Some Applications of a Desk-Top Computer[1]

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ABSTRACT

The more complex methods of programming the Olivetti 101 are discussed and illustrated with a set of examples taken from the field of Chemistry and Biochemistry. These examples begin with simple programs and graduate through programs which carry out complicated calculations of a repetitive nature from a minimum of data to programs which use special data storage techniques.

This communication will describe some of the more complicated programming methods and show how they can be used by a chemist or biochemist in his calculations. Most of my ideas are equally applicable to other desk-top computers taking into account their own idiosyncrasies of programming. These examples will not be especially orientated towards lipid chemistry but will serve to illustrate what the computer can do and in general how to go about programming the computer to do it.

I shall work mainly through the medium of flow charts because these are easier to comprehend for those unfamiliar with the computer. The program listings are obtainable from the author.

Because of the limited storage space available with desk-top computers a technique has been developed to increase the storage space by "packing registers." To form a packed register several small (e.g., three digit) numbers are joined together to form one large number so that they can be stored as a single number. The Olivetti Programma 101 and some of the other desk-top computers have the facility of transferring the decimal part of a number in the A register, into the M register while leaving everything unchanged. All of the figures after the decimal point are transferred irrespective of the decimal point setting of the computer.

If this instruction is followed by a subtraction we get

Register	M	A	R
Contents	1.0	3.52	4.50
Program instruction /↕			
New contents	0.52	3.52	4.50
Program instruction -			
New contents	0.52	3.00	3.00

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NUMBER GENERATION

			CODE	
	A/↑	INITIATOR		
123.456	R X			
	R -		0	S
	R +		1	↓
	R/↕	DECIMAL POINT	2	↑
	R ↑		3	↕
	D ↓	TERMINATOR	4	+
			5	-
R & D FOR +VE NUMBERS			6	x
F & E FOR -VE NUMBERS			7	÷
			8	◇
			9	*

FIG. 1. Program sequence and code for generating numbers in the program.

The numbers stored in a packed register can be brought into use one by one with this technique.

Programs involving the repetition of a calculation can often be shortened by the use of the so called "Domino technique"; that is, moving all the answers from one register to the next. The term "Domino" will be used in the flow charts to describe this technique.

Flow Chart	Programme		Before	After
↓	B ↕	B	1	3
DOMINO BCDB	C ↕	C	2	1
↓	D ↕	D	3	2
	B ↕			

Numbers, such as those used for indexing loops or constants employed in a calculation, can be generated in the M register by writing the appropriate instructions in the program. These instructions consist of an initiation instruction (A/↑) followed by the number in the code that the machine uses for numbers. This is illustrated in Figure 1. The number is read from right to left, each digit being made up of two symbols, the appropriate symbol for the number itself preceded by R if the number is positive and F if it is negative. D (or E if negative) is used to indicate the last digit of the number. The position of the decimal point is indicated by R/ (or F/, D/, E/ where appropriate) for the next digit after the decimal point reading from right to left.

Since the machine has a very limited capacity it is often necessary to use several programs linked together, so that they perform different parts of the calculation. When a program card is entered the F, E, D registers are overwritten by the contents of the card while the others (M, A, R, B, C) are unchanged. It may be necessary to transfer numbers in

LINEAR GRADIENT

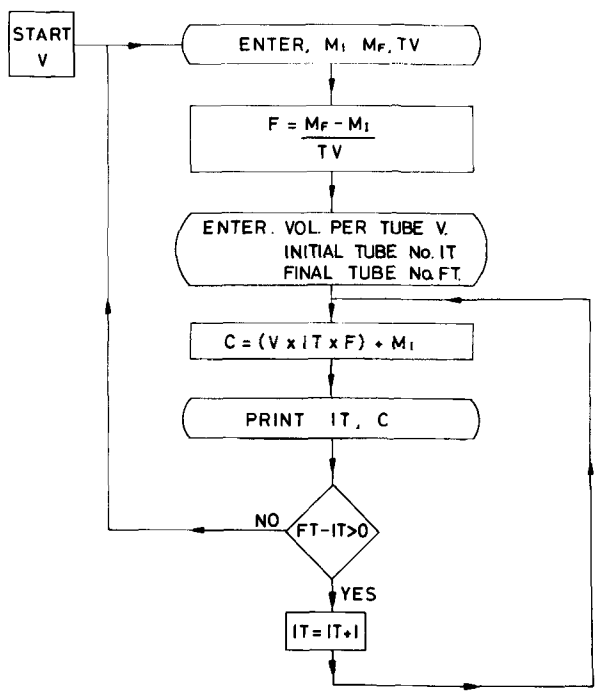


FIG. 2. Flow chart for the program to calculate a linear gradient.

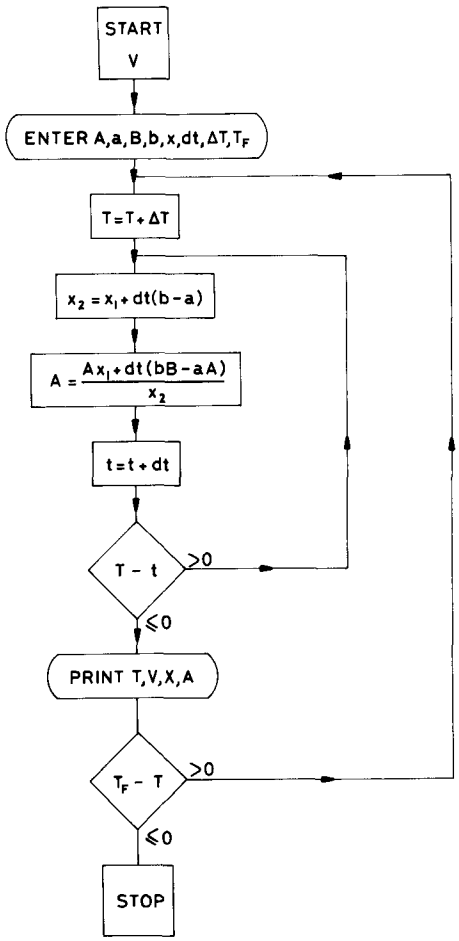


FIG. 3. Flow chart for the program to calculate a curved gradient generated by pumping a solution of constant concentration into a mixing chamber from which the output is taken at a rate which may be equal to or different from the inflowing rate.

F, E, D to M, A, R during the program changing. F and E can be stored in M and A while D is stored in R by means of the special instruction RS. The first instruction of the new card generally should be RS to retrieve the number from R. This instruction is also part of the sequence $\overset{R}{RS}^{*}$ which can be used to clear program instructions from the D register after they have been used, leaving it free for number storage.

A typical simple expression suitable for calculation on a desk-top computer would be the cross-link density of wool measured by swelling the wool in formic acid where

$$\text{cross-link density} = \left[\frac{Wt_w d_w}{(Wt_{a+w} - Wt_w)d_a + Wt_w d_w}\right]^{5/3}$$

The cube root cannot be evaluated by a single program step but is evaluated with a simple approximation (1):

$$\sqrt[3]{x} = y_{n+1} = y_n - \frac{1}{3}\left[y_n - \frac{x}{y^2_n}\right]$$

As an example of a long series of repetitive calculations carried out from a minimum of data entered into the computer, I have taken the calculation of the output from several devices used for automatically and continually changing the concentration of a solution supplied to a chromatographic column, known as gradient devices. Of these the most simple is the linear gradient generated from two identical interconnected vessels. The example shown in Figure 2 requires the initial and final concentrations, the total volume, the volume of each tube on the fraction collector, the initial and final tube numbers, and will print out the concentration in each tube between the two limits set.

The next stage of complexity is the pumped gradient device where buffer of concentration B is continuously pumped into a mixing chamber containing a buffer of different concentration A from which the output is taken by a second pump.

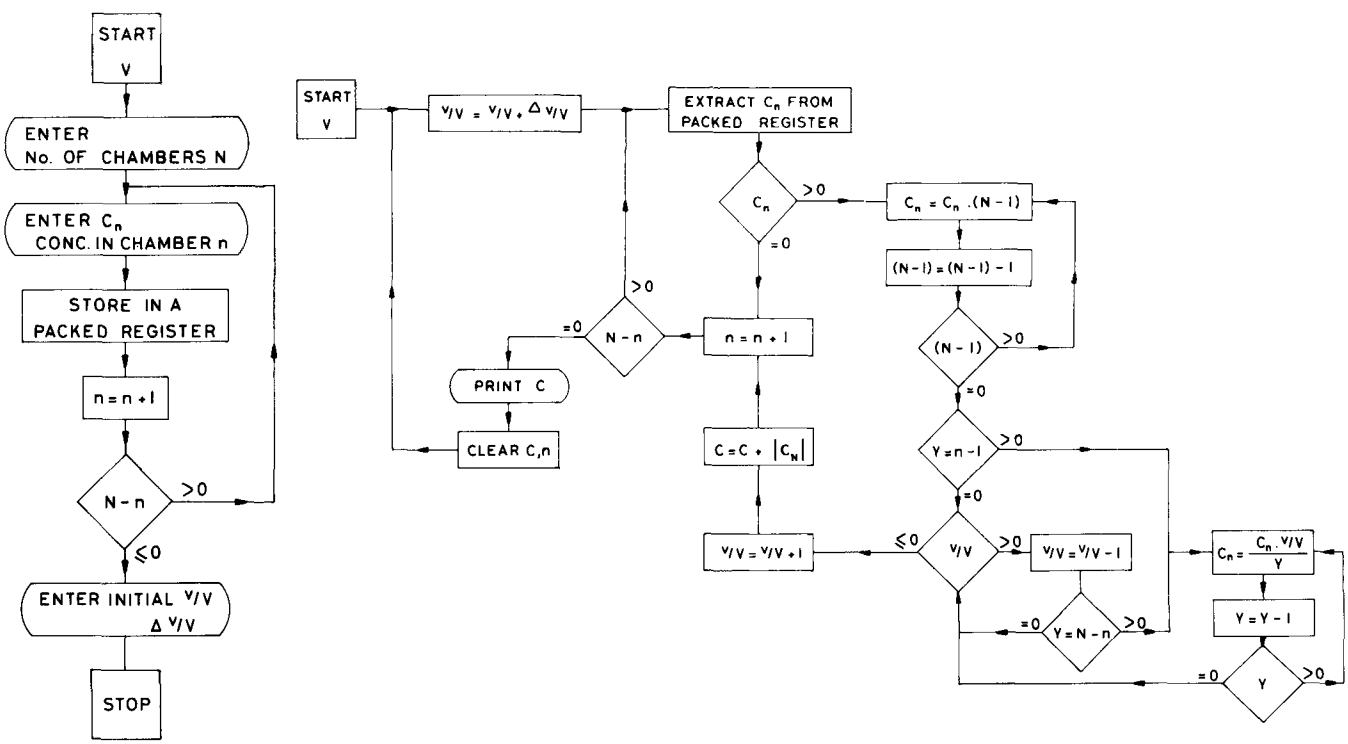


FIG. 4a,b. Flow charts for the programs to calculate the gradients from multichamber gradient devices (Varigrads) with up to nine chambers.

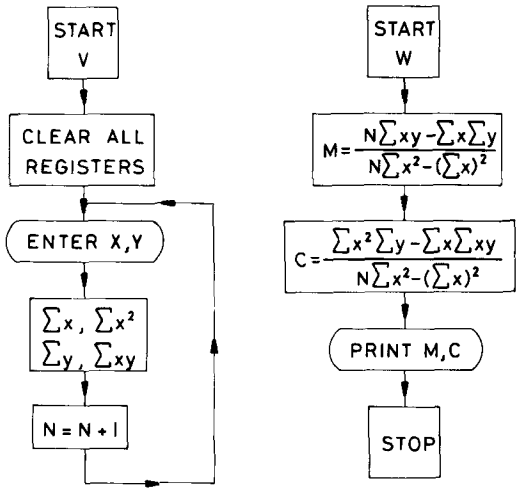
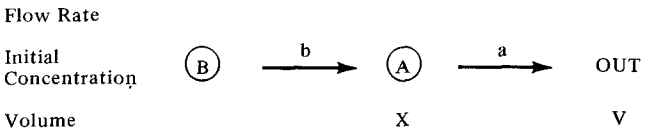


FIG. 5. Flow chart for the program to calculate the linear regression coefficients.



Convex, linear or concave gradients can be generated depending on the ratio of the flow rates a and b.

This type of gradient device has been used for chromatography and is finding increasing use in the generation of very precise gradients for gradient centrifugation in zonal rotors. A full treatment of this has been given by Hinton and Dobrota (2). The integral produced in the calculation is not calculable with a digital computer and instead an approximation must be used

$$C = \frac{AX + dt\,(bB - aA)}{X + dt\,(b - a)}$$

where C is the output concentration after a small interval of time. The value of dt is a compromise between accuracy and the time taken for computation; comparison between this calculation and the value found from integration indicates that dt does not have to be particularly small. The program (Fig. 3) requires as input A, a, B, b, dt, the time interval between printouts ΔT and the final time T_F. The computer will print out: time, total volume pumped out, volume in the mixing chamber, and concentration of the buffer flowing out. This printout will be repeated with the time increasing by the set amount ΔT each time until the final time T_F is reached when the calculation will terminate and the program resets back to the beginning ready to accept the parameters for another gradient if necessary.

More complex gradients can easily be generated in a variable gradient device (Varigrad) consisting of a number of identical chambers connected in series in hydrostatic equilibrium. Tables to calculate the outputs of such devices have been worked out (3). However it is time-consuming to calculate gradients from the Tables. The output of a gradient device of this kind is given by

$$C = \sum_{n=1}^{n=N} [L_n{}^{*}(N-1)!(1-v/V)^{N-1}\cdot (v/V)^{n-1}]/[(N-n)!(n-1)!]$$

where C = outflowing concentration; N = total number of chambers; L_n = initial concentration in chamber n; v/V = fraction of total volume that has flowed out of the device.

Figures 4a and b show the program that can be used to

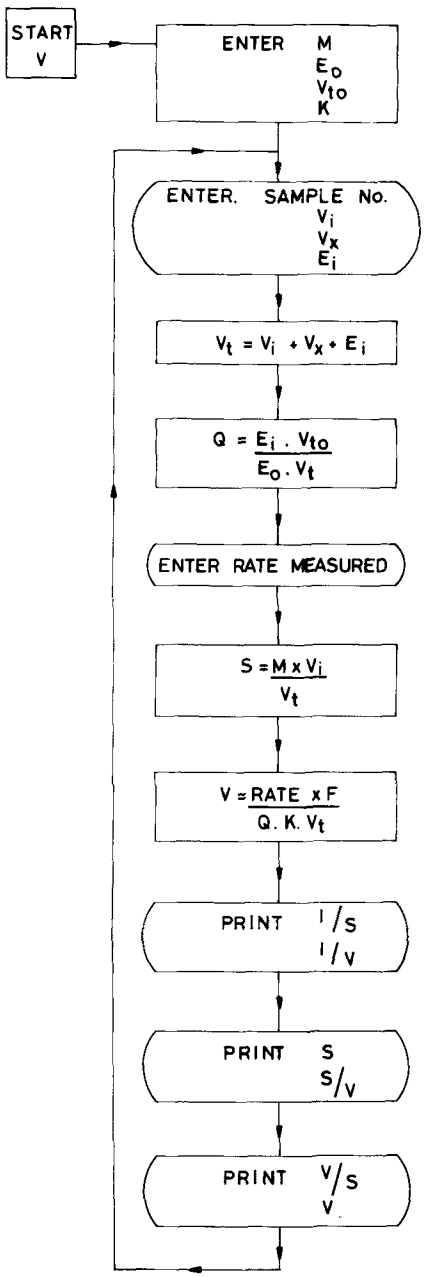


FIG. 6. Flow chart for the program to calculate S, V, 1/S, 1/V, S/V, V/S from experimental data for an enzymic reaction.

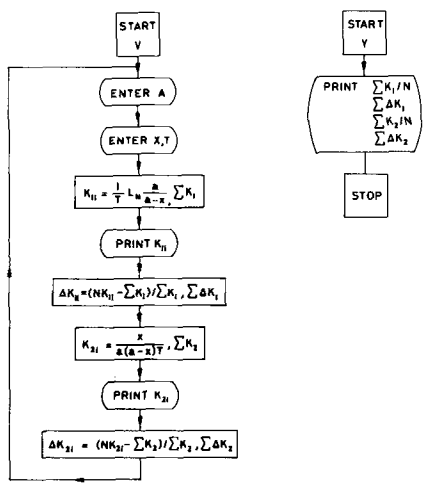


FIG. 7. Flow chart for the program to determine the order of a unisubstrate chemical reaction.

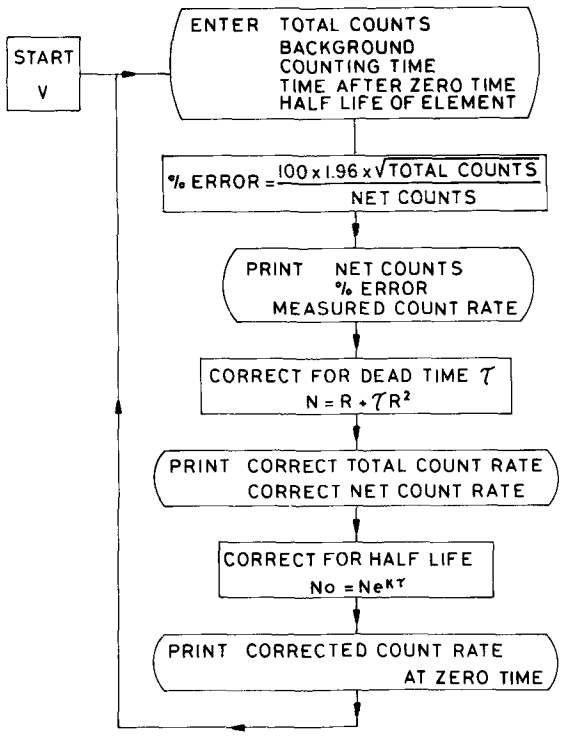


FIG. 8a. Flow chart for the program to correct the output of a Geiger-Muller counter (for background, dead time of the counter and the half-line of short lived radioactive elements).

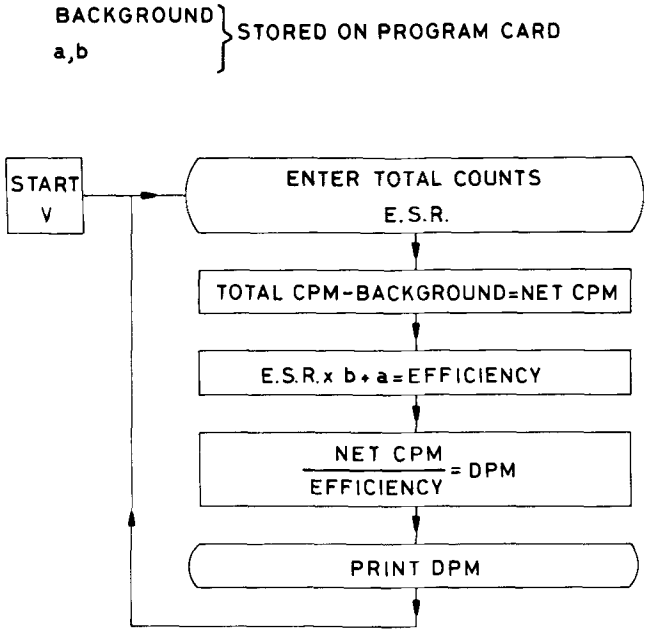


FIG. 8b. Flow chart for the program to correct the output of a scintillation counter (to convert cpm to dpm for a singly labeled sample with a linear quench correction curve).

calculate gradients up to nine chambers. The first program inputs the number of chambers, the concentrations in each chamber which are stored in a packed register, the initial value for v/V and the increment between printouts $\Delta v/V$. The second program calculates and sums the contribution the individual chambers make at the value of v/V in operation. This calculation is based on a simple routine to calculate $X^N \cdot N!$

A/V	C↕
C↕	F−
CX	/V
BX	

assuming that X is in the B register, N in the A register, and 1 is in the C and F registers. The outflowing concentration is printed out and then calculation begins for the new value of v/V, this will continue until v/V = 1, that is, when the gradient is completed. The computing time of course increases with the number of chambers used but once the computation has started no further operator attention is required until all the required values of concentration have been printed out.

There are many applications where experimental data has to be fitted either to a straight line or a quadratic. The gradient and intercept of a "best straight line fit" to a series of points are given by

$$m = (N\Sigma xy - \Sigma x\Sigma y)/(N\Sigma x^2 - (\Sigma x)^2)$$

$$c = (\Sigma x^2\Sigma y - \Sigma x\Sigma xy)/(N\Sigma x^2 - (\Sigma x)^2)$$

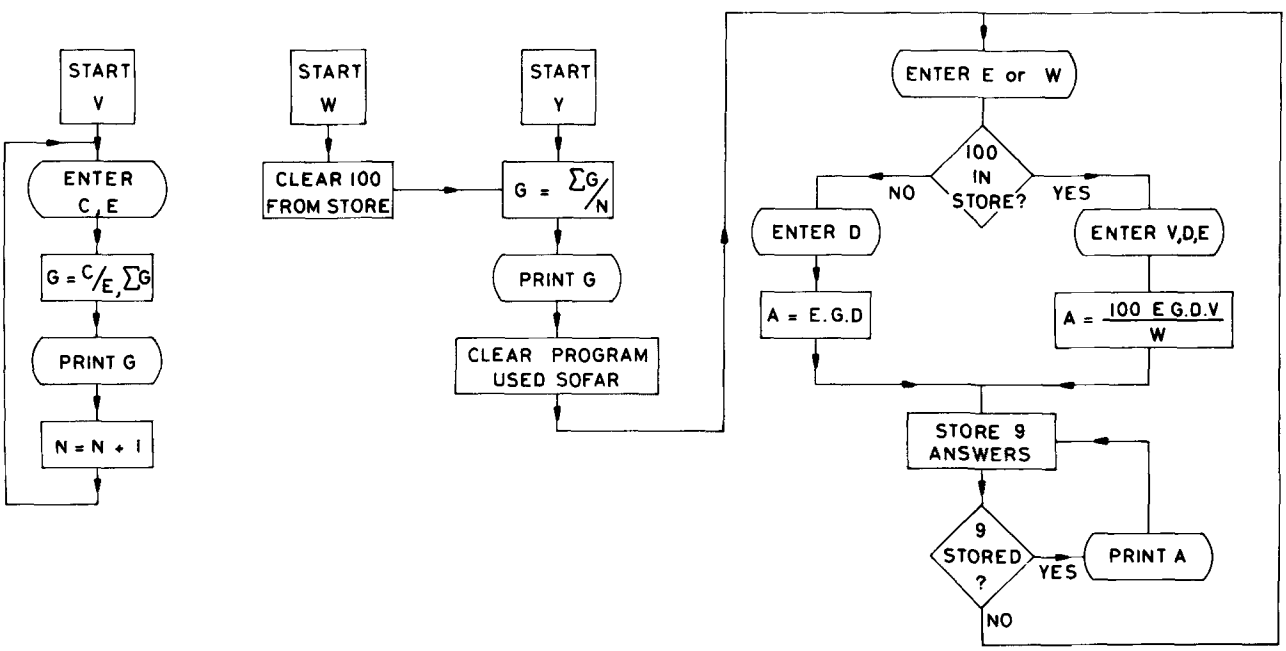


FIG. 9. Flow chart for the program to calculate the results from Atomic Absorption Spectroscopy in either concentration or percentage. Nine results can be stored and printed out together.

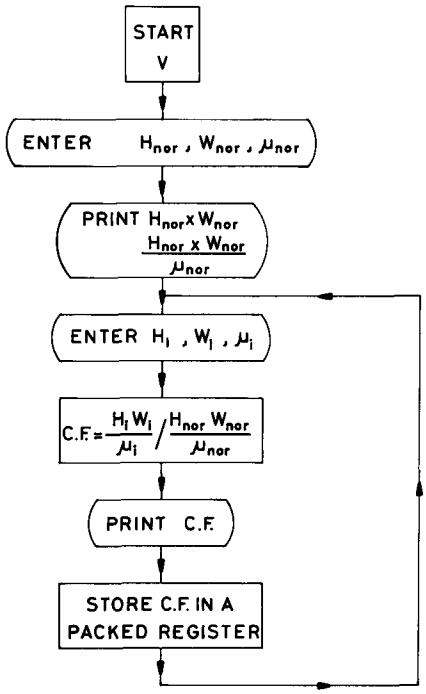


FIG. 10a. Flow chart for the program to calculate the color factors from an amino acid analysis of a standard mixture of amino acids using the "height x width" method of integration of the chart.

for the straight line $y = mx + c$.

Figure 5 indicates the type of program used to calculate the gradient and intercept. The regression coefficients for the quadratic $y = a + bx + cx^2$ are

$$a = \frac{A}{|A|}, \quad b = \frac{B}{|A|}, \quad c = \frac{C}{|A|}$$

where

$$a = \frac{A}{|A|} = \frac{\Sigma y(\Sigma x^2\Sigma x^4 - (\Sigma x^3)^2) - \Sigma xy(\Sigma x\Sigma x^4 - \Sigma x^2\Sigma x^3) + \Sigma x^2 y(\Sigma x\Sigma x^3 - (\Sigma x^2)^2)}{n(\Sigma x^2\Sigma x^4 - (\Sigma x^3)^2) - \Sigma x(\Sigma x\Sigma x^4 - \Sigma x^2\Sigma x^3) + \Sigma x^2(\Sigma x\Sigma x^3 - (\Sigma x^2)^2)}$$

$$b = \frac{n(\Sigma xy\Sigma x^4 - \Sigma x^2 y\Sigma x^3) - \Sigma x(\Sigma y\Sigma x^4 - \Sigma x^2\Sigma x^2 y) + \Sigma x^2(\Sigma y\Sigma x^3 - \Sigma xy\Sigma x^2)}{|A|}$$

$$c = \frac{n(\Sigma x^2\Sigma x^2 y - \Sigma x^3\Sigma xy) - \Sigma x(\Sigma x\Sigma x^2 y - \Sigma y\Sigma x^3) + \Sigma x^2(\Sigma x\Sigma xy - \Sigma x^2\Sigma y)}{|A|}$$

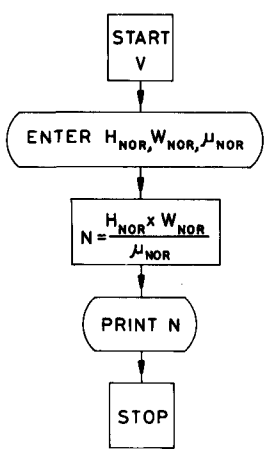


FIG. 10b. Flow chart for the programs to calculate the results from an amino acid analysis using the "height x width" method of integration of the chart.

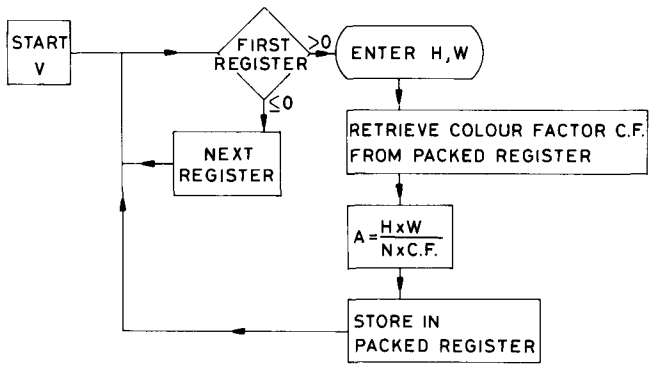


FIG. 10c. See legend for Figure 10a.

These are considerably more complicated, but they are still calculable with the Olivetti Programma 101. Extensive use has been made of these curvilinear regression expressions by Hultin et al. (4) to calculate the initial velocity of reaction of enzymic reactions.

For enzymic reactions which obey Michaelis Menton kinetics the initial velocity of reaction (V) and substrate concentration (S) are related by expressions such as

$$1/V = (K_m/V_{max}) \cdot 1/S + 1/V_{max}$$
$$S/V = S/V_{max} + K_m/V_{max}$$
$$V = V_{max} - K_m \cdot V/S$$

The data, after a suitable transformation, can be fitted to all of these expressions by means of the "best fit" straight line program (Fig. 5). For the transformation of the data a program such as that in Figure 6 is used where the experimental parameters are entered into the computer and the values for 1/S, 1/V; S, S/V; V/S, V are printed out as three pairs of numbers for each set of data entered. The flow chart indicates that these three pairs are separated on the printout by blank spaces so that they are easily discernible.

The computer can be used not only to provide numerical answers to suitable expressions but also to help investigate reaction mechanisms. For example the reaction

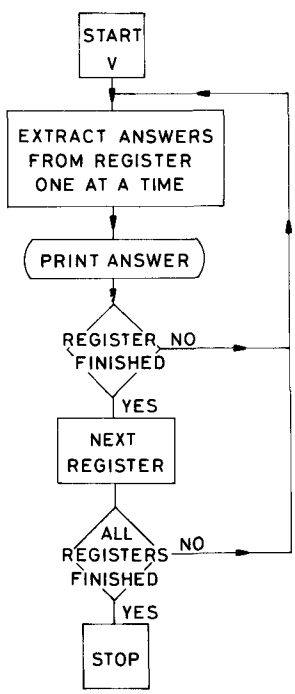


FIG. 10d. See legend for Figure 10a.

$$A \longrightarrow \text{products}$$

may be first order (where $K_1 = \text{Ln}(A/A\text{-}X)T$ or second order with respect to A[where $K_2 = X/(AT(A - X))$].

Figure 7 indicates how this can be accomplished. The initial concentration of A is fed in followed by the concentration of product at a time T. K_1 and K_2 are evaluated and printed for each set of values of product and time, followed by the mean and the proportional difference from the mean value. These differences are summed and at the end the mean values of K_1 and K_2 are printed together with the sum of the proportional differences from the mean. The first order reaction required a calculation of $\log_e$; this is accomplished using an approximation (1):

$$\text{Ln } X = 16(y + y^3/3 + y^5/5 \ldots)$$

$$\text{where} \quad y = ({}^8\sqrt{x} - 1)/({}^8\sqrt{x} + 1).$$

This preliminary treatment could be carried out with data read directly from the measuring apparatus. When the reaction mechanism has been established the accurate rate constant would be determined from a straight line plot of t against the relevant expression.

This computer has many applications in the field of molecular weight determination, for example in the calculation of molecular weight by osmotic pressure

$$M = RT/(\pi/c)_{c \to 0}$$

In this case the function π/c is plotted against c and the value of $(\pi/c)_{c \to 0}$ found from the intercept by means of the "best fit" straight line program.

It can be applied to the calculations involved in the various types of ultracentrifuge experiments such as the expressions for

(a) Low speed sedimentation equilibria

$$M_W = \frac{1}{XJ} \frac{dJ}{dx} \cdot \frac{RT}{(1 - \nu\rho)w^2}$$

where

$$X = A - (R_R - R_N)/F.$$

(b) Yphantis high speed sedimentation equilibrium

$$M_W = \frac{RT \cdot 4.862}{(1 - \nu\rho)w^2 X} \cdot \frac{d(\log y)}{dx}$$

(c) The number average molecular weight

$$M_N = \frac{RT}{(1 - \nu\rho)w^2} \cdot \frac{Y}{\Delta X/F\Sigma XY}$$

Many of the calculations used in radiochemical experiments are amenable to computation; Figure 8a illustrates a typical program used to correct the data obtained from a standard Geiger-Muller counter; corrections are provided for background count, dead time of the counter and correction back to a specified zero time for elements with a short half-life. The per cent error is also printed out for any required confidence level. The correction for half-life entails a calculation of an exponential. This is most easily accomplished with a Maclaurin series which takes very little programming space but does significantly increase the computation time (1):

$$e^x = 1 + x/1! + x^2/2! + x^3/3! \ldots .$$

The calculation of the data output from scintillation counters with desk-top computers has recently been reviewed by Grower and Bransome (5).

Disintegrations per minute (dpm)

$$= \frac{\text{counts per minute (cpm)} - \text{background} - \text{spillover}}{\text{efficiency}}$$

The counter itself usually prints cpm and External Standards Ratio (ESR) for each channel. The efficiency is calculated from a quench correction curve which is a plot of efficiency against ESR for a series of quenched standards. The spillover from one channel to another (e.g., $^{14}C \rightarrow {}^3H$) is calculated from a spillover curve of percentage of ^{14}C counts appearing in the ^3H channel against efficiency in the ^{14}C channel.

The quench correction and spillover curves can either be expressed by straight lines or quadratics for which the regression coefficients are easily calculated. Figure 8b shows a typical program used to convert cpm to dpm for singly labeled samples with a linear quench correction curve. For a double label experiment, the slope and intercept of two sets of quench correction curves must be stored as well as the spillover curves for ^{14}C to ^3H channel.

The examples used so far have simply shown the type of calculations that are carried out without any undue emphasis being placed on output presentation. The next example applicable to almost any analysis is designed to show how with a certain amount of attention to detail the output readibility can be improved.

The results of many routine analyses simply require an absorbance to be converted to a concentration by means of a factor found from an analysis at a known standard concentration. Normally with a desk-top computer the concentration is calculated and printed out directly. However with a large number of analyses considerable effort is needed to sort out all the answers from the roll of output paper, and some method of data storage is required to improve the output presentation. The answers could be stored in several ways: with a domino technique or by packing registers. The domino technique to store and print answers is embodied in the program in Figure 9, written to calculate results from Atomic Absorption Spectroscopy where the results may be required either as a concentration or as a percentage of the sample. Both calculations are on the same card and the computer decides, on the absence or presence of the constant used for the percentage calculation, whether the concentration or percentage version is to be used. After nine sets of readings have been entered the results are printed out together and the machine resets, ready to accept more data. These blocks of answers are easily spotted and recorded elsewhere as required. Should less than nine sets of data be entered the remaining results can be printed with a single command to the computer.

To carry the data storage a stage further—to the packed register technique—a set of programs (Fig. 10) has been written to calculate the results of amino acid analyses where the calculation is

$$M = \frac{\text{Area amino acid}}{\text{Area standard}} \times \frac{\text{M standard}}{\text{Color factor.}}$$

This type of calculation is applicable to any analysis that uses a chart output (for example the gas chromatograph or sugar analyzers) where each peak uses a different color factor.

Figure 10a illustrates the program required to calculate the color factors from a standard chromatogram. The answers are built up into three blocks of figures which are printed out and retained in the computer so that they can be recorded on program card 2 of the standard analysis (Fig. 10c). Figure 10b,c,d shows the three program cards required for a standard analysis.

Program card 1 simply calculates Area standard/M Standard. Card 2, which has the color factors stored on it, is used to calculate the analysis by extracting the color factors one at a time from their packed reigsters, carrying

out the computation, and storing the result in another packed register. The color factors are removed as they are used so that space is left to store the answers. Card 3 is used to print out the answers in a single column. It does this in such a way that the answers are retained in the computer.

The results of an amino acid analysis are very rarely reported simply as μmoles and are usually reported as: percentage amino acids, percentage nitrogen, or number of residues to a set molecular weight. Because the results of the analysis are retained in the computer these calculations can most conveniently be carried out simply by adding further program cards to the computer (6).

While this communication has not intended to be a review of all the applications it is hoped that sufficient applications have been demonstrated to stimulate people to evaluate the potential uses of this desk-top computer, bearing in mind that many of the more complex calculations could more simply be carried out on a larger computer.

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