A NEW VERSION OF MULTI (ELS) FOR EXTENDED NONLINEAR LEAST SQUARES

Kiyoshi Yamaoka and Hisashi Tanaka

Faculty of Pharmaceutical Sciences, Kyoto University, Sakyo-ku, Kyoto 606, Japan

(Received June 14, 1986)

A new version of MULTI (ELS) written in BASIC was presented for population pharmacokinetics for microcomputers. The program is provided with four algorithms of extended nonlinear least squares (steepest descent method, quasi-Newton method with DFP formula, quasi-Newton method with BFGS formula and simplex method). Four transformations of parameters can be selected to impose constraints on the parameters (no constraint on a parameter. $\Pi_i = Q_i$, $\Pi_i = B + (A - B) \cdot \sin^2(Q_i)$ and $\Pi_i = B + (A - B) \cdot \exp(Q_i)/(1 + \exp(Q_i))$, where $\Pi_i$ denotes a population mean parameter or variance of inter- and intra-individual variations, $Q_i$ is an intermediate parameter, $A$ and $B$ are lower and upper limits of $\Pi_i$. The definition of a population model and the modifications for BASIC compiler in the new version of MULTI (ELS) are the same as in the old version.

**Keywords** — population pharmacokinetics; extended least squares; quasi-Newton; DFP formula; BFGS formula; simplex; parameter transformation

INTRODUCTION

An extended nonlinear least squares program, MULTI (ELS), for microcomputers was announced in this journal. A new version of MULTI (ELS) has recently been developed. A new version written in the Microsoft BASIC or in FORTRAN 77 is now available. The purpose of the present report is to publish the new version of MULTI (ELS), to explain the usage of the MULTI (ELS) and to compare the convergence of the new version with that of the old version. The new version is simply called MULTI (ELS) in the subsequent sections.

**Algorithms for Extended Least Squares**

Figure 1 presents the source list of a new version (V. 1986) of MULTI (ELS) written in BASIC. While the old version is provided with two algorithms, MULTI (ELS) is provided with the following four extended least squares algorithms, i.e. (1) Steepest Descent Method, (2) Quasi-Newton Method with DFP Formula, (3) Quasi-Newton Method with BFGS Formula and (4) Simplex Method.

The first algorithm is the most simple one. The second which was first proposed by Davidon was followed by Fletcher and Powell. This algorithm is well known as Davidon’s method. The third algorithm was recently proposed by Broyden, Fletcher, Goldfarb and Shanno.

**MULTI (ELS) V1986**

5 DEFINT I-N:EP=1E-10:EM=1E+10:DF=.5:PC=.000001:DP=.001:DV=.01
10 PRINT"**************************************************"
11 PRINT"MULTI-LINES FITTINGS (1986)"
12 PRINT"BY EXTENDED LEAST SQUARES METHOD"
17 PRINT"**************************************************"
18 REM-- COPYRIGHT (C) MAY 1 (1986), BY KIYOSHI YAMAOKA--
19 REM-- FACULTY OF PHARMACEUTICAL SCIENCES IN KYOTO UNIVERSITY--
24 PRINT:PRINT"DEFINE EQUATIONS AT 1000, 1100, 1200, 1300, 1400."
25 PRINT:"CP IS DEPENDENT VARIABLE."DIM ME$(4)
27 PRINT:"T(1), T(2), T(3), ... ARE INDEPENDENT VARIABLES."
30 PRINT:"P(1), P(2), ..., ARE MEAN PARAMETERS TO ESTIMATE."
31 PRINT:"E(1), E(2), ..., ARE INTER-INDIVIDUAL VARIATIONS."
32 PRINT:"E(1), E(2), ..., ARE INTRA-INDIVIDUAL VARIATIONS."
33 PRINT:"** AN EXAMPLE FOR ONE-COMPARTMENT MODEL **"
34 PRINT"C1 1000 CP=(P(1)+E(1))*EXP(-(P(2)+E(2))*T(1))+E(1)"
36 ME$(1)="STEEPEST DESCENT":ME$(2)="QUASI-NEWTON(DFP FORMULA)"
37 ME$(3)="QUASI-NEWTON(BFGS FORMULA)":ME$(4)="SIMPLEX"
38 PRINT:FOR I=1 TO 4:PRINT"("":I"":):ME$(I)"": METHOD":NEXT I:PRINT
INPUT "WHICH ALGORITHM DO YOU SELECT (1.2.3.4)" : AL
IF (AL = 1) OR (AL = 2) OR (AL = 3) OR (AL = 4) THEN 40
PRINT : PRINT "NON-DIAGONAL ELEMENTS OF OMEGA MATRIX ARE ALL ZERO (Y/N)" : CO$$$
IF CO$$$ = "N" THEN SU = 1
PRINT : PRINT "* I BELIEVE YOU HAVE DEFINED EQUATIONS *"
INPUT "SUBJECT NAME " : NS$$
INPUT "NUMBER OF MEAN PARAMETERS (P) " : MP
PRINT "NUMBER OF INTER-INDIVIDUAL VARIATIONS (ES) " : ME
PRINT "NUMBER OF INTRA-INDIVIDUAL VARIATIONS (EE) " : MG
IF SU = 0 THEN M = MP + MG + ME : GOTO 52
M = MP + MG + ME $$ ME + 1)/2
M1 = MP + MG + ME
INPUT "NUMBER OF INDEPENDENT VARIABLES (TT) " : NV
INPUT "NUMBER OF GROUPS (CP) " : LN$$
DIM N(LN) FOR I = 1 TO LN
PRINT "NUMBER OF TIME COURSES IN GROUP (" : I : ")" : INPUT N(I) : NEXT I
NM = 0: FOR I = 1 TO LN: IF NM = N(I) THEN NM = N(I)
NEXT I: DIM NN(N(LN), NM) : N = 0: FOR I = 1 TO LN: PRINT FOR J = 1 TO N(I)
PRINT "NUMBER OF POINTS OF " : J : " TIME COURSE IN " : I : " GROUP:"
INPUT NN(I, J) : N = N + NN(I, J) : NEXT J: NEXT I : DIM PL(M), PU(M)
IF N(LN) = 1 THEN DIM V1(NM, NM)
IF N(LN) = 2 THEN DIM V2(NM, NM)
IF N(LN) = 3 THEN DIM V3(NM, NM)
IF N(LN) = 4 THEN DIM V4(NM, NM)
IF N(LN) = 5 THEN DIM V5(NM, NM)
FOR K = 1 TO LN: FOR J = 1 TO N(K): PRINT PRINT "* * * * GROUP: K: * * * *"
NEXT K: NEXT LN
FOR I = 1 TO VN PRINT "TT (" : L : ") OF " : I : " TH POINT:"
NEXT I: NEXT L
PRINT "CP OF " : I : " TH POINT:" : INPUT CY(K, J, I)
NEXT J: NEXT K : DIM CN(S)$$
PRINT : PRINT "* * * * CONSTRAINTS ON P(I) * * * * : CN(S) = " " NO CONSTRAINT"
CNS$$ = 2$$ P(I) = Q(I) * Q(I) : CNS$$ = " P(I) + B(A-B) * SIN^2(Q(I))"
CNS$$ = 4$$ P(I) = B(A-B) * EXP(Q(I)) / (1 + EXP(Q(I)))
PRINT FOR I = 1 TO 4: PRINT" (: I : ) " ; CNS$$ = I : NEXT I : PRINT
PRINT "WHICH CONSTRAINT DO YOU SELECT (1.2.3.4) " : NC
IF (NC = 1) OR (NC = 2) OR (NC = 3) OR (NC = 4) THEN 98
PRINT : PRINT "FOR I = 1 TO MP PRINT "INITIAL P (" : I : ") " : INPUT P(I)
IF NC = 2 THEN PRINT "LOWER. UPPER LIMITS OF P (" : I : ")": INPUT PL(I), PU(I)
NEXT I: FOR I = 1 TO MG PRINT "INITIAL SIGMA^2 (" : I : ")": INPUT P(MP + I)
NEXT I: FOR I = 1 TO MG PRINT "LOWER. UPPER LIMITS OF SIGMA^2 (" : I : ")": INPUT P(MP + MG + I)
NEXT I: FOR I = 1 TO MP PRINT "INITIAL OMEGA^2 (" : I : " )": INPUT P(MPG + I)
NEXT I: FOR I = 1 TO MP PRINT "LOWER. UPPER LIMITS OF OMEGA (" : I : ")": INPUT P(MPG + MG + I)
NEXT I: IF SU = 0 THEN 118
I = 0: FOR I = 1 TO ME: FOR J = I + 1 TO ME: I = I + 1
NEXT J: NEXT I
FOR I = 1 TO M: ON NC GOSUB 5000.5010.5020.5030: NEXT I
GOSUB 4000: OB = SS PRINT "INITIAL OBJECT FUNCTION = " : SS: IF AL = 4 THEN 3000
REM$$$ QUASI-NEWTON METHOD $$$
FOR I = 1 TO M: X0(I) = Q(I) : NEXT I: FOR I = 1 TO M: FOR J = I TO M
H(I, J) = 0: IF I = J THEN HH(I, J) = 1
NEXT J: NEXT I: FOR KK = 1 TO 200
FOR I = 1 TO M: Q(I) = X0(I) + DQ: GOSUB 4000.0000: DS = SS
Q(I) = X0(I) + DP: GOSUB 4000.0000: (DS - SS) / 2: DP: NEXT I: FOR I = 1 TO M
DP = 0: FOR J = I TO M: DD(I) = DD(I) - HH(I, J) * GR(I): NEXT J: NEXT I: AP = 1
NEXT I: IF K = 1 THEN M: XI = X0: AP = DD: NEXT 1
NEXT I = 1 TO M: Q(I) = XI(I): NEXT I: GOSUB 4000
IF SS < OB THEN AP = DP * AP: GOTO 180
IF ABS(OB - SS) < PC * ABS(OB) THEN 730: REM -- CHECK OF CONVERGENCE --
PRINT "OB = SS PRINT "LOOP = " : KK
FOR I = 1 TO MP PRINT "P (" : I : ") = " : P(I): NEXT I
FOR I = 1 TO MG PRINT "SIGMA^2 (" : I : " ) = " : P(MP + I): NEXT I
196 FOR I=1 TO ME:PRINT "OMEGA^2(";I");")=":P(MP+MG+1):NEXT I
197 IF SW=0 THEN 203
198 J=0:FOR I=1 TO ME-1:FOR J=I+1 TO ME:I=I+1
199 PRINT "OMEGA(";I");",":P(MI+J):NEXT J:NEXT I
200 PRINT "OBJECT FUNCTION=":SS
201 FOR I=1 TO M:Q(I)=X(I)+DP*:GOSUB 4000:DS=SS
202 Q=1:FOR I=1 TO M:Q(I)=X(I)+X(I):GG(I)=G(I)-GR(I):NEXT I
203 DG=0:FOR I=1 TO M:DG=DG+X(I):GG(I):NEXT I
204 IF AL=1 THEN 710
205 IF AL=2 THEN 500
206 REM**** CALCULATION BY BFGS FORMULA ****
207 FOR I=1 TO M:FOR J=1 TO M:A(I,J)=0:FOR K=1 TO M:FOR L=1 TO M
208 HH=0:IF K=L THEN HH=1
209 H1=HH*:XD(I)*GG(K)/DG
210 HH=0:IF L=J THEN HH=1
211 H2=HH*:XD(I)*GG(L)/DG
213 REM**** CALCULATION BY DFP FORMULA ****
214 FOR I=1 TO M:FOR J=1 TO M:H=HG+HH(I,J)*GG(I)*GG(J):NEXT J:NEXT I
215 FOR I=1 TO M:FOR J=1 TO M:H1=HH*:XD(I)*DG
216 H2=HH*:XD(I)*DG
217 NEXT K:NEXT H
218 NEXT K:NEXT J:GOTO 700
219 REM**** EXIT FROM LOOP ****
220 PRINT:"PRINT "+":ME$(AL)": METHOD"
221 PRINT:"- CONSTRAINTS ON P(I)=":CN$(NC)="-"'
222 PRINT "LOOP=":KK
223 FOR I=1 TO MP:PRINT "P(";I");")=":P(I):NEXT I
224 FOR I=1 TO MG:PRINT "SIGMA^2(";I");")=":P(MP+1):NEXT I
225 FOR I=1 TO ME:PRINT "OMEGA^2(";I");")=":P(MP+MG+1):NEXT I
226 IF SW=0 THEN 765
227 IF J=0 FOR I=1 TO ME-1:FOR J=I+1 TO ME:I=I+1
228 PRINT "OMEGA(I)=":I":")=":P(MI+J):NEXT J:NEXT I
229 PRINT "FINAL OBJECT FUNCTION=":SS:PRINT "AKAIKE'S AIC=":SS+2*M
230 PRINT "INPUT DO YOU DISPLAY INPUT AND PREDICTED VALUES(Y/N)";CO$'
231 IF CO$>"Y" THEN 840
232 FOR I=1 TO IG:LN:FOR J=1 TO N(IG):PRINT:PRINT "**** GROUP";IG:"****
233 PRINT "=":J":TH TIME COURSE="":2
234 FOR I=1 TO NN(IG,J):FOR L=1 TO NV:PRINT "T(";I");") OF");I":TH POINT=";
235 PRINT TX(IG,J,I,L);TT(L)=TX(IG,J,I,L):NEXT L:GOSUB 900
236 PRINT "CP OF")";I":TH POINT="":PRINT CY(IG,J,I,L);"):(PRED=":CP:"
237 NEXT I:NEXT J:NEXT I
238 PRINT:"FOR I=1 TO 4:PRINT(";I");")":ME$(I)"": METHOD";NEXT I
239 PRINT "(-1) END":PRINT
240 INPUT " WHICH ALGORITHM DO YOU SELECT(1,2,3,4 OR -1)";AL
241 IF AL=1 THEN END
242 IF AL=2 THEN 780
243 IF AL=3 THEN 880
244 IF AL=4 THEN 1500
245 PRINT:PRINT "GOTO 940"
246 REM-----------------------------------------------------------------------------------
247 REM**** GAUSS-JORDAN METHOD ****
248 FOR I=1 TO NS:IB(I)=I:NEXT I
249 FF=1:DE=1:FOR K=1 TO NS:PP=0:FOR J=K TO NS
250 IF ABS(PP)<ABS(B(K,J)) THEN L=J:PP=B(K,J)
251 NEXT J:IF ABS(PP)<EP THEN PRINT "MATRIX IS SINGULAR.";END
252 IF L=K THEN 2010
253 IF L=1 THEN 2070
254 IF (A(I)>1)*(A(I)>2)*(A(I)>3)*(A(I)>4) THEN 850
255 GOTO 940
256 REM-----------------------------------------------------------------------------------
257 REM-----------------------------------------------------------------------------------
New MULTI (ELS)
Constraints on Parameters to Estimate

The old version of MULTI (ELS) attains the imposition of constraints on the parameters by a simple clipping method. The new version performs the constraints by the following transformations of parameters to estimate, i.e. (1) No Constraints on Parameters, (2) $\pi_i = \frac{q_i^2}{\theta}$, (3) $\pi_i = B + (A - B) \cdot \sin^2(q_i)$, and (4) $\pi_i = B + (A - B) \cdot \exp(q_i) / (1 + \exp(q_i))$. $\pi_i$ specifies a population mean parameter of a variance of inter- and intra-individual variations, $q_i$ an intermediate parameter and $A$ and $B$ the lower and the upper limits of the constraints, respectively. $\pi_i$ always takes the positive value by transformation 2. Transformations 3 and 4 make $\pi_i$ take the values between $A$ and $B$. Even if constraint 1 is selected, MULTI (ELS) imposes constraint 2 on the variances of inter- and intra-individual variations (i.e. the diagonal elements of $\Sigma$ or $\Omega$ matrix) always take positive values. When one of the constraints from 2 through 4 is selected, MULTI (ELS) imposes these constraints not only on the population mean parameters but also on all elements of inter- and intra-individual matrices.

Comparison of MULTI (ELS) with old Version

Figure 2 presents an execution of MULTI (ELS) for five time courses which are given as example 2 in Table III of the reference. The underlines in Fig. 2 specify the input from the keyboard. The others specify the output from MULTI (ELS). The initial values for the parameters are purposefully deviated far away from the final converged values. Algorithm 4 (the simplex method) and constraint 2 ($\pi_i = \frac{q_i^2}{\theta}$) are selected in the execution. The converged values of the parameters and the final objective function (Ob = 12.65) agree with those given by NONMEM. Even when constraint 1 (no constraint on parameters) was selected, the simplex method gave reasonable converged values. On the other hand, the old version stopped the calculation after 200 loops to give the final objective function (Ob = 12.69) which is almost the
same as the new version. However, the efficiency of convergence of the old version is worse than that of the new version. Figure 3 shows an execution of MULTI (ELS), when algorithm 2 (quasi-Newton with DFP formula) and constraint 3 \( (P_i = B + (A - B) \cdot \sin^{2}(Q_i)) \) were selected. In the selection of constraint 3 or 4, the lower and upper limits must be directed. The converged values of parameters and the objective function agree with those given by NONMEM. The old version stopped the calculations after 19 loops to give an improper final object function \( (Ob = 181) \).

**EX. OF MULTI (ELS) V1986**

1000 CP=(P(1)+ES(1)) * EXP(-(P(2)+ES(2)) * TT(1)) + EE(1):RETURN

RUN

******************************************************************************
*  MULTI-LINES FITTINGS(1986)  *
*  BY EXTENDED LEAST SQUARES METHOD  *
******************************************************************************

DEFINE EQUATIONS AT 1000,1100,1200,1300,1400.
CP IS DEPENDENT VARIABLE.
TT(1),TT(2),TT(3), ... ARE INDEPENDENT VARIABLES.
P(1),P(2), ... ARE MEAN PARAMETERS TO ESTIMATE.
ES(1),ES(2), ... ARE INTER-INIVIDUAL VARIATIONS.
EE(1),EE(2), ... ARE INTRA-INIVIDUAL VARIATIONS.

** AN EXAMPLE FOR ONE-COMPARTMENT MODEL **
[ 1000 CP=(P(1)+ES(1)) * EXP(-(P(2)+ES(2)) * TT(1)) + EE(1) ]

( 1 ) STEEPEST DESCENT METHOD
( 2 ) QUASI-NEWTON(DFP FORMULA) METHOD
( 3 ) QUASI-NEWTON(BFGS FORMULA) METHOD
( 4 ) SIMPLEX METHOD

WHICH ALGORITHM DO YOU SELECT(1,2,3,4) 4

NON-DIAGONAL ELEMENTS OF OMEGA MATRIX ARE ALL ZERO (Y/N) Y

* I BELIEVE YOU HAVE DEFINED EQUATIONS *
SUBJECT NAME EXAMPLE2
NUMBER OF MEAN PARAMETERS(P) 2
NUMBER OF INTER-INIVIDUAL VARIATIONS(ES) 2
NUMBER OF INTRA-INIVIDUAL VARIATIONS(EE) 1
NUMBER OF INDEPENDENT VARIABLES(TT) 1
NUMBER OF GROUPS(CP) 1
NUMBER OF TIME COURSES IN GROUP( 1 ) 5

NUMBER OF POINTS OF 1 TH TIME COURSE IN 1 TH GROUP 5.
NUMBER OF POINTS OF 2 TH TIME COURSE IN 1 TH GROUP 5.
NUMBER OF POINTS OF 3 TH TIME COURSE IN 1 TH GROUP 5.
NUMBER OF POINTS OF 4 TH TIME COURSE IN 1 TH GROUP 5.
NUMBER OF POINTS OF 5 TH TIME COURSE IN 1 TH GROUP 5.

**** GROUP 1 ****
----- 1 TH TIME COURSE -----
TT( 1 ) OF 1 TH POINT 8.35
CP OF 1 TH POINT 8.35
TT( 1 ) OF 2 TH POINT 6.86
CP OF 2 TH POINT 6.86
TT( 1 ) OF 3 TH POINT 5.66
CP OF 3 TH POINT 5.66
TT( 1 ) OF 4 TH POINT 5.67
CP OF 4 TH POINT 5.67
TT( 1 ) OF 5 TH POINT 3.31
CP OF 5 TH POINT 3.31
**** GROUP 1 ****
---- 2 TH TIME COURSE ----
TT(1) OF 1 TH POINT 0
CP OF 1 TH POINT 11.6
TT(1) OF 2 TH POINT 3
CP OF 2 TH POINT 8.9
TT(1) OF 3 TH POINT 6.52
CP OF 3 TH POINT 7.92
TT(1) OF 4 TH POINT 1.2
CP OF 4 TH POINT 5.98

**** GROUP 1 ****
---- 3 TH TIME COURSE ----
TT(1) OF 1 TH POINT 0
CP OF 1 TH POINT 10.3
TT(1) OF 2 TH POINT 3
CP OF 2 TH POINT 8.78
TT(1) OF 3 TH POINT 6.5
CP OF 3 TH POINT 7.92
TT(1) OF 4 TH POINT 1.2
CP OF 4 TH POINT 5.21

**** GROUP 1 ****
---- 4 TH TIME COURSE ----
TT(1) OF 1 TH POINT 0
CP OF 1 TH POINT 8.09
TT(1) OF 2 TH POINT 3
CP OF 2 TH POINT 6.6
TT(1) OF 3 TH POINT 6.5
CP OF 3 TH POINT 7.1
TT(1) OF 4 TH POINT 1.2
CP OF 4 TH POINT 5.34

**** GROUP 1 ****
---- 5 TH TIME COURSE ----
TT(1) OF 1 TH POINT 0
CP OF 1 TH POINT 8.03
TT(1) OF 2 TH POINT 3
CP OF 2 TH POINT 7.26
TT(1) OF 3 TH POINT 6.46
CP OF 3 TH POINT 6.21
TT(1) OF 4 TH POINT 1.2
CP OF 4 TH POINT 5.22

**** CONSTRAINTS ON P(I) ****
(1) NO CONSTRAINT
(2) P(I)=Q(I)*Q(I)
(3) P(I)=B+(A-B)*SIN^2(Q(I))
(4) P(I)=B+(A-B)*(EXP(Q(I))/(1+EXP(Q(I))))

WHICH CONSTRAINT DO YOU SELECT(1,2,3,4) 2

INITIAL P(1) 20
INITIAL P(2) 1
INITIAL SIGMA^2(1) 1
INITIAL OMEGA^2(1) 1
INITIAL OMEGA^2(2) 1
INITIAL OBJECT FUNCTION= 373.791

*EXAMPLE2* BY SIMPLEX METHOD
- CONSTRAINTS ON P(I): P(I)=Q(I)*Q(I) -
LOOP= 187
P( 1 )= 9.15267
P( 2 )= .490044
SIGMA^2( 1 )= .389476
OMEGA^2( 1 )= .977343
OMEGA^2( 2 )= 8.4232E-04
FINAL OBJECT FUNCTION= 12.6511
AKAIKE'S AIC= 22.6511

DO YOU DISPLAY INPUT AND PREDICTED VALUES(Y/N) N

( 1 ) STEEPEST DESCENT METHOD
( 2 ) QUASI-NEWTON(DFP FORMULA) METHOD
( 3 ) QUASI-NEWTON(BFGS FORMULA) METHOD
( 4 ) SIMPLEX METHOD
(-1 ) END

WHICH ALGORITHM DO YOU SELECT(1,2,3,4 OR -1)=1

FIG.2

Comments on MULTI (ELS)

There are three important variables (PC, DP and DV) at line 5 in Fig. 1. These variables may be changed by the user to attain the optimum computation of the extended nonlinear least squares method. PC is the criterion for convergence. The small PC value specifies the severe convergent condition. DP is used to calculate the numerical differentials for population mean parameters (lines 150—160 and lines 204—207). DV is used to calculate the differentials for the inter- and intra-individual variations (lines 4010—4029). If the user needs a calculation of double precision, the single precision variables (DE, PP, B (1,j), W and AI) which appear at LINES 2000—2190 can be changed to the double precision variables.

*********************************************************
* MULTI-LINES FITTINGS(1986)                          *
* BY EXTENDED LEAST SQUARES METHOD                     *
*********************************************************

DEFINE EQUATIONS AT 1000.1100.1200.1300.1400.
CP IS DEPENDENT VARIABLE.
TT(1),TT(2),TT(3), ... ARE INDEPENDENT VARIABLES.
P(1),P(2), ... ARE MEAN PARAMETERS TO ESTIMATE.
ES(1),ES(2), ... ARE INTER-INDIVIDUAL VARIATIONS.
EE(1),EE(2), ... ARE INTRA-INDIVIDUAL VARIATIONS.

** AN EXAMPLE FOR ONE-COMPARTMENT MODEL **
[ 1000 CP=(P(1)+ES(1))×EXP(-(P(2)+ES(2))×TT(1))+EE(1) ]

( 1 ) STEEPEST DESCENT METHOD
( 2 ) QUASI-NEWTON(DFP FORMULA) METHOD
( 3 ) QUASI-NEWTON(BFGS FORMULA) METHOD
( 4 ) SIMPLEX METHOD

WHICH ALGORITHM DO YOU SELECT(1,2,3,4)=2

*** CONSTRAINTS ON P(1) ***
( 1 ) NO CONSTRAINT
( 2 ) P(1)=Q(1)×Q(I)
( 3 ) P(1)=B+(A-B)×SIN^2(Q(I))
( 4 ) P(1)=B+(A-B)×EXP(Q(I))/(1+EXP(Q(I)))

WHICH CONSTRAINT DO YOU SELECT(1,2,3,4)=3
INITIAL P(1)  20.
LOWER, UPPER LIMITS OF P(1)  5, 30
INITIAL P(2)  1
LOWER, UPPER LIMITS OF P(2)  0, 2
INITIAL SIGMA^2(1)  1
LOWER, UPPER LIMITS OF SIGMA^2(1)  0, 2
INITIAL OMEGA^2(1)  1
LOWER, UPPER LIMITS OF OMEGA^2(1)  0, 2
INITIAL OMEGA^2(2)  1
LOWER, UPPER LIMITS OF OMEGA^2(2)  0, 2
INITIAL OBJECT FUNCTION= 373.792

*EXAMPLE2* BY QUASI-NEWTON(DFP FORMULA) METHOD
- CONSTRAINTS ON P(I): P(I) = B+(A-B)*SIN^2(Q(I)) -
LOOP= 18
P(1) = 9.14635
P(2) = .490221
SIGMA^2(1) = .391782
OMEGA^2(1) = .971462
OMEGA^2(2) = 7.54476E-04
FINAL OBJECT FUNCTION= 12.6519
AKAIKE'S AIC = 22.6519

DO YOU DISPLAY INPUT AND PREDICTED VALUES(Y/N)? N

( 1 ) STEEPEST DESCENT METHOD
( 2 ) QUASI-NEWTON(DFP FORMULA) METHOD
( 3 ) QUASI-NEWTON(BFGS FORMULA) METHOD
( 4 ) SIMPLEX METHOD
(-1 ) END

WHICH ALGORITHM DO YOU SELECT(1,2,3,4 OR -1)? -1

FIG.3

REFERENCES