A LOW COST, BBC MICROCOMPUTER-BASED SYSTEM FOR RECORDING THE ELECTROCARDIOGRAM

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The recording of the electrocardiogram (ECG) is a common component of undergraduate practical courses in biological sciences. The equipment traditionally used to record the ECG is often expensive and has limited versatility. Here we describe a system which allows students to record and analyse their own ECG's which is low in cost and makes use of the BBC microcomputer, a machine with a variety of other applications. This system complements a computer assisted learning program, featuring simulated ECG records, previously described (Brown & Dewhurst, 1988).

The hardware features a differential amplifier with good common mode rejection ratio (C.M.R.R.) receiving signals from two high impedance pre-amplifiers and incorporates opto-isolation. The output is filtered and transferred to the analogue port of a BBC microcomputer. Apart from availability, in both secondary and tertiary educational establishments, the BBC microcomputer was chosen for the ease with which it can be interfaced and the quality of its' graphics. Controls on the hardware are simple and robust and allow the student to record from either standard bipolar limb leads or unipolar limb or chest leads to obtain a conventional twelve lead ECG.

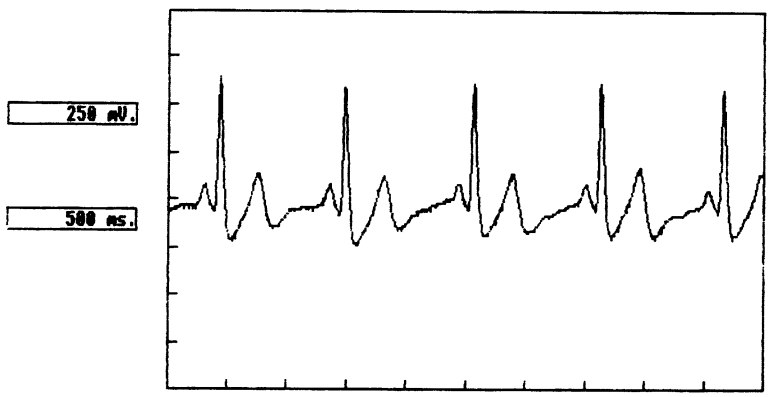

Figure 1. Typical ECG record - bipolar lead I.

The software used to display the recorded signal is a modified version of that previously reported (Dewhurst & Meehan, 1987). Briefly, the microcomputer stores a trace and reproduces it, using high resolution graphics, on an oscilloscope-like display (Figure 1). Students are able to scrutinise the signal, varying time and voltage scales and can thus expand any portion of the stored trace. Stored traces can be filed on disk and printed copies can be obtained by those with an EPSON compatible printer.

Brown, G.J. & Dewhurst, D.G. (1988) Br. J. Pharmac. (in press).
Dewhurst, D.G. & Meehan, A.S. (1986) Br. J. Pharmac. 89, Proc Suppl., 881P.

MICRO-COMPUTER PHARMACOKINETIC CURVE FITTING USING THE METHOD OF RESIDUALS WITH "ON SCREEN" LINE DRAWING

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The method of residuals has long been applied to solving pharmacokinetic models (Riggs 1970) but graphic methods are slow if several attempts are required to obtain a reasonable fit. Graphic methods for microcomputers which use cursor keys to draw lines are not ideal. However, the availability of a mouse system and a language written to utilize one makes "on screen " graphic curve fitting practicable.

Four programs have been written to take into account different routes of administration:

1) first order elimination from multi-compartment models (i.v. injections)
2) first order input and elimination (oral,i.m..,s.c. etc)
3) single zero order input (constant rate infusions)
4) consecutive zero order inputs (consecutive loading and maintenance infusions).

Time-concentration data, loaded from data files, are examined for minimum and maximum values so the screen can be suitably scaled. The data are plotted as log(concentration) verses time. Using the mouse the first construction line is drawn through the terminal points. The computer calculates the equation of this line, subtracts values from the data and plots the residuals. The time axis is re-scaled to expand the residual plot and the process repeated until all the exponential phases are resolved.

The programs calculate AUC(0-Tlast) and AUC(0-inf.) using the trapezoidal method and the AUC(0-inf.) using the fitted model for comparison. The residual sum of squares and AIC are presented to give an indication of "goodness of fit". **GRAFIT 1** allows a maximum of 5(!) compartments. The maximum number for **GRAFIT 2** is 2,but this program calculates any lag-time.

The fitted curves can plotted to screen or printer. The derived parameters can be printed out and/or saved to file ready for use as the first estimates in iterative curve fitting programs.The whole process can take as little as 2 minutes even though this may be the first time the data have been plotted.

The programs were written in Locomotive Basic2 (v1.21) on an Amstrad PC 1512 with 640K memory. Basic2 is available for other PC based systems and I am grateful to N.J.Loftus , M.D.Hall and their colleagues at ICI Pharmaceuticals who have been testing the programs for about 12 months on their IBM systems.

Riggs,D.S. (1970) "The Mathematical Approach to Physiological Problems" MIT Press, Cambridge, Massachusetts

AN IMPROVED APPARATUS FOR THE MEASUREMENT OF RAT FOOT VOLUME BY WATER DISPLACEMENT

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A standard method for studying inflammation in rats is that of measuring the degree of swelling produced after injection of an inflammation-inducing substance into the foot.

The apparatus to be demonstrated was designed to simplify the measurement procedure and increase the accuracy of the results.

Two cylindrical chambers are connected at their bases by a flexible tube which incorporates a T-piece for refilling when necessary and a short length of stainless steel tubing. (i.d. 2.2mm). This forms a U-tube which is partly filled with saline containing a wetting agent (1 ml Paterson Anti-static Wetting Agent/litre of saline). One chamber has an i.d. of 21 mm and is wide enough to accommodate the rat's foot. The other chamber has an i.d. of 9 mm and contains a wire electrode which is raised and lowered by a stepper motor (Airpax digital linear actuator type L92121-P2, McLennan Servo Supplies Ltd., Camberley, Surrey) to sense the level of saline in the chamber. The short length of stainless steel tubing in the connecting tube near to the base of the narrow chamber forms the return electrode for the level-sensing current and also constricts the flow of saline between the chambers preventing oscillations in level when the foot is immersed.

Electronic logic circuitry controls the stepper motor and a three-digit electronic display which counts the upward and downward steps of the electrode, keeping a record of its position. The sequence of events is as follows:

1. The electrode is lowered to the saline's surface where it stops and the counter is zeroed.
2. The electrode is raised 200 steps (10 mm) so the counter now displays 200.
3. The rat's foot is immersed to a known depth causing the saline level to rise in both chambers.
4. The electrode is lowered to the saline's surface while the display counts downwards. It stops on reaching the saline and the display shows a count proportional to the rise in saline level and so proportional to the volume of the saline displaced.
5. The rat's foot is removed from the saline and the apparatus is ready to take the next reading.

The improved apparatus gives results of superior accuracy to those obtained using equipment which measures the volume of water required to replace the overflow caused by immersion of the rat's foot (e.g. Garland et al, 1968) because such equipment is subject to errors caused by loss of water on the foot when it is removed.

To illustrate the accuracy of the new apparatus a test object, similar in size to a rat's foot, was measured fifty times giving a value of 69.94 ± 0.066 units (mean ± SEM).

Garland, L. G., Smith, S. J. and Sim, M. F. (1968). J. Pharm. Pharmacol., 20, 236-238.

THE USE OF STELLA SOFTWARE FOR THE TEACHING OF PHARMACOKINETICS IN THE UNDERGRADUATE PHARMACY AND MEDICAL SCIENCES COURSES

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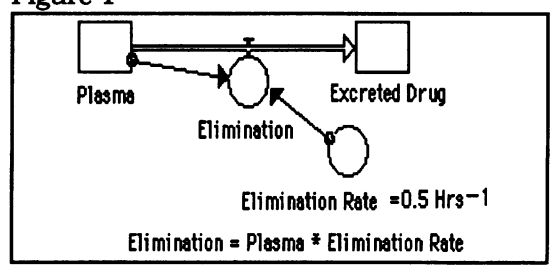
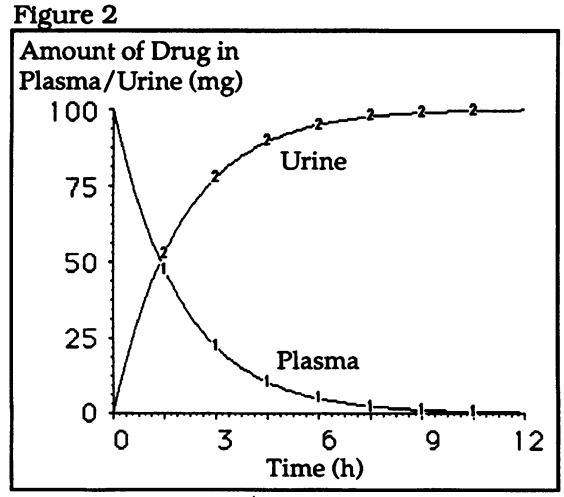
The use of computer programmes to model the absorption, distribution and clearance of drugs is well established and main frame or mini-computers are widely used for the teaching of pharmacokinetics. However, in the past, the construction of flexible and versatile pharmacokinetic models has required a high level of programming expertise, was time-consuming and demanded considerable effort. It is questionable whether this approach is of immediate use to the student of pharmacokinetics. The current trend in software design is to produce 'user-friendly' systems which allow the student to perform a wide variety of tasks without programming knowledge. The recent introduction of STELLA® (Structural Thinking, Experimental Learning Laboratory with Animation), a graphics based software package for the Apple Macintosh® microcomputer, allows the simulation of a wide variety of time-dependent processes. It operates by allowing the user to construct the system as a diagram from a set of subunits representing compartments and transfer rates and the programme derives and solves the corresponding sets of differential equations using iterative procedures (Eulers or Runge-Kutta methods). Such a programme has obvious applications in the teaching of pharmacokinetics.

Figure 1



A example of a simple model of drug elimination from the body and cumulative excretion in the urine following i.v. bolus administration is shown in Figure 1. The compartments represent the drug in the plasma and urine, being linked by the transfer rate. When the model is run, the corresponding concentration-time profiles in the compartments are displayed (Figure 2). A wide range of models simulating repeated oral dosing and multiple compartment equilibria can be easily developed by the student after a few hours of training. Alternatively, the user may experiment with selected models to examine the effect of changes of different parameters on the plasma concentration-time curve.

Figure 2



The models constructed by the students have been expanded to include a wide range of physiological and physico-chemical factors, such as the influence of intestinal transit times on absorption. This programme package has many applications in the undergraduate course where access to a Macintosh computer is possible.

Stella is a registered tradename of High Performance Systems, USA and Macintosh is a trademark licensed to Apple Computer Inc., USA.