EDUCATION

SESSION

AN INTRODUCTION TO MICROCOMPUTING IN PHARMACOLOGY

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The digital microcomputer represents a powerful, but flexible, tool for laboratory based data manipulation and simulation in pharmacology teaching. However, efficient use of these machines requires a basic understanding of the principles of operation, data storage and programming to enable the user to appreciate the potential, and limitations, of the system. Microcomputing encompasses a large and confusing range of terms relating to the internal structure, and operation of the machine. An attempt will be made to outline the main principles of microcomputer operation, commencing with the central microprocessor unit, and gradually building up the internal and external structure of the unit, so that the use and action of each component is fully explained. A brief survey of data storage systems will be presented, together with an appraisal of the relative advantages and disadvantages of each system.

Finally, a review of the major programming language BASIC will be presented so that the potential user will be able to appreciate the ease with which initial steps in microcomputing may be undertaken.

A glossary of major terms will be provided, together with a series of demonstrations of microcomputer usage.

MEASUREMENT AND ANALYSIS OF TISSUE RESPONSES USING MICROCOMPUTERS

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A wide range of powerful analyses can be carried out when response data from pharmacological experiments are collected and stored using microcomputer techniques. Such numeric data are easily analysed by simple arithmetic techniques and, if necessary, can be reanalysed in a different way without any need for further measurements.

The analogue electrical signals produced by the transducers monitoring the pharmacological response must be digitised before they can be stored in a microcomputer. The continuous analogue singal is sampled at regular intervals to produce a series of binary numbers each of which represents the magnitude of the analogue signal at the instant of sampling. This process is carried out by an analogue to digital converter (ADC). All but the most recent microcomputers work with 8 digit (bit) binary numbers and so it is easiest to interface them with ADC's which produce 8 digit binary numbers. The number of bits to which the ADC digitises governs the resolution of the conversion process. Thus the voltage range across which an 8 bit ADC operates can be divided into 256 steps. Ten, 12 or 16 bit ADC's are available if greater resolution is necessary but are more difficult to interface to the microcomputer. The choice of sampling rate is determined by the application thus a rate of 1 Hz might be suitable for monitoring a slowly changing parameter such as temperature while 1 KHz would be necessary for skeletal muscle twitches. As a rough guide the sampling frequency should be at least twice that of the highest frequency component in the input signal. If the signal is contaminated with high frequency noise it should be low pass filtered before submission to the ADC to avoid the need for very high sampling rates.

The ADC is usually in a separate unit from the microcomputer and contains its own power supplies. The connections between this interface unit and the microcomputer are optically isolated to prevent any high voltages accidentally fed to ADC damaging the computer. To allow the computer to initiate external events such as electrical stimulation, output lines are often routed through the interface unit.

A program in the microcomputer supervises the collection of the digital data from the interface unit and interacts with the user to allow him to control the progress of the experiment. The bulk of this program is usually written in BASIC, however, BASIC does not execute quickly enough to collect data from the ADC at sampling frequencies greater than 1 Hz and so the portion of the program directly involved in the collection of data from the ADC must be written in assembly language. The digital data are collected into the computer's memory from where they are written to a floppy disk for permanent storage. The data stored on the floppy disk can be recovered easily into the computer memory where they can be analysed by other programs. The analysis programs are usually written in BASIC.

These aspects will be discussed in relation to the development of a microcomputer technique for the analysis of the effects of drugs on the responses of the rat vas deferens to electrical field stimulation (Marshall & Sparks, 1981).

Marshall, R.W. & Sparks, M. (1981). Br. J. Pharmac. 74, 988P.

A COMPUTER-CONTROLLED SELF-TEACHING AND SELF-ASSESSMENT SYSTEM BASED ON MULTIPLE CHOICE QUESTIONS

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"I thought I knew it until I saw those MCQ questions". This comment, made by a Pharmacology student at the end of the first year examinations, prompted the development of a system which allows students access to our bank of multiple choice questions (MCQs) in Pharmacology for the purpose of self-assessment and self-teaching.

The system is written in BASIC and utilises a 64k Northstar Horizon microcomputer with assosicated VDU and teletype printer and is located in the main teaching laboratory. Some 1200 MCQs are stored on 3 floppy discs and are grouped into 17 topics:- biotransformation; absorption, distribution and excretion of drugs; cholinergic and noradrenergic systems; antidepressants; major and minor tranquilisers; sedatives, hypnotics and antiepileptics; local and general anaesthetics; pharmacological chemistry; cardiovascular; receptors; chemotherapy; autacoids; analgesics; interactions. On initiating the system a student states his course (medicine, dentistry or science) together with the subject on which he wishes to be questioned and the degree of difficulty required (easy, normal or hard). A suitable question is then selected at random from the question bank and is displayed on the screen.

Each question consists of a stem and 5 alternative completions each of which must be answered true (T), false (F) or don't know (K). When all 5 responses have been entered the correct answers are displayed together with a reference to a standard text-book for each incorrect answer given by the student. For most subjects the student may then ask for 'help' which will provide an explanation of the answers together with the original question. Another question is then presented as required. When the student finishes, an overall score is given (+1 for correct; -0.5 for each incorrect answer given) with comments appropriate to the mark obtained. The system is popular with the students and is used extensively throughout the year. Between January 1981 and June 1981 the system presented 20,592 questions and was used on 1387 separate occasions.

The same computer system also provides a simulated guinea-pig ileum programme which allows the 'addition' of agonists in the presence or absence of antagonists to a 'guinea-pig ileum' and presents a trace of the 'response' produced. A wide range of agonists and antagonists can be used at any concentration. If a student's practical work fails to provide suitable data an experiment can thus be simulated and a usable trace obtained.

Because of overcrowding on the single access terminal it has become necessary to mount the system on the University mainframe computer which can be accessed through the multiuser terminal network.

I would like to express my thanks to the Yapp Education and Research Trust and to the Nuffield Foundation for financial assistance.

MICROCOMPUTERS IN BEHAVIOURAL RESEARCH

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The use of microcomputers in behavioural research has been encouraged by recent reductions in cost, the development of suitable interfaces for existing equipment, and of user oriented high level languages - such as Acorn Computers' OnliBasic (Fray, 1980). In contrast to the high degree of computing skill demanded by earlier machines, modern systems are easy to use, requiring little knowledge of computing and have made computer controlled experimentation a reality for a number of laboratories. Microcomputer systems such as Apple, Pet, and Acorn, offer sufficient flexibility to simultaneously run several independent experiments, are able to store the data generated over extended periods of time, and are limited only by the number of Input/Output lines available and nominal speed/space restrictions.

The interpretation of data from such commonly used paradigms as rotation and locomotor behaviour can be immediately improved by recording the observed responses over successive time intervals. Drugs producing superficially similar results using conventional counters may yield completely different behavioural profiles when detailed studies of the time courses involved are analysed: similar scores could be achieved by differing effects on onset time, intensity and duration of responding. As a further example counts recorded from different photocells within a single test-chamber can be dissociated to reveal where and when activity occurred, whether it was confined to one section of the chamber (cf stereotypy), or more evenly distibuted as locomotor behaviour per se.

The computer can provide excellent digital or analogue control of experiments. Complex experiments involving multiple contingencies and responses, such as recognition memory, can be readily programmed and the rate of presentation, complexity etc. of the stimuli varied according to the subjects trial by trial performance. Such control is either difficult or impossible using conventional equipment. The computer is of particular value to those clinical studies requiring accurately drawn and controlled visual stimuli - for example in vigilance and sensorimotor tasks used to assess drug effects on cognitive mechanisms. The ability to generate and display moving or stationary figures of varying complexity on a monitor will be of critical importance to future research of this nature. In addition to the oppotunities for the instantaneous presentation of results, disc storage of data provides an opportunity for subsequent overall statistical analysis and/or graphical representations.

In conclusion, the computer is proving itself a valuable experimental tool with on-line control providing an elegant and occasionally unique method of studying behavioural phenomenom.

Fray, P.J. (1980) Trends Neurosci. 3 (12), XII - XIV

A MICROCOMPUTER SYSTEM FOR THE COLLECTION AND ANALYSIS OF DATA FROM BODY TEMPERATURE EXPERIMENTS

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A scanning tele-thermometer based on a microprocessor and interfaced with a microcomputer has been developed for the collection and analysis of body temperature data from experimental subjects. The thermometer has, in addition to and independent of the microcomputer, a light emitting diode (LED) display of the current sample (thermistor number and °C) and an analogue output to a chart recorder (Rikadenki B-34).

Analogue signals from up to 16 thermistors enter a multiplexer sampled by an 8-bit analogue to digital converter with an automatic adjustable offset, giving a resolution of 0.08°C over the range 0-50°C. Programs for either manual or automatic sampling (10s, 1 min or 6 min/input) of thermistor inputs are selected by operating manual keyswitches. Sampling programs are machine coded in a 2K read-only memory which can be erased and reprogrammed (EPROM, Acorn Computers). The EPROM is carried on a printed circuit board which also holds a 6502 microprocessor, a 1K random access memory and two peripheral interface adapters. One interface controls the keyswitches and the LED, the second provides control lines and an output port to the microcomputer (a Commodore PET 2001 with 8K of memory). Thermistor identification and temperature data are passed to the microcomputer as 8-bit binary numbers during thermistor change over.

The microcomputer is progammed in BASIC to display the data from the thermometer as °C on its visual display unit (VDU) together with the time of input from an internal clock. The BASIC instructions POKE and PEEK are used to store data in, and then examine and display the contents of screen memory locations (Dunn & Morgan, 1981). The screen display of data is thus updated continually and shows the identity of the input sampled last with the time this sample was gathered, and the last six temperature samples from all thermistors. An event marker, together with the time of marking, can be entered into the data collected and displayed for a specified input by the use of the microcomputer keyboard. The collected data in the computer memory is written to a cassette tape for storage. A record of the total number of samples written to the tape is shown on the VDU.

Data stored on tape can be retrieved for display on the VDU or for analysis on the same microcomputer using a BASIC program. The control temperature for a specified thermistor input is taken as being the mean of the samples collected before the occurrence of the event marker, which is now set at time zero for the data in that memory. Changes in temperature from the control value (Δ°C) are displayed on the VDU together with an index of this change (temperature response index, Δ°C x min) determined by trapezoidal approximation and the sample time (min) relative to the event marker. The maximum and minimum Δ°C and their incidence times are also presented. Each sample is indexed and can be removed, if necessary, from the analysis.

We thank Dr. R.W. Foster for his assistance in writing the analysis program.

Dunn, S. & Morgan, V. (1981). The PET Personal Computer for Beginners (Prentice-Hall: London).

AN APPLE MICROCOMPUTER CONTROLLED DATA LOGGING SYSTEM FOR pH AND OXYGEN MICROELECTRODES

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Microelectrodes are being used to record changes in oxygen tension and pH in the micro environments around marine fouling invertebrates. In these studies the recording of results and control of experiments is carried out by an Apple microcomputer.

Four pH electrodes and one oxygen electrode were previously used, each being buffered using an appropriate amplifier and its output connected to a pen recorder.

In the computer controlled system reported here, absolute records are obtained by the use of a digital voltmeter (DVM), which is connected to the computer via a general purpose interface bus (GPIB). This enables the computer to directly record the DVM reading. In order that the DVM can take readings from each of the five electrodes a multiplexer is connected between the DVM and the outputs of the electrode buffer amplifiers. The multiplexer is controlled directly from the computer via an interface card (6522). The electrode voltages are switched by reed relays which have been selected for their low thermal drift.

The data is stored in two ways: (i) onto floppy discs and (ii) printed out directly onto an Epson MX100 printer. The Apple microcomputer is fitted with a clock card to enable sampling of the electrodes to be carried out in real time. This card is used to set the sampling interval. During experiments the Apple system is programmed to sample each electrode every thirty seconds, print the time and each voltmeter reading and then store the uncalibrated data as a series of string variables. A calibration program provided hard copy output via the printer. In this system the maximum sampling speed is one sample every four seconds.

The use of this system enables more frequent and accurate data acquisition. The advantages of this system are convenience of data storage on discs and readily available calibrated data shortly after the end of the experiments. This system is currently in use, utilises readily available hardware cards and is easily programmable for various electrode combinations. Although pO_2 and pH changes are recorded with the system described, it can be adapted to record from other ion sensitive microelectrodes. Figure 1 illustrates the system.

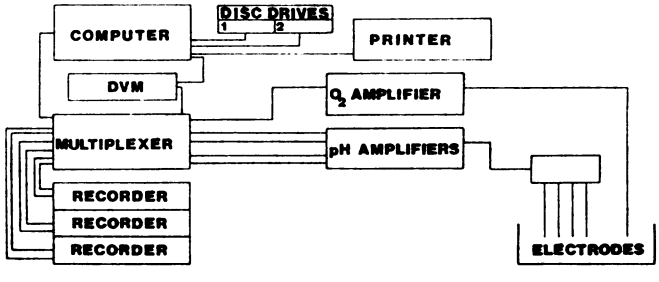

Figure 1 Apple controlled data logging system

USING A STUDENT ANSWER MACHINE (SAM) AND MULTIPLE CHOICE QUESTIONS TO DETECT LEARNING AND TEACHING PROBLEMS

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A lecture theatre has been equipped with an apparatus similar to that described by Garbutt & Laws (1977) with switches allowing up to 100 students each to register a response in the form True, False or Don't Know to Multiple Choice Questions (MCQs) displayed on a screen. Each switch is connected to an electronic console which has a digital display indicating the number of students participating and the percentage making each type of response to a particular MCQ option. The equipment is collectively called a Student Answer Machine (SAM).

We use MCQs of the determinate response type each with 5 options, any number of which may be true or false. The options are shown one at a time, and the students indicate their choice of response by operating the appropriate switch. Between 5 to 15 seconds is usually sufficient for over 95% of students to respond. The percentage number of students making each type of response is noted down from the reading on the console. We have found that 8 or 10 MCQs is a suitable number for a teaching session lasting about 30 minutes. After such a session a printed sheet with the questions and correct answers is distributed. Each question is then reviewed, and any options which did not achieve a correct response from 70% of students is considered to have created a problem, and some explanation is offered. A discussion frequently ensues at this stage, as a result of which a learning difficulty may be revealed. Commonly identified problems include unfamiliarity with drug names, inattention to material presented in practical classes and occasionally inadvertent omission of formal instruction on a particular topic by a teacher.

SAM sessions are now a regular part of the preclinical pharmacology course, and performance in MCQ components of formal examinations has improved over the three years during which the system has been in use.

Garbutt, P. & Laws, C.M. (1977) A low-cost electronic teaching aid. Br.J. Pharmac., 59, 524-525P

QUANTITATIVE RADIO-CHROMATOGRAM SCANNING

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The traditional method of quantifying levels of radioactivity on a thin layer chromatography (t.l.c.) plate is to locate it by autoradiography etc., elute the regions of interest and estimate levels by liquid scintillation counting. This is time-consuming, costly and destroys the sample. A high performance liquid chromatograph (h.p.l.c.) with autosampler, and a radioactivity flow detector is an alternative but for simplicity, high sample throughput and low running costs direct t.l.c. quantation is the better option. Integrators may be used in conjunction with t.l.c. radioscanners but subsequent data handling is very limited.

We have chosen to interface two instruments with PET computers, disk drives and printers. One instrument employs a proportional gas flow detector which scans a t.l.c. plate at selectable speeds and detects the radioactivity through a small slit. The more recently acquired instrument is an automatic linear analyser which has a large inlet diaphragm. This enables simultaneous examination of the full width of a 20x20 cm t.l.c. plate with resolution 0.2 mm. Quantitative raw data from both instruments are stored on disk and a normalised chromatogram automatically printed out. Peak search routines enable the level of radioactivity in any component (comprising 1-2 becquerels ^{14}C) to be automatically expressed as total counts or as a percentage of the total radioactivity on the plate.

A separate data processing station, comprising PET, disk drive and printer, allows users to re-evluate raw data in any way.

DATA HANDLING FOR SUPERFUSED BRAIN SLICE EXPERIMENTS

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The use of superfusion experiments to study the effects of drugs upon spontaneous or induced release of neurotransmitters from brain slices pre-loaded with radioactively-labelled neurotransmitter is well established. Such experiments produce large quantities of data which require arithmetic or mathematical manipulations. These are frequently subjected to error when calculated manually. A program has been developed for use with the Hewlett-Packard HP-85 microcomputer (but easily adaptable to other machines) with the following aims:
1) To accept the raw data, with facilities for correcting errors in terms of counts per minute per aliquot of superfusate.
2) To correct for variations in counting efficiency of the samples by the liquid scintillation counter using pre-determined quench correction curves.
3) To express the release of neurotransmitter in a convenient way i.e. fractional release per minute, such that the effects of drugs upon either spontaneous or evoked release can be assessed.
4) To tabulate and print the results in a clear format.
5) To plot the results graphically (using an external plotter).
6) To store the raw data and calculated results upon tape cassette in a standard, easily accessible format.

A further program has been produced which can:
1) Retrieve, from the tape cassette, the results from groups of experiments.
2) Analyse the results using simple statistical tests i.e. mean, standard deviation and standard error of the mean.
3) Tabulate the grouped results.
4) Plot graphically the results in terms of mean ± S.E.M..
5) Store the analysed results upon tape cassette.

The storage of data in a standard format enables subsequent programs to be devised without unnecessary recourse to the original data. The use of such programs enables large quantities of data to be handled both quickly and accurately and for the results to be both tabulated and expressed pictorially.

MICROCOMPUTER-CONTROLLED AUTOMATIC BEHAVIOURAL MONITORING

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A system has been designed to monitor automatically two aspects of behaviour, gross locomotor activity and rearing activity, for prolonged periods in groups of free-living rats housed in self-contained inhalation chambers. The accumulation of data and its print-out at pre-determined time intervals is controlled by a Commodore PET 8K microcomputer.

Inhalation chambers, modified from Littleton and Umney (1977) have been used to administer nicotine chronically by aerosol to groups of rats in an effort to detect behavioural changes. Both nicotine-treated test and untreated control groups are assessed concurrently. Locomotor activity is measured using LKB-Farad Animex Type S activity meters: the capacity of a resonance circuit tuned to an oscillator is altered by movement of the rats across the cage floor. If this change is sufficiently large to pass the threshold of a schmitt-trigger, a count is registered. Rearing activity is measured using a series of light beams and detectors arranged at a pre-set height along opposite sides of the cage. Interruption of the light beams is registered by a small electric pulse. Digital pulses thus generated pass to individual accumulators set up in the PET by the computer program. A total of four accumulators (locomotor and rearing activity for both test and control groups) are monitored simultaneously. The number of counts (a numerical assessment of activity) within each accumulator is displayed continuously on the screen together with a clock which may be pre-set either to real time or system elapsed time. The displayed information is updated from the accumulators every second. At regular, pre-programmed time intervals, hard copies of the displayed information together with the clock time are printed. The accumulators are subsequently reset to zero and the cycle repeated.

The system has demonstrated its reliability in experiments of up to five weeks duration, with activity being monitored for 24 hours daily. Further development should enable the system to control additionally the automatic switching on and off of the aerosol generators.

Littleton, J.M. & Umney, N.C. (1977) J. Physiol. (Lond) 266, 11P-12P.

MICROCOMPUTER SIMULATION OF ISOLATED TISSUE PREPARATIONS

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Although microcomputer technology is now making inroads into pharmacology the practical teaching applications have been limited. This demonstration shows the simulation of standard in vitro pharmacological experiments for the purposes of undergraduate teaching and teaching reinforcement. The system uses a Commodore CBM 8032 microcomputer feeding generated data, via a multiplexed digital to analogue output module (Biodata), to a Washington chart recorder.

The program presented for this demonstration shows the simulation of contractions of frog rectus abdominis muscle and guinea pig ileum and allows the "addition", via the computer keyboard, of appropriate agonists and antagonists. The program generates output data which is sigmoidally related to input data and thus allows the production of typical dose response curves on a chart recorder. The appropriate dissociation constants for the agonists and affinity constants (K_B) for the antagonists are incorporated in the program. Thus responses generated in the presence of antagonist are suitably reduced, according to the Gaddum-Schild equation. After obtaining responses to doses of agonist in the absence and presence of antagonist, the student should, by measurement and calculation, be able to determine the appropriate parameters, i.e. K_B and pA_2 for the antagonist used. Should the student select an inappropriate agonist/antagonist combination, the program will give the option of reselecting the antagonist or of proceeding, as K_B and pA_2 are calculable for any agonist/antagonist combination.

At run time the computer delivers a menu giving a number of options concerning tissue, agonist, antagonist, etc, from which the student makes his choice. The program then issues prompts on the VDU requesting concentrations for the selected agonist and, on the basis of information given, outputs the calculated response to the chart recorder in a form which mimics the shape and time course of a response to the agonist. When the response reaches a predetermined percentage of the theoretical maximum response, another prompt is issued asking for antagonist and its concentration. The "addition" of agonist is then again requested. After the completion of each dose response curve in the presence of antagonist, options are presented either to restart/terminate the program or to proceed to a graphics routine. This displays the data entered previously in the form of appropriately scaled dose response curves.

The system can thus be used for undergraduate group teaching or for individual teaching reinforcement as students can revise experiments previously performed in the laboratory, either originally by computer or on animal tissues. A suite of programs is presently under development encompassing a wide range of undergraduate teaching experiments, e.g. the effects of drugs on haemodynamic and respiratory function, heart rate and their relative physiological reflex interactions in the cat. Examples such as this, as well as providing increased versatility, could lead to a considerable financial saving in animal costs in courses using such preparations, and also could go some way towards reducing the number of animals used in undergraduate teaching. This technique has several obvious advantages over the use of animal tissue, in that mistakes, e.g. massive overdosage, can be immediately rectified without damage to the "preparation"; experiments can be repeated as often as required; programs can be run in accelerated mode to reduce experimental time. These and other factors constitute an improvement in teaching methods which must be considered in the use of microcomputers in pharmacology.

SIMULATION OF ISOLATED ORGAN EXPERIMENTS USING A MICROCOMPUTER

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A simulation of the isolated guinea-pig ileum preparation has been developed using a Commodore 4032 microcomputer with associated disk drive (4040) and matrix printer (3032). The simulation allows undergraduate students to investigate the effect of various agonists and antagonists on the preparation model, and to generate representative data for further analysis.

The model is based upon the relationship between agonist concentration (D) and percentage maximum response (y) given by the equation:-

$$y = \frac{\alpha[D]}{[D]+K_D} * 100$$

Information representing the agonist doses is stored in the program, and the appropriate values for intrinsic activity (α) and the dissociation constant (K_D) are obtained from the program when the agonist is chosen by the student. When the program is run an agonist dose is read, converted to $\mu mol.l^{-1}$, and then substituted into the equation. The resulting value for the percentage maximum contraction is then "randomised" to simulate a degree of biological variation. The modified value is then used to generate a simulated contraction which may be either written to the screen, or printed out as hard copy. The program then loops back to read the next agonist dose, generating a complete concentration-response curve.

When the program is completed the student is given the choice of repeating the curve to generate another set of data or of selecting an antagonist. On selection of an antagonist, the program loops through a routine to include a simulation of the effect of that antagonist. Using the pA_2 value of the antagonist and the slope of the Schild plot (presumed to be unity) an appropriate dose ratio is calculated for a given antagonist concentration. This value is then used to modify the agonist concentration before calculation of the response.

Using the model described the student may rapidly investigate drug-receptor interactions and study the effects of varying parameters such as the intrinsic activity of agonists and the pA_2 of antagonists. Data is generated rapidly and each student is provided with hard copy of their experiment.

MICROCOMPUTER AIDED COLLECTION AND ANALYSIS OF DATA FROM TISSSUE BATH EXPERIMENTS

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A microcomputer system to aid the collection and analysis of response data from tissue bath experiments will be demonstrated. The system is based on a CBM 3032 microcomputer with 32K of memory and 400K double density compthink floppy disk drives (Marshall & Sparks, 1981).

Response data in the form of analogue electrical signals from upto four strain guages is digitised to 8-bit resolution at a sampling rate of 50 Hz by an interface unit. The interface unit is designed to accept the output from the conditioning preamplifiers of a standard chart recorder (Devices, Ormed). Two output lines are also routed through the interface unit to allow the computer to initiate periods of electrical stimulation.

The microcomputer collects data from the control of the program written partly in BASIC and partly in machine code. The program divides the four transducers and their associated tissue baths into two "stations" each comprising two transducers. Either station can function independently of the other, allowing two independent workers to use the system simultaneously. Choices are offered in the form of a menu to allow the operator(s) to determine such parameters as, the interval between periods of data collection, whether electrical stimulation should be initiated and whether the data collected should be stored on floppy disk. The actual data collection is carried out by a machine code subroutine. During data collection the input from each transducer is displayed on the VDU. The binary data collected from each transducer is stored as single bytes in specific areas of computer memory. On completion of a period of data collection control is returned to the BASIC part of the program which then supervises the transfer of the data to floppy disk. The internal clock of the computer is used to time the interval between periods of stimulation. During these intervals the various parameters can be changed (without stopping the program) and the last set of data can be displayed in graphical form on the VDU. The data from each period of stimulation is transferred to floppy disk immediately after collection, so in the event of an equipment failure only the current data is lost. Prior to analysis the data from many experiments (upto 3800 sets of data) is compressed and stored as records in a large random access file. Storage in this form allows comparison of responses from different experiments.

A suite of BASIC programs has been developed to analyse the data collected. For example, one program scales responses from several experiments into grams and combines them to produce a mean response which can be plotted on a printer in either numeric or graphical form. The mean responses from several sets of data can be calculated and plotted simultaneously to allow comparison of various treatments. Other programs calculate and display the mean differences between several sets of paired responses.

Marshall, R.W. & Sparks, M. (1981). Br. J. Pharmac. 74, 988P.

MICROCOMPUTER CONTROL OF EXPERIMENTS ON ISOLATED TISSUES

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A videotape will be used to illustrate how a microcomputer can be employed to control experiments on isolated tissues and to analyse the results during the experiments. The system illustrated utilises stepper-driven and pneumatically-driven syringes to inject small volumes of drug solutions into the organ bath. The microcomputer-controlled system relieves the experimenter of tedious repetitive tasks but more importantly produces a great improvement in the quality and quantity of information which can be obtained from each experiment.

AUTOMATIC BIO-ASSAY CONTROLLER FOR IN VITRO SMOOTH MUSCLE PREPARATIONS

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The bio-assay controller is built using a modular technique incorporating eurocard size printed circuit boards which plug into a common backboard. The LSI microprocessor (National SC/MP) is used, under software control to implement various operations and timing set up by the operator. The software is contained within an EPROM (eraseable, programmable, read only memory) chip, and may be altered for different applications. The bio-assay unit is coupled to tube squeezers which allow the automatic introduction of drugs or physiological fluids on a regular basis to various smooth muscle preparation. The time cycle and drug contact time is variable and up to two rest periods can be incorporated into any time cycle to suit the requirements of the different preparations. A facility is also included which allows either the automatic or manual application of drug; in the manual mode there is an audible signal for drug application. These units are ideally suited for bioassay and PA_2 studies in a wide range of smooth muscle preparations.

A COMPUTER-BASED APPROACH TO ANALYSIS OF CARDIAC FUNCTION

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A system has been devised to record and analyse analogue data obtained from an isolated working heart preparation and, in conjunction with additional data entered by the operator, to calculate a number of parameters relating to cardiac function.

The hardware consists of a 32K Apple II + microcomputer containing an Apple communication interface card, Apple analogue to digital conversion card (16 channel, 0-5V, 8 bits), Mountain Hardware Inc. clock card and Apple disk drive card. Additional equipment includes 2 Apple floppy disk drives and a Hitachi 9" video monitor. The mini-computer is a DEC PDP 11/60 running RSTS/E version 6C to 7.0.

Left ventricular pressure is recorded from the isolated working heart via a short fluid-filled cannula connected to a pressure transducer and Devices chart recorder. The Apple II data system uses machine code programmes to record 5 secs of this analogue data at 1KHz via the Devices pre-amplifier and display it graphically to allow the operator to inspect the recorded data. An Applesoft programme records additional data including aortic flow, coronary flow and other experimental details and stores the information on floppy disk. Data are then processed to give heart rate, peak left ventricular pressure, maximum rate of rise of left ventricular pressure, ejection time, mean systolic pressure and pressure-time integral. These data are stored as an output file on floppy disk. The Apple is then connected via a RS232 line to the PDP and the output file transmitted and stored. The raw data are kept on Apple floppy disk until a group of hearts has been completed and the processed results checked. The operator adds wet and dry heart weights when available and further processing of weight related parameters is then performed using the PDP. Parameters calculated include aortic flow, coronary flow, cardiac output, external pressure-volume work, kinetic work and total external work. The processed data are stored on the PDP. The operator can recall data and tabulate them together with the mean, standard deviation and standard error of the mean for each parameter.

This system provides the user with the flexibility of dedicated data collection whilst having the wider capabilities of data management and tabulation of a mini-computer.

We would like to acknowledge contributions to development by:
J.G. Bartlett, I. Brooks and P.F. Davies.

AN AUTOMATIC, MICROPROCESSOR CONTROLLED METHOD FOR THE DETERMINATION OF THE REFRACTORY PERIOD OF THE GUINEA-PIG ATRIUM

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The introduction of microprocessors has enabled apparatus to be constructed which will perform complex tasks which were either impossible, required a high level of skill and attention or used apparatus not widely available (Geivers et al, 1972). One such example is the use of a microprocessor controlled stimulator for the automatic determination of the refractory period (Stimulator IR, Hugo Sachs Elektronik, Freiburg, West Germany).

The basic principle of the equipment is as follows: An isolated left atrium is stimulated using suprathreshold stimuli at a set frequency (eg 1Hz). After a predetermined period of standard, single pulse stimulation, a second pulse of an identical width & voltage is applied to the preparation (initially well inside the refractory period) & on successive 'double pulsing' the time interval between the basic frequency & the second pulse is extended by a fixed interval of, for example, 2 ms. Eventually a time interval is reached when the second pulse falls outside the refractory period & an enhanced response is seen. If this enhancement is a fixed percentage above the control level, a double check is made, the time interval between the two pulses determined by the microprocessor & passed to a printer for a permanent record. The basic frequency is then readopted until the predetermined interval is completed after which 'double pulsing' for another refractory period measurement is commenced. All parameters are preset by the experimenter on the IR Stimulator which can control and measure 4 tissues simultaneously.

The use of such a microprocessor controlled device will be demonstrated.

Geivers, H. Van Nueten, J.M. & Schaper, W. (1972) Med. & biol. Engng., 10, 193-199.

PROGRAM FOR ADJUSTMENT OF AMINOGLYCOSIDE DOSAGE

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Microcomputers are being introduced into the diagnostic laboratories of clinical microbiologists. A drug dosage program has been developed which is compatible with PET or APPLE equipment. This helps the microbiologist to predict an individualised dosage schedule when recommending the administration of an aminoglycoside antibiotic to a particular patient. As with earlier programs developed in this department (Mawer, 1976) the daily dosage rate is scaled to creatinine clearance, which is either known or predicted from age, sex, body weight and serum creatinine concentration.

Mawer, G.E. (1976) Clinical Pharmacokinetics, 1, 67-78.

MICROCOMPUTER-BASED COMPUTING INTEGRATOR FOR ANALYSIS OF CHROMATOGRAPHIC PEAKS

M.C. Elphick (introduced by D.R. Tomlinson), Digital Measurement & Analysis Ltd., 906 Woodborough Rd., Nottingham, NG3 5QR

The microcomputer is being used in an increasing number of applications in the laboratory. The low cost of these computers together with the availablity of equally inexpensive interface units makes for the development of some powerful yet cost-effective data acquisition and control systems. One limiting factor in their use is the development of suitable operating software; this is often very costly in terms of time spent by the programmer. Moreover, there is a good deal of duplicated work between one establishment and another in solving the same problems. However, as time goes by, more commercial microcomputer-based systems are becoming available to perform standard laboratory procedures. The system described here is just one of these, and was developed in order to give the chromatographer a software/hardware integration system around which his/her own more specific BASIC programmes could be written.

The system consists of a CBM* computer (model 4032), an analogue to digital convertor (A/D) with a front-end programmably attenuated amplifier, and operating software held on a read only memory integrated circuit (ROM). The A/D samples the output of the chromatograph and converts the signal, with 12-bit resolution (plus one bit polarity), for input into the computer via the IEEE port.

The software is written entirely in machine code, thus enabling integration to be performed in real-time and at high sampling rates (up to 15 area slices per sec.). The integration routine is called from a BASIC programme and returns with peak heights, areas and area allocation codes left in variable arrays. These can then be used directly for further calculations.

The 4-K of machine code operates the A/D on 'auto-attenuation' giving very large dynamic range. Eight parameters are required by the integrator. These allow the integration routines to deal with a variety of conditions. For example there is a software filter for noisy signals, an offset, a threashold parameter, spike rejection and programmable sampling rates as well as timed parameters such as start and stop of integration.

Baseline correction is achieved with four time-programmable baseline tracking modes. These can be switched into operation at any time during and on up to eight different occasions during a run.

The obvious advantage of this system over that of a conventional integrator lies in the power and simplicity of BASIC, first for setting up the integration parameters, but most of all for processing the raw data once integration has finished. Compounds can be indentified, detector response factors applied and finally the compounds can be quantified with reference to a standard and dilution factors. The final results can then be printed or saved on disk for later statistical analysis.

The most important feature of the system, however, lies in its precise and accurate integration routines. Results compare very favourably with conventional integrators.

* Trade Mark of Commodore Business Machines.

USING A CHEAP MICROCOMPUTER FOR STUDENT SELF-ASSESSMENT WITH FEEDBACK

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On the basis of our experience using equipment collectively called a Student Answering Machine (SAM) installed in a lecture theatre, as described by D'Mello & Kruk (this meeting), we were convinced that Multiple Choice Questions (MCQs) could be valuable for teaching pharmacology. In order to use SAM a specific lecture theatre must be booked for a large number of students with staff in attendance. As an alternative, we decided to investigate the use of a micro-computer to administer, mark and offer feedback on a set of MCQs on defined topics so that students could use this teaching facility in their own time. The apparatus is the Sinclair ZX81 with 16 K RAM, the cheapest micro-computer available. A television and a cassette tape recorder are also needed.

The program is written in Basic, and either a listing with full description, or a master cassette with loading instruction is available from us at the above address.

The program will administer up to 8 MCQs and it would be easy to alter it to allow marking schemes other than the determinate response type which is most commonly used (i.e. a reply is required to each option and any number of these is true or false). The student enters his responses on the keyboard, and when a question is completed his answer and the correct responses are displayed. At this stage the student can request some feedback on options which he did not attempt or which were answered incorrectly. The question, options, the correct responses and the student's responses are then displayed, as well as some explanatory text.

We have found that 8 to 10 MCQs on a particular topic result in a session lasting 20 to 30 minutes. At the end of the questions a score is given, together with a display of the number of options answered correctly, incorrectly or not attempted.

The program will be demonstrated during the meeting.

D'Mello, A. & Kruk, Z.L. (1982) This meeting