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Simulation of Chromatography: The Relationship between Position Peak and Exit Peak

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A set of three programs for the simulation of chromatography based on the discrete flow model (one of plate theories) in the linear isotherms were developed. The main of them is that of the relationship between position peak and exit peak (chromatogram). This program represents the elemental processes of column operations and the resulting exit peak by step-by-step operations, and satisfactory results were obtained. The other two, those of position peak and exit peak, were developed for the need of explanations, though these kinds of programs were already reported by other investigators. Using these programs, especially the "tailing" of chromatogram in linear isotherm is discussed.

One of the most simple theories of chromatography is the discrete flow model (one of plate theories). This model has been well-illustrated using counter-current chromatography (CCC), because the theory is simple[1, 2]. Programs and/or results for the simulation of chromatography based on the theory for the linear isotherms were already reported[2, 3]. Two kinds of chromatographic peaks exist: that are still on a column (position peaks) and for these peaks as they leave the column (exit peaks or chromatograms)[2]. The reported programs and/or results are for the two kinds of peaks, and they are useful themselves. However, they alone can not give a thorough understanding of chromatographic basis, especially of the relationship between the position and exit peaks. Therefore, the author developed a program to understand the relationship. Further, the programs for the position and exit peaks were also developed for the need of explanations.

Theory

In CCC, column operations consist of two kinds of elemental processes: the equilibration of solute molecules between the stationary and mobile phases in each tube and the subsequent transfer of the series of mobile phases to the next tubes. Alternate repetitions of these two processes transfer the solutes at their intrinsic velocities. Thus, the solutes are separated. Each tube corresponds to a theoretical plate in the plate theory[2].

At equilibrium, the solute is partitioned between two phases according to the capacity factor, k', as follows:

$$k' = n_S/n_M = (C_S V_S)/(C_M V_M) = K (V_S/V_M) \qquad \cdots\cdots(1)$$

In Eq 1, n, C, V and K represent amount of the solute, concentration of the solute, volume of the phase and partition coefficient of the solute, respectively. Subscripts S and M represent the stationary and mobile phases, respectively. If the conditions of CCC remain constant, the phase ratio (V_S/V_M) is to be constant. Solutes have their intrinsic values of K; these values are independent of the concentrations in linear isotherms.

Equations representing the position and exit peaks are derived from the theory mentioned above; they are Eqs. 2 and 3, respectively[1, 2]. The exit peak also can be drawn using Eq. 2. In this paper, the presentation of these equations are arranged in my style.

$$Q_{n,j} = Q_0 \frac{n!}{(n-j)!j!} \cdot \frac{k'^{n-j}}{(1+k')^n} \qquad (j \leqq n) \qquad \cdots\cdots(2)$$

$$Q_n = Q_0 \frac{(n-1)!}{(n-N)!(N-1)!} \cdot \frac{k'^{n-N}}{(1+k')^n} \qquad (n \geqq N) \qquad \cdots\cdots(3)$$

In these equations, Q_0, n, j and N represent the total amount of the solute, the number of transfers (start from 0), the plate number (start from 0) and the number of theoretical plates (start from 1), respectively. $Q_{n,j}$ in Eq. 2 denotes the amount of the solute in a given plate, whereas Q_n in Eq. 3 denotes that in a mobile phase which leave the column.

Position peak approaches Gaussian distribution with increasing number of n (see below), then it is also represented as Eq. 4[4]. The exit peak can be drawn using Eq. 4 also.

$$Q_{n,j} = Q_0 \frac{1+k'}{\sqrt{2\pi n k'}} \exp\left\{-\frac{[j(1+k')-n]^2}{2nk'}\right\} \qquad \cdots\cdots(4)$$

Results and Discussion

Position Peak

A program for the position peak was developed (Program 1, see the appendix) based on Eq. 2. The peaks are represented stepwise by doing "hit space key". Three stages of them are copied (**Fig. 1**). At the last stage, Gaussian distribution based on Eq. 4 is also drawn (lines in **Fig. 1c**). Although the number of n is small, **Fig. 1** represents satisfactory results; the peaks approach Gaussian distributions and are separated mutually. Eq. 2 is not usable with large number of n; in these cases, only Eq. 4 should be used. If G$ = "N" in line 100 is changed to G$ = "G", only the peak based on Eq. 4 is drawn. Remark, the symmetry of peak is kept at any stage in the case of $k' = 1$.

Exit Peak

A program for the exit peak was developed (Program 2) based on Eq. 3. Two examples of the peaks are shown (**Fig. 2**). The peaks based on Eq. 4 is also drawn by doing "hit space key" (lines in **Fig. 2**). If G$ = "N" in line 100 is changed to G$ = "G", only the peak based on Eq. 4 is drawn. All the peaks exhibited "tailing" to various extents (**Fig. 2**). The degree of "tailing" decreases and the peak becomes more Gaussian as the number of N and the value of k' become larger[2]. Actually a short or an inefficient column is one of the causes of "tailing"[5]. Remark, the peak in the case of $k' = 1$ exhibits "tailing" as a matter of course.

Relationship between Position Peak and Exit Peak

The two kinds of programs mentioned above are useful themselves. However, they alone can not give a thorough understanding of chromatographic basis. For example, these are not so useful to understand instantaneously that the Gaussian (symmetry) distribution in position peak causes the "tailing" of exit peak. Therefore, the author developed a new program (Program 3); the program exhibits the elemental two processes in a column, the equilibration and the transfer (see above), and the resulting exit peak stepwise. Although this program can be used with various values of parameters of course, an example with very small number of N ($N = 6$) and $k' = 1$ (refer to the above remarks) is shown for the simplicity of presentation (**Fig. 3**). From this, the fact that the symmetry of position peak is not kept in

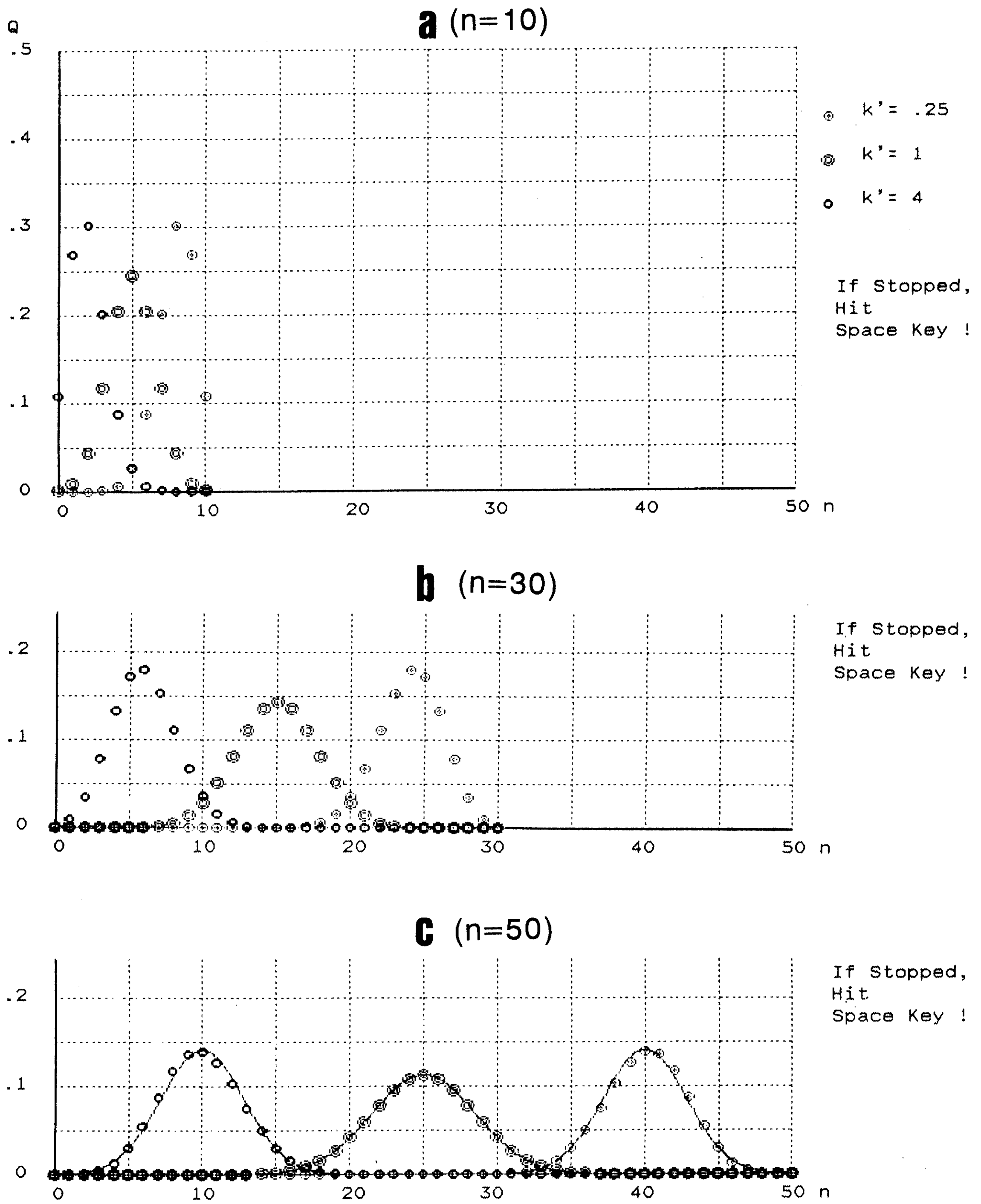

Fig. 1 Three Stages of an Example of the Simulation of "Position Peak" (produced by Program 1)

the exit peak can be grasped confidently.

In conclusion, Program 3 is very useful to understand the elemental two processes, the equilibration and the transfer of mobile phases, and the relationship between the position and exit peaks. If Program 3 is used together with Programs 1 and 2, more effective educational results will be obtained.

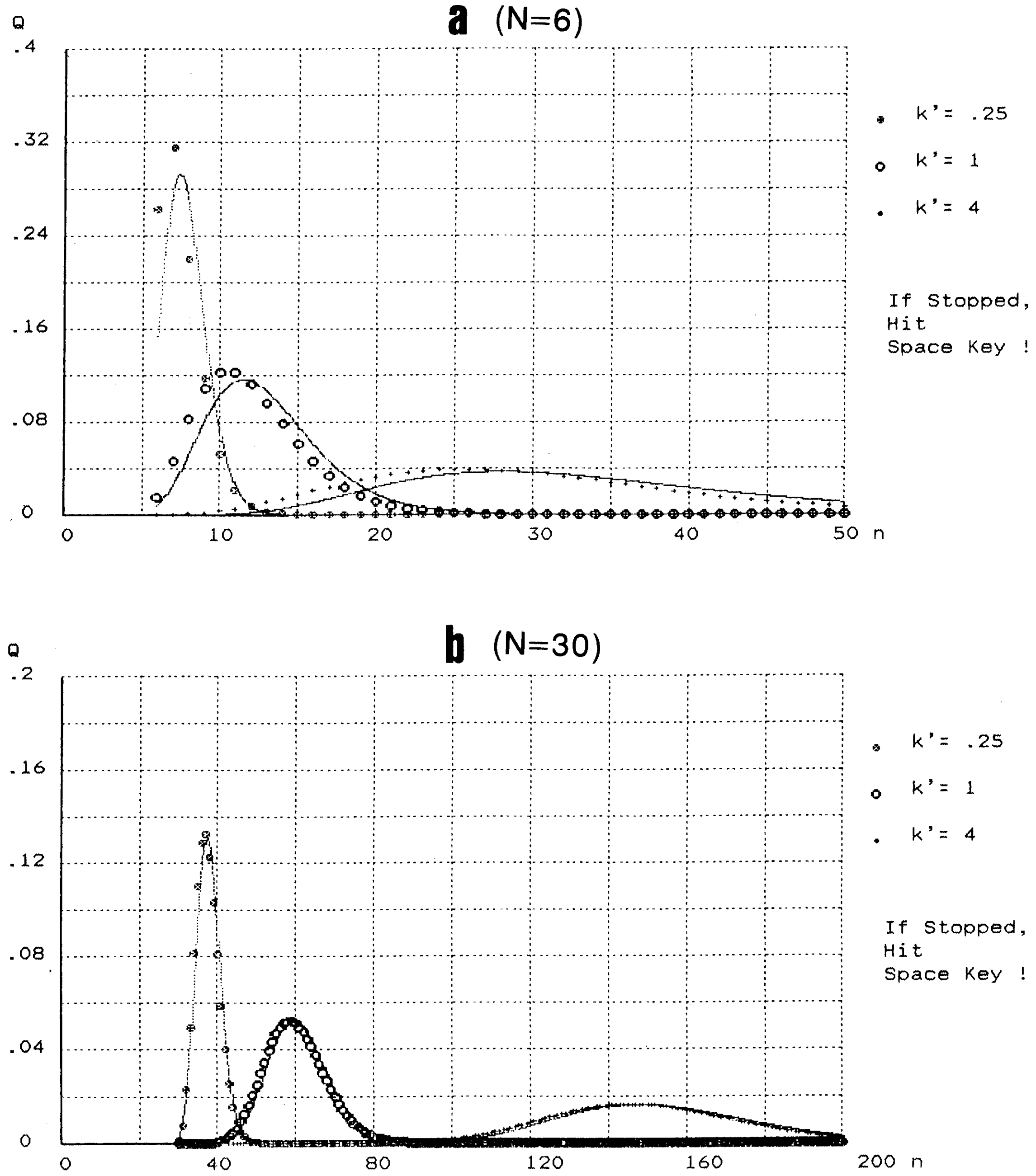

Fig. 2 Two Examples of the Simulation of "Exit Peak" (produced by Program 2)

Appendix

Programs developed in this paper are as follows, and they are written by N_{88}-BASIC using an NEC Model PC-9801 personal computer.

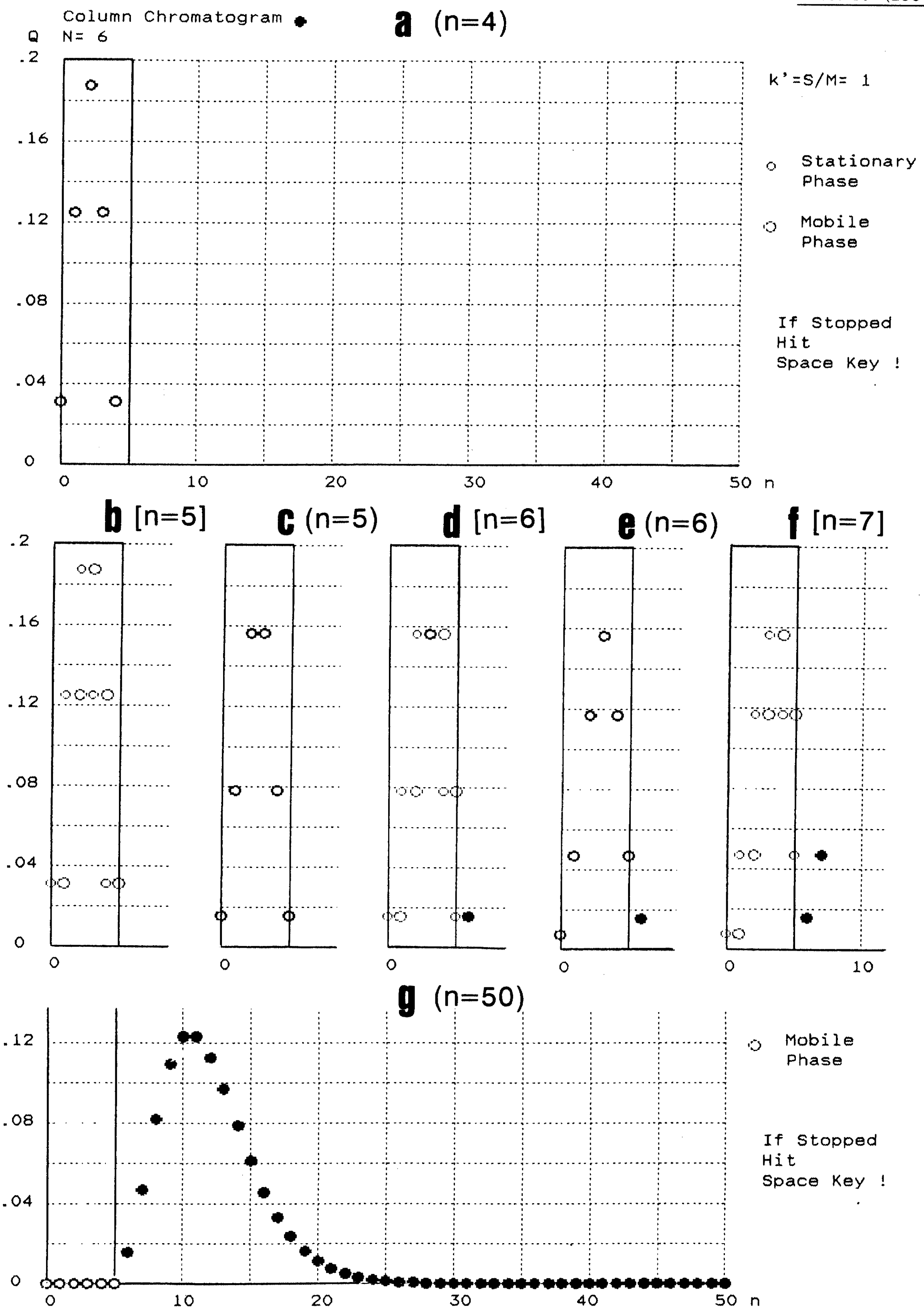

Fig. 3 Seven Stages of an Example of the Simulation of "Relationship between Position Peak and Exit Peak" (produced by Program 3)

The numbers n in ( ) represent the equilibrated states and those in [ ] represent the instants of transfers of mobile phases.

Program 1

```
10 '    *****************  Position Peak  *************
20 '
30 CLS 3 :CONSOLE ,,0,1 :SCREEN 3 :COLOR 6
40 PRINT "*****  Position Peak  *****":COLOR 7:PRINT
50 '
60 '      ---------------  PARAMETERS  -----------
70  INPUT "Parameter Change (Y/N)";Z$ :CLS 3
80  IF Z$="Y" GOTO 90 ELSE 100
90   LIST 100-150
100  N1=5  :N2=50   : ST=5 :FX=50  :FY=.5   :G$="N"
110  K1=.25  :K2=1  :K3=4     :Q1=1  :Q2=1  :Q3=1
120  C10=1 :C11=3  :C20=2 :C22=4  :C30=2 :C33=3
130 ' Step-by-step Presentation(N1,N2,ST), Only Gaussian distribution(N -> G)
140 ' Full scales of X-axis( FX ) and Y-axis( FY )
150 ' Capacity Factor,k'(K), Amount of Substance(Q), Scales of Circles(C10··)
160   CLS 3
170 '      ------------  PRESENTATION OF THE BACKGROUND  ------
180 '
190   LINE(40,40)-(40,360) :LINE(40,360)-(510,360)
200   FOR I=1 TO 10 :LINE(40+47*I,40)-(40+47*I,360),7,,&HCCCC
210   LINE(40,360-32*I)-(510,360-32*I),7,,&HCCCC :NEXT I
220   LOCATE 1,2 :PRINT "Q" :LOCATE 2,23 :PRINT "0"
230   FOR I=2 TO 6 :LOCATE 0,27-4*I :PRINT .2*FY*(I-1) :NEXT I
240   LOCATE 5,25:PRINT "0          ";.2*FX;"         ";.4*FX;"         ";.6*FX;"
    ";.8*FX;"         ";FX;"n"
250   CIRCLE(530,90),C10,5 :CIRCLE(530,90),C11,5  :LOCATE 69,5:PRINT "k'=";K1
260   CIRCLE(530,122),C20,2:CIRCLE(530,122),C22,2 :LOCATE 69,7:PRINT "k'=";K2
270   CIRCLE(530,154),C30,4:CIRCLE(530,154),C33,4 :LOCATE 69,9:PRINT "k'=";K3
280   LOCATE 67,13 :PRINT "If Stopped," :LOCATE 67,14 :PRINT "Hit"
290   LOCATE 67,15 :PRINT "Space Key !"
300 '
310 '      ----------------------  CALCULATION  ---------------
320 IF G$="G" GOTO 540 ELSE 330
330 FOR N=N1 TO N2 STEP ST
340   Q10=Q1*(K1/(1+K1))^N :Q20=Q2*(K2/(1+K2))^N :Q30=Q3*(K3/(1+K3))^N
350   NN=N-ST :Q11=Q1*(K1/(1+K1))^NN :Q22=Q2*(K2/(1+K2))^NN
360            Q33=Q3*(K3/(1+K3))^NN
370   FOR X=0 TO N
380       XX=40+470*X/FX
390     M=N-ST :IF M<0 GOTO 450
400       IF X=0 GOTO 420
410       Q11=Q11*(M-X+1)/(X*K1):Q22=Q22*(M-X+1)/(X*K2):Q33=Q33*(M-X+1)/(X*K3)
420       CIRCLE(XX,360-320*Q11/FY),C10,0 :CIRCLE(XX,360-320*Q11/FY),C11,0
430       CIRCLE(XX,360-320*Q22/FY),C20,0 :CIRCLE(XX,360-320*Q22/FY),C22,0
440       CIRCLE(XX,360-320*Q33/FY),C30,0 :CIRCLE(XX,360-320*Q33/FY),C33,0
450     M=N
460       IF X=0 GOTO 480
470       Q10=Q10*(M-X+1)/(X*K1):Q20=Q20*(M-X+1)/(X*K2):Q30=Q30*(M-X+1)/(X*K3)
480       CIRCLE(XX,360-320*Q10/FY),C10,5 :CIRCLE(XX,360-320*Q10/FY),C11,5
490       CIRCLE(XX,360-320*Q20/FY),C20,2 :CIRCLE(XX,360-320*Q20/FY),C22,2
500       CIRCLE(XX,360-320*Q30/FY),C30,4 :CIRCLE(XX,360-320*Q30/FY),C33,4
510   NEXT X
520   IF INKEY$="" THEN GOTO 520
530 NEXT N
540   FOR X=0 TO N2 STEP FX/1000
550       DM1=1+K1 :DM2=1+K2 :DM3=1+K3 :PI=3.14159 :XX=40+470*X/FX
560       Q10=Q1*DM1/((2*PI*N2*K1)^.5)*EXP(-(X*DM1-N2)^2/(2*N2*K1))
570       Q20=Q2*DM2/((2*PI*N2*K2)^.5)*EXP(-(X*DM2-N2)^2/(2*N2*K2))
580       Q30=Q3*DM3/((2*PI*N2*K3)^.5)*EXP(-(X*DM3-N2)^2/(2*N2*K3))
590       PSET(XX,360-320*Q10/FY),5 :PSET(XX,360-320*Q20/FY),2
600       PSET(XX,360-320*Q30/FY),4
610   NEXT X
620   IF INKEY$="" THEN GOTO 620
630 GOTO 30
640 END
```

Program 2

```
10 '    ****************  Exit Peak (Chromatogram)  **************
20 '
30  CLS 3 :CONSOLE ,,0,1 :SCREEN 3 :COLOR 6
40  PRINT "*****  Exit Peak (Chromatogram)  *****":COLOR 7:PRINT
50 '
60 '      ------------------  PARAMETERS  -----------
70  INPUT "Parameter Change (Y/N)";Z$ :CLS 3
80  IF Z$="Y" GOTO 90 ELSE 100
90  LIST 100-150
100  CLM=20   :NL=100  :FY=.2  :FX=NL :G$="N"
110  K1=.25  :K2=1  :K3=4    :Q1=1  :Q2=1  :Q3=1
120  C10=1 :C11=3   :C20=2 :C22=4   :C30=2 :C33=3
130 ' Number of theoretical plates(CLM), Last number of transfers(NL)
140 ' Only Gaussian derived(N -> G), Full scales of X- and Y-axis(FX,FY)
150 ' Capacity Factor,k'(K), Amount of Substance(Q), Scales of Circles(C10··)
160 CLS 3
170 '       ---------  PRESENTATION OF THE BACKGROUND  ----------
180 '
190   LINE(40,40)-(40,360) :LINE(40,360)-(510,360)
200   FOR I=1 TO 10 :LINE(40+47*I,40)-(40+47*I,360),7,,&HCCCC
210   LINE(40,360-32*I)-(510,360-32*I),7,,&HCCCC :NEXT I
220   LOCATE 1,2 :PRINT "Q" :LOCATE 2,23 :PRINT "0"
230   FOR I=2 TO 6 :LOCATE 0,27-4*I :PRINT .2*FY*(I-1) :NEXT I
240   LOCATE 5,25:PRINT "0          ";.2*FX;"          ";.4*FX;"          ";.6*FX;"
   ";.8*FX;"          ";FX;"n"
250   CIRCLE(530,90),C10,5 :CIRCLE(530,90),C11,5  :LOCATE 69,5:PRINT "k'=";K1
260   CIRCLE(530,122),C20,2:CIRCLE(530,122),C22,2 :LOCATE 69,7:PRINT "k'=";K2
270   CIRCLE(530,154),C30,4:CIRCLE(530,154),C33,4 :LOCATE 69,9:PRINT "k'=";K3
280   LOCATE 67,13 :PRINT "If Stopped," :LOCATE 67,14 :PRINT "Hit"
290   LOCATE 67,15 :PRINT "Space Key !"
300 '
310 '      -------------------  CALCULATION  -----------
320 IF G$="G" GOTO 480 ELSE 330
330     Q10=Q1/(1+K1)^CLM :Q20=Q2/(1+K2)^CLM :Q30=Q3/(1+K3)^CLM
340 FOR N=CLM TO NL
350     IF N=CLM GOTO 390
360         Q10=Q10*((N-1)/(N-CLM))*(K1/(1+K1))
370         Q20=Q20*((N-1)/(N-CLM))*(K2/(1+K2))
380         Q30=Q30*((N-1)/(N-CLM))*(K3/(1+K3))
390         XX=40+470*N/FX
400        CIRCLE(XX,360-320*Q10/FY),C10,5
410        CIRCLE(XX,360-320*Q10/FY),C11,5
420        CIRCLE(XX,360-320*Q20/FY),C20,2
430        CIRCLE(XX,360-320*Q20/FY),C22,2
440        CIRCLE(XX,360-320*Q30/FY),C30,4
450        CIRCLE(XX,360-320*Q30/FY),C33,4
460 NEXT N
470 IF INKEY$="" THEN GOTO 470
480   FOR N=CLM TO NL STEP FX/2000
490      PI=3.14159 :IF N=0 GOTO 570
500      Q10=Q1/((2*PI*N*K1)^.5)*EXP(-(CLM*(1+K1)-N)^2/(2*N*K1))
510      Q20=Q2/((2*PI*N*K2)^.5)*EXP(-(CLM*(1+K2)-N)^2/(2*N*K2))
520      Q30=Q3/((2*PI*N*K3)^.5)*EXP(-(CLM*(1+K3)-N)^2/(2*N*K3))
530      XX=40+470*N/FX
540      PSET(XX,360-320*Q10/FY),5
550      PSET(XX,360-320*Q20/FY),2
560      PSET(XX,360-320*Q30/FY),4
570   NEXT N
580 IF INKEY$="" THEN GOTO 580
590 GOTO 30
600 END
```

Program 3 (1)

```
10 '   *********  Relationship between Position Peak and Exit Peak  *********
                                                        (Chromatogram)
20 '
30 CLS 3 :CONSOLE ,,0,1 :SCREEN 3 :COLOR 6
40 PRINT "*****  Relationship between Position Peak and Exit Peak  *****"
50 COLOR 7:PRINT
60 '
70 '      ---------------------  PARAMETERS  -----------------
80 '
90   CLM=6  :N1=4  :N2=50  :FY=.2  :K=1       :Q=1 :CS=3 :CM=4 :ST=1
100  INPUT "Parameter Change (Y/N)";Z$ :IF Z$="Y" GOTO 110 ELSE 170
110  PRINT :INPUT "Number of theoretical plates, N( 1 - ab. 50 )";CLM :PRINT
120  PRINT "Range of Step-by-step Presentation (from n1 to n2 )"
130  INPUT "    n1 ( 0 - smaller than N )";N1
140  INPUT "    n2 ( 50, 100, 150 or 200 etc. larger than N )";N2
150  PRINT  :INPUT "Full Scale of Y-axis ( 0.1, 0.2, 0.25, 0.5, 1 etc.)";FY
160  PRINT  :INPUT "k'( ab. 0.2 -10 )";K
170  FX=N2  :KS=K/(K+1) :KM=1/(K+1)
180  CLS 3
190 '     ------------  PRESENTATION OF THE BACKGROUND  -----------
200 '
210  LINE(40,40)-(40,360) :LINE(40,360)-(510,360)
220  X1=40+470*(CLM-1)/FX
230  LINE(40,39)-(X1,39),4
240  LINE(40,40)-(X1,40),4:LINE(X1,40)-(X1,360)
250  FOR I=1 TO 10
260    LINE(40+47*I,40)-(40+47*I,360),7,,&HCCCC
270    LINE(40,360-32*I)-(510,360-32*I),7,,&HCCCC
280  NEXT I
290  COLOR 4:LOCATE 5,1:PRINT "Column"
300  LOCATE 5,2 :PRINT "N=";CLM :COLOR 5
310  LOCATE (6+58.8*(CLM-1)/FX),1:PRINT "Chromatogram":COLOR 7
320  CIRCLE (156+470*(CLM-1)/FX,9),CM,5
330  PAINT (156+470*(CLM-1)/FX,9),5,5
340  LOCATE 2,2 :PRINT "Q" :LOCATE 2,23 :PRINT "0"
350  FOR I=2 TO 6
360    LOCATE 0,27-4*I :PRINT .2*FY*(I-1)
370  NEXT I
380  LOCATE 5,25:PRINT "0         ";.2*FX;"        ";.4*FX;"         ";.6*FX;"
    ";.8*FX;"        ";FX;"n"
390  LOCATE 66,3  :PRINT "k'=S/M=";K
400  CIRCLE(530,122),CS,2
410  LOCATE 69,7  :PRINT "Stationary" :LOCATE 69,8 :PRINT "Phase"
420  CIRCLE(530,170),CM,5
430  LOCATE 69,10 :PRINT "Mobile" :LOCATE 69,11 :PRINT "Phase"
440  LOCATE 67,15 :PRINT "If Stopped" :LOCATE 67,16 :PRINT "Hit"
450  LOCATE 67,17 :PRINT "Space Key !"
460 '
470 '     -----------------  CALCULATION  -------------
480 FOR N=N1 TO N2 STEP ST
490    Q0=Q*KS^N
500    IF N>CLM-1 GOTO 520
```

Program 3 (2)

```
510     N0=N :GOTO 530
520     N0=CLM-1
530     FOR X=0 TO N0
540       IF X=0 GOTO 560
550       Q0=Q0*(N-X+1)/(X*K)
560       QS=Q0*KS:QM=Q0*KM
570       CIRCLE(40+470*X/FX,360-320*QS/FY),CS,2
580       CIRCLE(40+470*X/FX,360-320*QM/FY),CM,5
590     NEXT X
600   IF INKEY$="" THEN GOTO 600
610     IF N=N2 GOTO 1000
620     Q0=Q*KS^N
630     IF N>CLM-1 GOTO 650
640     N0=N :GOTO 660
650     N0=CLM-1
660     FOR X=0 TO N0
670       IF X=0 GOTO 690
680       Q0=Q0*(N-X+1)/(X*K)
690       QM=Q0*KM
700       CIRCLE(40+470*X/FX,360-320*QM/FY),CM,0
710     NEXT X
720     Q0=Q*KS^N
730     IF N>CLM-1 GOTO 750
740     N0=N :GOTO 760
750     N0=CLM-1
760     FOR X=0 TO N0
770       IF X=0 GOTO 790
780       Q0=Q0*(N-X+1)/(X*K)
790       QM=Q0*KM
800       IF X=(CLM-1) GOTO 820
810       CIRCLE(40+470*(X+1)/FX,360-320*QM/FY),CM,5
820     NEXT X
830     IF N<CLM-1 GOTO 860
840     CIRCLE(40+470*(N+1)/FX,360-320*QM/FY),CM,5
850     PAINT(40+470*(N+1)/FX,360-320*QM/FY),5,5
860   IF INKEY$="" THEN GOTO 860
870     Q0=Q*KS^N
880     IF N>CLM-1 GOTO 900
890     N0=N :GOTO 910
900     N0=CLM-1
910     FOR X=0 TO N0
920       IF X=0 GOTO 940
930       Q0=Q0*(N-X+1)/(X*K)
940       QS=Q0*KS:QM=Q0*KM
950       CIRCLE(40+470*X/FX,360-320*QS/FY),CS,0
960       IF X=(CLM-1) GOTO 980
970       CIRCLE(40+470*(X+1)/FX,360-320*QM/FY),CM,0
980     NEXT X
990 NEXT N
1000 END
```

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