically in an effective manner. A variety of models are available to describe the experimental reciprocal relaxation times in terms of individual rate constants.

REFERENCES