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DECUS NO.	FOCAL8-93
TITLE	DOSE-RESPONSE ROUTINE
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DOSE-RESPONSE ROUTINE

DECUS Program Library Write-up

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ABSTRACT

The S-shaped log dose-response curve, so widely encountered in biomedical analysis, is approximately linear only over its midportion. Comparative statistics are greatly simplified by transforming the curve to a straight line which is accomplished by probit conversion. This program outputs log dose and probit values for subsequent plotting by the user on linear graph paper.

The expanded program for 8K systems additionally plots a scaled log dose versus probit scattergram.

INTRODUCTION

Probits derive from the cumulative probability curve where, instead of percentage response, the normalized deviation from the mean (t-value) is computed. By this convention the midpoint has a value of 0 with a corresponding cumulative probability of 50%. Responses less than 50% are expressed in negative units (e.g., -2 standard deviations from the mean). To circumvent the use of negative numbers, 5 is added to the normalized deviate, yielding the so-called probit. The probit value of the median (t=0) then is $0 + 5 = 5$; that of two standard deviations to the left (t=-2) is 3.

Note that probits merely are a handy convention of transforming a curve to a straight line. Interpolation of the line to the midpoint (probit = 5) yields the corresponding log dose that affects 50% of the sampled population (median effective dose or ED₅₀).

PROGRAM DESCRIPTION

After initialization, the program requests the dose and calculates the log (base 10) of the dose. The user then is asked to input the percent response, from which the cumulative normal distribution function is computed. The x-coordinate corresponding to the cumulative area under the curve is then found by integration and expressed in units of standard deviation from the mean. Adding five to this t-value yields the probit of the percentage response.

The program initially calculates and stores the t-values for responses of 16% (approximately -1 S.D.), 50% (zero S.D.), and 84% (approximately +1 S.D.). Using these data as starting points for subsequent response entries from the user, the computer proceeds much more quickly to the final answer than it would were it to start from zero each time.

OPERATION

Load FOCAL into core. When FOCAL is ready, an asterisk (*) is typed in the left margin. Now load the paper tape marked DOSE-RESPONSE ROUTINE.

When loaded, the program first requests the dose, then the percentage response to that dose. These responses are typed in by the operator, each being terminated by pressing the space bar. Up to two places to the right of the decimal point are accepted. Integration being fairly slow, a few seconds may elapse before the computer prints the log dose and probit values.

In its present form the program achieves good accuracy, at reasonable computational speed, with the base of the integration rectangle set to 0.04 times the standard deviation. Greater accuracy, albeit at reduced speed, is obtained by a finer division of the area under the curve. Conversely, faster computation but at the price of reduced accuracy, is achieved by resetting this variable (HOR) from 0.04 to 0.1. HOR is initialized on line 01.10 in the program.

The 8K version is similar to the preceding except that it incorporates a plotting routine, and signals the operator with the typewriter bell that calculation is in progress. In this version, the user terminates data input and initiates the plotting routine by typing ZEZE. Having stored the lowest and highest log dose values the program then scales these to the nearest logarithmic multiple of two and increments the scale by two if an even multiple is encountered. With scaling completed, a log dose-probit response scattergram is printed. Log dose and its antilog appear on the bottom of the horizontal coordinate.

REFERENCES

A worthwhile discussion of the log dose-response curve and probit transformation may be found in *BIostatISTICS* by Avram Goldstein (MacMillan Co., New York, 1964). The subject is treated exhaustively in *PROBIT ANALYSIS* by D. J. FINNEY (Cambridge University Press, Cambridge, 1964).

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*
*C-8K FOCAL @1969
*
*01.05 TYPE !"DOSE-RESPONSE ROUTINE"!;ERASE                                4K VERSION
*01.10 SET HOR=0.04
*01.11 TYPE !"USE THE SPACE BAR BETWEEN DATA"!
*01.15 TYPE !!!"WORKING - PLEASE WAIT"!;GOTO 11.1
*01.17 ASK "DOSE"LO;DO 4
*01.20 SET X=-5;SET A=0;ASK "      % RESPONSE", RE,!;TYPE %5.04 "LOG"LO
*
*02.10 IF (RE-17)10.3;SET N3=0;DO 3
*02.20 IF (RE-51)10.5;SET N3=2;DO 3
*02.30 IF (RE-85)10.5;SET N3=4;DO 3;GOTO 10.5
*
*03.10 SET A=AV(N3);SET X=AV(N3+1)
*
*04.05 IF (LO)4.1,1.17,4.1
*04.10 SET LO=FLOG(LO)/FLOG(10);RETURN
*
*05.50 TYPE %4.02 "      PROBIT"X+5,!!;GOTO 1.17
*
*10.30 SET A=<[1/FSQT(2*3.14159)]*FEXPL[-(X*X/2)]>*HO+A
*10.35 IF (RE/100-A) 5.5,5.5
*10.50 SET X=X+HO
*10.55 IF (X-5+HO) 10.3;GOTO 5.5
*
*11.10 SET X=-5;SET A=0;SET RE=16;DO 12
*11.20 SET RE=50;DO 2.1;DO 10.5;DO 12
*11.30 SET RE=84;DO 2.2;DO 10.5;TYPE !;DO 12;SET N=1;GOTO 1.17
*
*12.10 DO 10.3;IF (RE/100-A) 12.3,12.3;DO 10.5;GOTO 12.1
*12.30 SET AV(N)=A;SET AV(N+1)=X;SET N=N+2
*G

```

DOSE-RESPONSE ROUTINE

USE THE SPACE BAR BETWEEN DATA

WORKING - PLEASE WAIT

DOSE:7.5 % RESPONSE:3
LOG= 0.8751 PROBIT= 3.12

DOSE:10 % RESPONSE:60
LOG= 1.0000 PROBIT= 5.24

DOSE:12.5 % RESPONSE:95
LOG= 1.0969 PROBIT= 6.64

DOSE:15 % RESPONSE:100
LOG= 1.1761 PROBIT= 10.00

```

01.05 T !"DOSE-RESPONSE CURVE"!;E
01.10 S HOR=0.04;S LK=99;S LG=-99
01.11 T !"USE THE SPACE BAR BETWEEN DATA"! "TERMINATE WITH ZEZE"
01.15 T " AFTER DOSE IS ASKED"!!"WORKING - PLEASE WAIT"!;G 11.1
01.17 A "DOSE"PL(N);I (0ZEZ-PL(N))7.05,7.05;S LO=PL(N);D 4;S PL(N)=LO
01.20 S X=-5;S A=0;A " % RESPONSE", RE,1;T %5.04 "LOG"PL(N)
01.40 I (PL(N)-LG)1.5;S LG=PL(N)
01.50 I (LK-PL(N))2.1;S LK=PL(N)

02.10 I (RE-17)10.3;S N3=0;D 3
02.20 I (RE-51)10.5;S N3=2;D 3
02.30 I (RE-85)10.5;S N3=4;D 3;G 10.5

03.10 S A=AV(N3);S X=AV(N3+1)

04.05 I (LO) 4.1,1.17,4.1
04.10 S LO=FLOG(LO)/FLOG(10);R

05.50 S PL(N+1)=X+5;S N=N+2;T %4.02 " PROBIT"X+5,!!;G 1.17
05.60 S N=N-1;T !! "PROBITS";F X=1,18;T " "
05.65 T "PROBITS VS LOG DOSE"!;S X=0
05.70 T %4.02 10-X/4,#;D 6;S X=X+1;I (X-4)5.8;T 1;G 5.85
05.80 T !;G 5.7
05.85 T " "
05.91 T "I";F X=1,14;T "- "
05.94 D 5.91;D 5.91;D 5.91;T "I"
05.95 T ! " %4.01,LK
05.97 S A=(LG-LK)/4;D 5.85;T A+LK;D 5.85;T 2*A+LK;D 5.85;T 3*A+LK
05.98 D 5.85;T LG,!;F X=1,33;T " "
05.99 T " LOG DOSE";D 8;D 1.1;S N=1;G 1.17

06.40 S PL=1
06.50 I (PL(PL+1)-(10-X/4)+0.125)6.55;G 6.65
06.55 S PL=PL+2;I (PL-N)6.5;R
06.65 T " ";F N3=LK,(LG-LK)/60,PL(PL);T " "
06.70 S PL(PL+1)=-1;T "*"#;G 6.55

07.05 T !;S X=1;S A=0
07.10 S LO=X;D 4;I (LK-LO)7.4,7.55,7.2
07.20 S X=X*2;S A=A+1;S LO=X;D 4.1;I (LK-LO)7.5,7.55,7.2
07.40 S X=X/2;S A=A-1;G 7.1
07.50 S LK=FLOG(X/2)/FLOG(10);G 7.6
07.55 S X=X*2;S A=A+1;G 7.5
07.60 S X=1
07.65 S LO=X;D 4.1;I (LO-LG)7.7,7.95,7.75
07.70 S X=X*2;S A=A-1;G 7.65
07.75 S X=X/2;S A=A+1;S LO=X;D 4.1;I (LG-LO)7.75
07.77 S A=FABS(A);I (A/2-FITR(A/2))7.9,7.9;S X=X*2
07.90 S LG=FLOG(X*2)/FLOG(10);G 5.6
07.95 S X=X/2;S A=A+1;G 7.77

08.10 S X=LK;D 8.5;T 1,%4.02," "X;S X=A+LK;D 8.6;S X=2*A+LK;D 8.6
08.20 S X=3*A+LK;D 8.6;S X=LG;D 8.6;T 1;F X=1,33;T " "
08.30 T "TRUE DOSE"!!!!;R
08.50 S X=FEXP(X*FLOG(10))
08.60 D 8.5;D 5.85;T X;R

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10.30 S A=<[1/FSQT(2*3.14159)]*FEXP[-(X*X/2)]>*H0+A
10.35 I (RE/100-A) 5.5,5.5
10.50 S X=X+H0;S LC=LC+1;I (LC-20)10.55;S LC=0;T ""
10.55 I (X-5+H0) 10.3;G 5.5

11.10 S X=-5;S A=0;S RE=16;D 12
11.20 S RE=50;D 2.1;S X=X+H0;D 12
11.30 S RE=84;D 2.2;S X=X+H0;T !;D 12;S N=1;O 1.17

12.10 D 10.3;I (RE/100-A) 12.3,12.3;S X=X+H0;G 12.1
12.30 S AV(N)=A;[AV(N+1)=X;S N=N+2

DOSE-RESPONSE CURVE

8K VERSION

USE THE SPACE BAR BETWEEN DATA
TERMINATE WITH ZEZE AFTER DOSE IS ASKED

WORKING - PLEASE WAIT

DOSE:.81 % RESPONSE:30
LOG=-0.0915 PROBIT= 4.48

DOSE:2.43 % RESPONSE:38
LOG= 0.3856 PROBIT= 4.68

DOSE:7.29 % RESPONSE:62
LOG= 0.8627 PROBIT= 5.32

DOSE:21.9 % RESPONSE:73
LOG= 1.3405 PROBIT= 5.60

DOSE:65.7 % RESPONSE:85
LOG= 1.8176 PROBIT= 6.04

DOSE:ZEZE

PROBITS

PROBITS VS LOG DOSE

- = 10.00
- = 9.75
- = 9.50
- = 9.25
- = 9.00
- = 8.75
- = 8.50
- = 8.25
- = 8.00
- = 7.75
- = 7.50
- = 7.25
- = 7.00
- = 6.75
- = 6.50
- = 6.25
- = 6.00
- = 5.75
- = 5.50
- = 5.25
- = 5.00
- = 4.75
- = 4.50
- = 4.25
- = 4.00
- = 3.75
- = 3.50
- = 3.25
- = 3.00
- = 2.75
- = 2.50
- = 2.25
- = 2.00
- = 1.75
- = 1.50
- = 1.25
- = 1.00
- = 0.75
- = 0.50
- = 0.25
- = 0.00

	I		I		I		I		I
=	0.3	=	0.3	=	0.9	=	1.5	=	2.1
					LOG DOSE				
=	0.50	=	2.00	=	8.00	=	32.00	=	128.0
					TRUE DOSE				

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