A SET OF COMPUTER PROGRAMS FOR ELECTROPHYSIOLOGICAL ANALYSIS OF END PLATE CURRENT CHARACTERISTICS

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A system of programs will be demonstrated for the routine computer analysis of data obtained from voltage clamp experiments on the neuromuscular junction. The programs make use of a CED 502 (Cambridge Electronic Design) high performance analogue-digital converter interfaced, via a SILO temporary storage memory, to a PDP11/23 (Digital Equipment Corp.) computer with a 10 Mbyte Winchester disc. The 4 us A/D conversion time of the CED 502, its capacity to store digitised data temporarily in the SILO, coupled with the fast data writing rate of the Winchester disc allow continuous sampling at the rate of 25000 samples per second, up to the capacity of the disc. Results are presented on a cathode ray tube (CRT) display and on a daisywheel printer. Analysis is performed off-line, from signals stored on FM magnetic tape, to make the most economical use of the computer.

The programs are written in the FORTRAN language with time critical subroutines written in assembler language. The user operates all programs in a similar manner, by selecting options from a series of menus and sub-menus. Three programs will be shown:

i) An end plate current (EPC) collection and analysis program. Series of nerve-evoked EPCs or spontaneous MEPCs can be collected, averaged, and double exponential curves fitted to their decay phases using a non-linear least squares method. The program continuously samples the signal from the tape recorder, using a pulse from a hardware spike detector to signify the presence of an EPC or MEPC, which is then copied on to the disc. By this means, pre-trigger information on spontaneous MEPCs can be acquired. The signals stored on disc can be viewed on a CRT and included in, or rejected from, further stages of analysis.

ii) A current fluctuation analysis program. Steady state currents through ACh channels can be collected, power spectra calculated, and single and double Lorentzian curves fitted.

iii) A single channel current analysis program. Channel open/close fluctuations can be collected and analysed with varying degrees of automation. Open/close state dwell time histograms can be compiled and exponential curves fitted.

Supported by Organon Scientific Development Group, and the Unversity of Strathclyde Research and Development Fund.

ANALYSIS OF LIGAND BINDING DATA USING A MICROCOMPUTER

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Of the numerous methods which exist for the analysis of radioligand binding data, the most reliable have utilised a strictly analytical approach whereby the constants describing the binding reaction are determined using non-linear iterative curve fitting techniques (Munson & Rodbard, 1980). This approach, although highly effective, requires extensive computing facilities because of the size and complexity of the programmes and in consequence its use is restricted to those establishments with ready access to a desk top computer system.

Recently a method for the analysis of competition binding data using a graphical approach has been developed for use on a more readily available microcomputer system (Humrich & Richardson, 1983). Results obtained with this approach have been shown to be comparable to those obtained using more complex non-linear curve fitting techniques. In the present demonstration we report on a programme developed for use on the BBC microcomputer which utilises both graphical and analytical techniques in the analysis of competition data from binding studies.

The experimental data is initially entered using a prefitting programme which creates a disk-based data file. The analysis programme automatically accesses this data file and requests initial estimates of the binding parameters (eg total and non specific binding, number of sites, IC_{50} and % of specific binding for each site). Thereafter, the data are expressed in a log concentration-response format and the binding isotherm associated with the initial estimates superimposed on this plot.

Following this initial and all subsequent estimates of the binding parameters the residual sum of the squares associated with the fit are calculated to enable a crude test for "goodness of fit" to be made. The initial fit is improved by manually adjusting the binding parameters with the cursor controls and the binding isotherm redrawn. This procedure may be repeated until a satisfactory fit to the data has been achieved, at which point an iterative curve fitting section of the programme may be entered which utilises the best fit parameters achieved manually as initial estimates. Following the iterative fitting section the best fit parameters are graphically displayed with the experimental data. On completion of a session the parameters are stored on the data file and may be recalled instantaneously if further analysis of the data is required.

Results obtained using this system are in close agreement with those obtained when a more complex analytical approach is used (e.g LIGAND, Munson & Rodbard, 1980). The graphical fitting section of the programme represents a useful method for detecting deviations from a particular model and enables detection of incorrectly entered or spurious data points and prevents ill-conditioning when analysing data using the iterative curve fitting section of the programme.

A modified version of the programme in which data are analysed according to the Hill equation may be used in both ligand binding studies and for applications in which the observed response may be described in terms of the logistic function

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LESSONWRITER:- A SIMPLE AUTHORING SYSTEM FOR THE PRODUCTION OF COMPUTER ASSISTED INSTRUCTION LESSONS IN PHARMACOLOGY

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The rapid development of microcomputer technology, together with the decrease in capital cost of computer hardware, now means that most departments of pharmacology have access to a number of microcomputers for student use. In turn, these developments have resulted in many departments investigating the use of Computer Assisted Instruction (CAI) techniques in an attempt to cope with the rapidly increasing scope and complexity in the field of pharmacology (Doull and Walaszek, 1978; Pagliaro, 1981). However, the need to master high-level mainframe languages, or to spend time learning programing techniques for microcomputers tends to prevent academic staff and students from gaining the benefits to be obtained from CAI. Furthermore, the differences between high level languages, such as 'Tutor' makes the problem of software portability one of major importance.

Lessonwriter is a suite of programs, written in Commodore Basic 4.0 and running on a Commodore 4032 microcomputer with a 4040 disk drive, which enables non-computer individuals to create, edit and run CAI lessons using commands and data entry in English without the need to have detailed knowledge of computer programing techniques.

Lessonwriter is divided into two areas. The first program "Input" enables a CAI lesson to be created, edited and stored on floppy disk. The second program "Run" enables a student to select and run a CAI lesson.

When "Input" is run the user is presented with the options to either create a new lesson, or edit an existing one. If the user elects to create a new lesson they are presented with a series of input requests concerning the title and author(s) of the lesson. When these have been entered and verified a menu of 'frametypes' is presented, each one representing one particular method of presenting a screen of information. Selection of the required 'frametype' enables the author to enter data and/or question answer routines at the keyboard without recourse to problems concerning the layout of the screen. The program handles all text layout and enables the author to check input before committing it to store. When satisfactory, the frame data is stored on floppy disk as a sequential file. Similarly the 'edit' function enables an author to alter the information in any frame of a given CAI lesson and restore the new information on disk.

The use of "Run" enables the student to select a given CAI lesson from the disk. When the lesson is selected "Run" automatically takes the student through the lesson presenting the frame data in the correct order, handling the screen layout and receiving student responses.
The use of Lessonwriter enables authors to encode CAI lessons without prior knowledge of computer programing techniques and thus encourages the rapid accumulation of banks of CAI programs for student use. Furthermore the use of Basic in this package ensures that versions may be readily available to run on all microcomputers supporting sequential disk files.

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Pagliaro,L.A. (1981) Proc. West. Pharmacol. Soc., 24, 113-115.

PATIENT ANTHROPOMETRIC ASSESSMENT AND STORAGE UTILIZING A CHEAP MICROCOMPUTER SYSTEM

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An Apple II microcomputer, monitor, dual floppy disc and printer are programmed in Basic to analyse and assess a series of body measurements. The system makes the necessary calculations, prints out the records with comments, and files relevant information. The patient is supplied by the program with a reference number, and is further identified by name, address and date of birth. The examination date and time are provided from the computer clock.

A short history of the patient's occupation, social grouping, current physical activity, current medication, smoking habits, fat proportion, weight, blood pressure, psychical stress and family arterial disease are taken into account and the subject is graded in terms of potential coronary risk factors before testing work capacity. Finally, standing and sitting heights, forced expiratory volume in 1 second and forced vital capacity are recorded.

The measured fat proportion is calculated from formulae derived from Tables published in Durnin and Wormersley (1974):

Female fat% = $30.76 \log_{10}$ (4 skinfolds) + 0.24 age - 31.68

Male fat% = $30.76 \log_{10}$ (4 skinfolds) + 0.24 age - 39.14

The programme prints its analysis of the patient with some licence. For example, the coronary risk factor is weighted with regard to "excess" obesity, smoking habits and high blood pressure. Excess is an inaccurate term and the following "target" formulae provided the patient with comparative values from peer population studies (to be published):

Target weight

Female (kg) = 62 trunk height + 33 standing height - k_1

Male (kg) = 72 trunk height + 39 standing height - k_2

(k_1 for small, medium and large frame - 53, 49, 45 and k_2 - 69, 64, 59 respectively).

Target fat

Female (%) = 0.25 age + 14

Male (%) = 0.20 age + 10

Target FEV 1.0

Female (BTPS) = 3.49 standing height - 0.025 age - 1.93

Male (BTPS) = 5.07 standing height - 0.035 age - 3.42

Target FVC

Female (BTPS) = 4.22 standing height - 0.021 age - 2.68) (ht in m and age in yrs)

Male (BTPS) = 7.05 standing height - 0.026 age - 2.37)

Heights and weights are printed in imperial measure as well as S.I.U. and the Garrow (1979) ratio (wt/ht^2) is included for target comparisions. Target values are "best guesses" but nevertheless offer useful guides to individuals belonging to normal adult populations (Barr & Thompson, 1978). An individuals anthropometry must still be judged within the bounds of his individual characteristics.

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