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A PROGRAMMABLE CALCULATOR PROGRAM FOR RAPID LOGARITHMIC EXTRAPOLATION, AND CALCULATION OF MEAN TRANSIT TIME FROM AN INDICATOR-DILUTION CURVE

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Reconstruction of the primary indicator-dilution curve is accomplished by exponential curve-fit from a set of points obtained on the downslope of the curve. Curve-fit is simplified by requiring entry of indicator concentrations (Y_i) only, where time increments (X_i) are made self-generating in the program. Similarly, calculation of mean transit time requires only the entries of Y_i. Stored values supply the needed quantities for calculations of cardiac output and the central blood volume as defined by the injection and the sampling sites. The Texas Instrument TR 52 model hand-held programmable calculator is utilized in this program but it should be adaptable to other programmable calculators. The present program provides a procedure for rapid reconstruction of the primary indicator-dilution curve, and hence calculations of cardiac output, mean transit time and central blood volume.

Indicator-dilution curve Logarithmic extrapolation Cardiac output Mean transit time Texas Instrument TR52

1. Introduction

Recirculation of the pulse injected indicator in the circulatory system necessitates reconstruction of the primary dilution curve by, e.g., the exponential extrapolation method [1,2]. The burden of this tedious analysis of the indicator-dilution curve has lessened by commercially available analog computers which determine the area under the recirculation free concentration–time curve and which calculate cardiac output taking into account the amount of indicator injected and a calibration factor [3]. These devices make on-line determination of cardiac output possible during the catheterization procedure. However, these computers are expensive and task specific.

Various short-cut methods are available for estimation of cardiac output from indicator-dilution curves. All these methods try to circumvent the extrapolation process which is the most time consuming. Williams et al. [4] utilized the mathematical property of the exponential decay by finding two points, (X_1, Y_1) and (X_2, $\frac{1}{2}Y_1$), on the exponential portion of the downslope of the dilution curve. The area from X_2 to ∞ is equal to that defined by time X_1, X_2 and their corresponding concentrations, Y_1 and $\frac{1}{2}Y_1$. This principle was adopted in a simplified planimetry procedure [5], and in a nomogram [6]. Others have treated the dilution curve as a gamma function with good results [7–10]. Killen and France [11] described a 'simple' curve-fit method for defining the downslope decay constant. Empirical estimations of the area under the dilution curve with triangles were tried with some success [12–15].

This communication presents a simplified procedure for exponential extrapolation of the downslope of the dilution curve by simply entering successive indicator concentrations, Y_i (e.g., indicator concentration at 1 s intervals) into a programmable calculator. The elapse time, X_i, was made self-generating in the program. In the process, information is accumulated for calculations of the decay constant (b), the Y-intercept (a), the correlation coefficient (r^2), and generation of successive Y values for correction of recirculation. Different parts of the same program were made to compute mean transit time (t_m). Cardiac output and the central blood volume can then be calculated from the stored values.

2. Program description

The present program consists of two parts:

(i) Exponential fitting of the downslope and generation of extrapolated values;

(ii) Calculation of the mean transit time.

A Texas Instrument (TR 52) calculator is used. The registers and the user defined labels are assigned as in table 1.

In the first part of the program, an exponential function of the form:

$$Y = ae^{bx} \text{ or } \ln Y = \ln a + bx \tag{1}$$

was fitted by the least squares method from a set of points, (X_i, Y_i) found on the downslope portion of the indicator-dilution curve in the period after the peak indicator concentration and before the recirculation. Where:

X_i is time

Y_i is indicator concentration at X_i

$i = 1, 2, 3, ..., n$

Since successive X_i-values increase at constant intervals (e.g., 1 s intervals or any other convenient constant time intervals), it was made self-generating in the program, eliminating the need for entering both X_i and Y_i. After each successive Y_i is entered, the coefficients a and b, and the correlation coefficient, r^2 are calculated and stored by a single key instruction. These coefficients are calculated according to:

$$a = \exp\left[\frac{\Sigma \ln Y}{n} - b\frac{\Sigma X}{n}\right] \tag{2}$$

$$b = \frac{\Sigma X \ln Y - (\Sigma X \Sigma \ln Y/n)}{\Sigma X^2 - ((\Sigma X)^2/n)} \tag{3}$$

$$r^2 = \frac{[\Sigma X \ln Y - (\Sigma X \Sigma \ln Y/n)]^2}{[\Sigma X^2 - ((\Sigma X)^2/n)][\Sigma(\ln Y)^2 - ((\Sigma \ln Y)^2/n)]} \tag{4}$$

Extrapolated values for each increment of X_i are calculated from eq. (1) by continuous successive pressing of a single user defined key (see example), as many values as desired. X_i is also made self-generative in this program.

Mean transit time (t_m) is calculated in the second part of the program, by:

$$t_m = \frac{\Sigma X \cdot Y}{\Sigma Y} \tag{5}$$

X_i in this portion of the program is also supplied by the program so that only entering of Y_i is required. Calculations of cardiac output and the central blood volume are not included in the program but can be

Table 1
Assignment of registers and user-defined keys

Registers	Curve-fit program	t_m program	User-defined keys	
00	n	n	A	to enter Y_i for curve-fit
01	ΣX	X	A [a]	to complete the curve fitting, calc. a, b, r^2 and store them
02	ΣX^2	Y		
03	$\Sigma \ln Y$	ΣXY	B	to obtain successive Y_i
04	$\Sigma X \ln Y$	ΣY	B [a]	to recall a
05	$\Sigma(\ln Y)^2$		C	not used
06	–		C [a]	to recall b
07	$x \ln Y$		D	to enter Y_i for t_m calculation
08	b		D [a]	to display t_m
09	a		E	to initiate either curve-fit or t_m program
10	$\Sigma X \ln Y - (\Sigma X \Sigma \ln Y/n)$		E [a]	to recall r^2
11	$\Sigma X^2 - (\Sigma X)^2/n$			
12	r^2			

[a] Denotes second function keys

Table 2
The program

LOC	CODE	KEY	LOC	CODE	KEY	LOC	CODE	KEY	LOC	CODE	KEY	LOC	CODE	KEY	LOC	CODE	KEY
000	46	*LBL		44	0		40	*x^2	112	23	lnX		46	*LBL		02	2
	15	E		00	0		55	÷		42	STO		18	*C		44	SUM
	25	CLR	040	04	4		43	RCL		00	0	152	43	RCL		00	0
	47	*CMS		43	RCL		00	0		09	9		00	0		04	4
	81	HLT		00	0	080	00	0		43	RCL		08	8	192	65	X
005	46	*LBL		00	0		54	)	117	01	1		81	HLT		53	(
	11	A		81	HLT		42	RCL		00	0		46	*LBL		43	RCL
	23	lnX	045	46	*LBL		01	1		40	*x^2	157	10	*E		00	0
	42	STO		16	*A		01	1		55	÷		43	RCL		01	1
	00	0		53	(	085	95	=		43	RCL		01	1	197	85	+
010	07	7		43	RCL		42	STO	122	01	1		02	2		01	1
	44	SUM		00	0		00	0		01	1		81	HLT		54	)
	00	0	050	04	4		08	8		55	÷	162	46	*LBL		42	STO
	03	3		75	-		25	CLR		53	(		12	B		00	0
	40	x^2		43	RCL	090	53	(		43	RCL		01	1	202	01	1
015	44	SUM		00	0		43	RCL	127	00	0		44	SUM		95	=
	00	0		01	1		00	0		05	5		00	0		44	SUM
	05	5	055	65	X		03	3		75	-	167	00	0		00	0
	01	1		43	RCL		55	÷		43	RCL		43	RCL		03	3
	44	SUM		00	0	095	43	RCL		00	0		00	0	207	43	RCL
020	00	0		03	3		00	0	132	03	3		00	0		00	0
	00	0		55	÷		00	0		40	*x^2		65	X		01	1
	43	RCL	060	43	RCL		75	-		55	÷	172	43	RCL		81	HLT
	00	0		00	0		43	RCL		43	RCL		00	0		46	*LBL
	00	0		00	0	100	00	0		00	0		08	8	212	19	*D
025	44	SUM		54	)		08	8	137	00	0		95	=		43	RCL
	00	0		42	STO		65	X		54	)		22	INV		00	0
	01	1	065	01	1		43	RCL		95	=	177	23	lnX		03	3
	49	*PROD		00	0		00	0		42	STO		65	X		55	÷
	00	0		55	÷	105	01	1		01	1		43	RCL	217	43	RCL
030	07	7		53	(		55	÷	142	02	2		00	0		00	0
	40	*x^2		43	RCL		43	RCL		81	HLT		09	9		04	4
	44	SUM	070	00	0		00	0		46	*LBL	182	95	=		95	=
	00	0		02	2		00	0		17	*B		81	HLT		81	HLT
	02	2		75	-	110	54	)		43	RCL		46	*LBL	222		
035	43	RCL		43	RCL		22	INV	147	00	0		14	D			
	00	0		00	0		TEXAS INSTR			09	9		42	RCL		TEXAS INSTR	
	07	7	075	01	1		INCORPORA			81	HLT	187	00	0		INCORPORA	

calculated from the stored values in the above computations.

Thus:

$$\text{Cardiac output} = \frac{(\text{Amount of indicator injected})}{\frac{\Sigma(\Delta t)\,Y}{(\Delta t)\,n}\,(\text{calib. factor}) \times n} \qquad (6)$$

Where $\Sigma(\Delta t)\,Y/(\Delta t)n$ is the average concentration of the indicator under the curve, sampled at Δt intervals, and n is the number of Δt. $(\Delta t)n$ is the elapse time since the injection to the completion of the primary curve. If Δt is taken to be 1 s, eq. (6) can be simplified to:

$$\text{Cardiac output} = \frac{\text{Amount indicator injected}}{\Sigma Y\,(\text{calib. factor})} \qquad (7)$$

ΣY is stored in R_4 in the t_m program. Of course, one can determine the area by planimetry and calculate the cardiac output conventionally. Central blood volume is the product of t_m and cardiac output:

$$\text{Central blood volume} = (\text{cardiac output})(t_m) \qquad (8)$$

3. Operating procedure and example

Figure 1 represents a typical dye-dilution curve. Cardiogreen, 5 mg, was injected at $t = 0$ into the right atrium of a dog weighing 19.6 kg. The dye concentration was plotted on the ordinate in arbitrary units against time in seconds. Five points (○) on the downslope of the curve were taken for the program to generate the subsequent points (●). The calibration factor was 0.75 mg/l/unit height. The operating procedure is as follows:

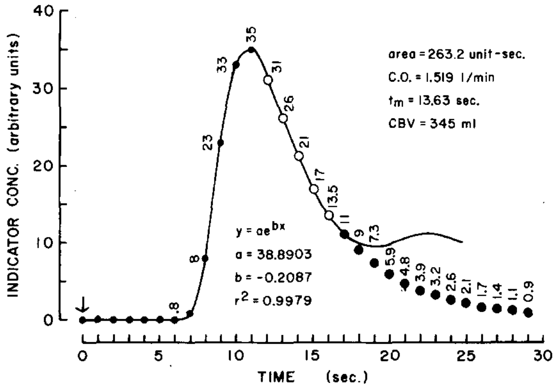

Fig. 1. Typical dye-dilution curve. Cardiogreen, 5 mg, was injected at $t = 0$ into the right atrium of a dog weighing 19.6 kg. The dye concentration was plotted on the ordinate in arbitrary units against time in seconds. Five points on the downslope (○) were taken for the program to generate the subsequent points (●). The calibration factor was 0.75 mg/l/unit height. CO, t_m and CBV represent cardiac output, mean transit time and central blood volume, respectively.

Procedure and example

A. Exponential curve-fit

Step	Press key	Display
1. Enter program		
2. Initialize	E	0
3. Enter Y_i (repeat for all i)	A	n
Example see fig. 1		
$Y_1 = 31$	A	1
$Y_2 = 26$	A	2
⋮	⋮	⋮
$Y_5 = 13.5$	A	5
4. Complete the program	*A	$r^2 = 0.9979$

*Denotes second function keys

$a = 38.8903$ (in R_9)
$b = -0.2087$ (in R_8)

Exponentiality of the downslope can be judged at this point, an r^2 value of better than 0.99 should be accepted

5. To obtain Y_6 to Y_n	B	$Y_6 = 11$
Example see fig. 1	B	$Y_7 = 9$
	B	$Y_8 = 7.3$
	⋮	⋮
	B	$Y_{29} = 0.7$

B. For t_m

Step	Press key	Display
1. Initialize	E	0
2. Enter Y_i beginning		
with 1 s	D	$Y_1 = 0$
after the injection to	D	$Y_2 = 0$
the completion of	⋮	⋮
the primary dilution		
curve (see fig. 1)	D	$Y_{10} = 35$

⋮
D $Y_{28} = 1.1$
D $Y_{29} = 0.9$
3. To obtain t_m *D $t_m = 13.63$
*Denotes second function keys

C. Cardiac output

According to eq. (7):

$$CO = \frac{5\ (\text{mg}) \times 60\ (\text{s/min})}{\dfrac{263.2\ (\text{ht} \cdot \text{unit-s})}{29\ (\text{s})} \times 0.75\ \dfrac{\text{mg/l}}{\text{ht} \cdot \text{unit}} \times 29\ (\text{s})}$$

$$= 1.519\ \text{l/min}$$

$\Sigma Y = 263.2$ is stored in register 4 (see table 1)

D. Central blood volume

According to eq. (8):

$$CBV = CO \times t_m = 1519\ (\text{ml/min}) \times \frac{13.63}{60}\ (\text{min})$$

$$= 345\ \text{ml}$$

Although the present program was made on the Texas Instrument TR 52 calculator, it should be adaptable to other programmable calculators which cost a small fraction of the commercially available task specific computers. Earlier, Shinozaki and Hanson [16] made a program on an Olivetti programma 101 for the same purpose. With the cost of these calculators continuing to fall, rapid computation of indicator-dilution results should be available to those who desire them. The present program is a simplified exponential curve-fit by eliminating entry of X_i. The process is thus greatly facilitated. The reconstruction of the primary dilution curve takes only 60 s at the most, such as the example shown in fig. 1. Once the recirculation is removed, there are choices of methods for obtaining the area under the reconstructed curve, such as planimetry, summation by trapezoid rule, or by Simpson rule. Equation (7) represents a trapezoid rule of summation which is known to generate results with sufficient accuracy. Its accuracy is limited by the Δt chosen. High accuracy can be obtained by a smaller Δt. A Δt of 1 s is generally adequate. It is hoped that the present program will be utilized by those who do not have the cardiac output computer to facilitate their calculations.

Acknowledgement

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Appendix

Program listing

The program listing is consistent with the program manual supplied by Texas Instruments. Asterisks denote second function keys.

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