THEORY OF PARTITION CHROMATOGRAPHY

II. NUMERICAL CALCULATIONS

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The theoretical treatment of partition chromatography, advanced in an earlier article[1], has now been supplemented by numerical calculations performed on a digital computer. In the present calculations the treatment in ref. 1 has been closely followed and therefore only a short summary of the method is given here.

In the model used in the theory, the chromatographic column is divided into cells of equal width and the operation of the column is assumed to take place in discontinuous steps. During a step the solution in the mobile phase of a cell is allowed to exchange solute with the stationary phase of that cell (lateral diffusion) and with solutions of the mobile phase in neighbouring cells (longitudinal diffusion). At the end of the step the solutions of the mobile phase in each cell are instantaneously shifted one step to the adjacent cells and the equilibration procedure is repeated. The solute concentration in the mobile phase of a particular cell is designated $f_{i,j}$, where i is the number of the cell and j the time (with the duration of a step being taken as the time unit). Thus $f_{i,j}$ defines a matrix where the ith row gives the solute concentration in the ith cell at different times and the jth column gives the distribution of the solute concentration in the mobile phase over the entire chromatographic column at the time j. The elements of the matrix $f_{i,j}$ are calculated from the characteristic parameters and the initial conditions of the column operation according to Eqns. (23) and (24) in ref. 1.

In order to simplify the treatment the last term in Eqn. (24) is neglected, *i.e.* longitudinal diffusion in the stationary phase is not taken into account. This approximation is of minor significance for the theory, but it makes possible the use of a single recursion formula for the determination of $f_{i,j}$. It takes the form:

$$f_{i+1,j} = {}^1/_2\,\alpha_1 f_{i+1,j-1} + (1 - \alpha_1 - \eta) f_{i,j-1} + {}^1/_2\,\alpha_1 f_{i-1,j-1} + \\ + \eta(1-\xi) f_{i,j-2} + \eta(1-\xi)\,\xi f_{i,j-3} + \ldots + \eta(1-\xi)\,\xi^{j-3} f_{i,1} \qquad (1)$$

where:

$$\alpha_1 = \frac{2D_1}{\tau v^2}$$

$$\xi = \frac{\gamma V_2}{V_1 + \gamma V_2}\left(1 + \frac{V_1}{\gamma V_2}\,e^{-m\tau}\right)$$

$$\eta = \frac{\gamma V_2}{V_1 + \gamma V_2}\,(1 - e^{-m\tau})$$

with:

$$m = \frac{2D_2}{V_2}\left(\frac{\gamma}{V_1} + \frac{1}{V_2}\right)^*$$

The following parameters characterize the column operation:

V_1, V_2 = volumes per interphase area of mobile and stationary phase respectively
D_1, D_2 = diffusion coefficients in mobile and stationary phase respectively
γ = partition coefficient
v = translational velocity of the mobile phase.

The initial conditions are given by the elements $f_{0\,j}$ and $f_{1\,j}$ in Eqn. (1), and were in all cases chosen to represent a rectangular concentration peak in the solution entering the chromatographic column.

The results were abstracted from the computor in the form of a few selected columns of a matrix, representing the concentration distribution in the mobile phase of the chromatographic column at different times. For a detailed characterization of the distributions their zeroth, first and second moments, with respect to the origin and with the cell width as unit of length, were also calculated. For the jth column they are defined in the following way:

$$A_0 = \sum_i f_{i\,j} \tag{2}$$

$$A_1 = \sum_i i\, f_{i\,j} \tag{3}$$

$$A_2 = \sum_i i^2 f_{i\,j} \tag{4}$$

It was found during the course of the calculations that the zeroth moment A_0 (representing the amount of solute in the mobile phase) in a given matrix generally very rapidly converges to a constant value. Hence a normalization on a common basis of the distributions represented by the different matrix columns is possible. The normalized distributions may then be characterized by the mean μ and the second moment around the mean μ_2. They are defined as follows:

$$\mu = A_1/A_0 \tag{5}$$

$$\mu_2 = A_2/A_0 - \mu^2 \tag{6}$$

In addition the mode M, defined as the location of the maximum of the smoothed distribution curve, was also determined.

Both μ and M are measures of location of the distribution, whereas μ_2 is a measure of dispersion. Further, as a measure of skewness Pearson's measure S is used. It is defined in the following way:

$$S = \frac{\mu - M}{\sqrt{\mu_2}} \tag{7}$$

In the following the results will in general be given in terms of the parameters A_0, M, μ, μ_2 and S.

* Here the dependence of m on the partition coefficient γ is taken different from that in ref. 1. It takes into account the assumption that diffusion in the stationary phase is the rate determining step in lateral diffusion. It simply states that the volume term of the mobile phase (where the concentration is kept uniform by convection) is changed in proportion to γ.

The present calculations were carried out with the Facit digital computer and matrixes of the order 200 were evaluated. The effective time for the evaluation of a matrix was about one hour.

RESULTS

In the calculations the above mentioned characteristic parameters were varied in order to determine their effect on the column operation. The parameters occur in the coefficients of Eqn. (1) only in form of the combinations $D_2\tau/V_2^2$, $V_1/\gamma V_2$ and $D_1/v^2\tau$. Therefore, not all of the parameters need be varied independently, and in the present calculations thus only the parameters D_1, D_2 and γ were varied. The others were kept fixed and had the values:

$$v = 0.01\ cm \cdot sec^{-1} \tag{8}$$

$$V_1/V_2 = 0.35 \tag{9}$$

$$V_2 = 0.01\ cm \tag{10}$$

Relation (9) refers to a column filling consisting of tight-packed spherical beads. According to (10) the radius of a bead is then 0.03 cm.

Convergence of the numerical solutions

In the numerical calculations the column operation occurs in discontinuous steps. As the exact solution is approached only in the limit when the number of steps tends to infinity, it is necessary to examine the convergence of the numerical solutions. For this reason calculations were carried out using alternatively 10, 20, 50 and 200 cells for the same length of a given column. The corresponding matrixes are numbered 1, 2, 3 and 4, respectively. In all cases the characteristic parameters have the same values, namely $D_1 = 10^{-5}$ cm$^2 \cdot$sec^{-1}, $D_2 = 5 \cdot 10^{-6}$ cm$^2 \cdot$sec^{-1} and $\gamma = 1$. The initial conditions are:

$$f_{1\,j} = \begin{cases} 1 \text{ for } j = 1, \cdots, n \\ 0 \text{ for } j = n + 1, \cdots, 200 \end{cases} \tag{11}$$

$$f_{0\,j} = \begin{cases} 1 \text{ for } j = 1, \cdots, n - 1 \\ 0 \text{ for } j = n, \cdots, 199 \end{cases} \tag{12}$$

$$f_{i\,1} = 0 \text{ for } i = 2, \cdots, 200 \tag{13}$$

In order to represent the same initial concentration peak the value of n in (11) and (12) is 1, 2, 5 and 20 for the matrixes 1, 2, 3 and 4, respectively. The cell width in the corresponding column models is 0.1, 0.05, 0.02 and 0.005 cm and the equilibration time τ has the values 10, 5, 2 and 0.5 sec, respectively. The results are recorded in Table I in the form of μ and μ_2 values for the 10th, 20th, 50th and 200th columns of the respective matrixes, representing the situation at the same nominal time instances. In Fig. 1 plots of μ and μ_2 against $1/n$ are shown. These curves indicate the way of convergence to the solutions of continuous column operation, represented by the extrapolated values on the ordinate axis.

TABLE I

MATRIX NOS. 1, 2, 3 AND 4

Matrix No.	*1*	*2*	*3*	*4*
Column No.	*10*	*20*	*50*	*200*
μ	4.1086	3.4014	3.0498	2.9028
μ_2	1.6891	1.211	1.037	1.006

Influence of diffusion and partition coefficients

The influence of both the lateral and longitudinal diffusion coefficients and the partition coefficient is established by separately changing these parameters. In all these calculations the value $n = 5$, in the initial conditions (11) and (12), is used and the value of τ is 2 sec giving a cell width of 0.02 cm. The conditions are then reasonably close to those of continuous column operation.

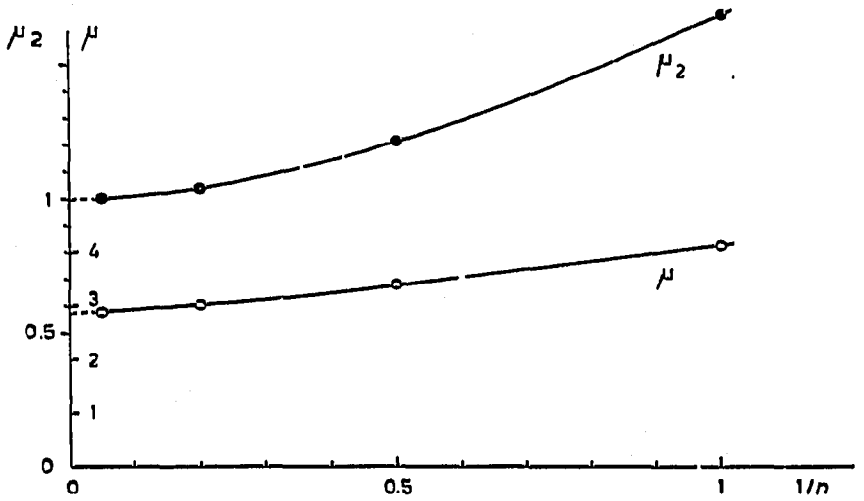

Fig. 1. Convergence of solutions from discontinuous column operation.

In the matrixes numbered 5, 6 and 7 different longitudinal diffusion coefficients are used, D_1 having the values 0, 10^{-5} and $5 \cdot 10^{-5}$ cm$^2 \cdot$sec^{-1}, respectively. (The results are recorded in Table II.) In the matrixes numbered 8, 9 and 10, different lateral diffusion coefficients are used, the values of D_2 being ∞, 10^{-6} and 10^{-7} cm$^2 \cdot$sec^{-1}, respectively. (The results are recorded in Table III). To this group belongs also matrix No. 5 in Table II, for which $D_2 = 5 \cdot 10^{-6}$ cm$^2 \cdot$sec^{-1}. Finally, in the group of matrixes numbered 11, 12, 13, 14, 15 and 16 the partition coefficient is varied, the values of γ being 0, 0.1, 0.2, 0.5, 2 and 5, respectively. (The results are shown in Table IV). To this group belongs also matrix No. 6 in Table II, for which $\gamma = 1$.

DISCUSSION

From the results in Tables II–IV it is seen that in all cases, except matrix No. 10, steady state conditions are established in the chromatographic column. The steady state is characterized by constancy in the value of total solute concentration in the

TABLE II

MATRIX NOS. 5, 6 AND 7

D_1 = 0, 10^{-5} and $5 \cdot 10^{-5}$ $cm^2 \cdot sec^{-1}$, respectively
D_2 = $5 \cdot 10^{-6}$ $cm^2 \cdot sec^{-1}$
γ = 1

Matrix No.	*Parameter*	*Column number*				
		25	*50*	*100*	*150*	*200*
5	A_0	1.2963	1.2963	1.2963	1.2963	1.2963
	μ	8.7187	15.201	28.165	41.129	54.092
	M	7.841	14.285	27.237	40.197	53.159
	μ_2	11.35	24.40	50.53	76.54	102.7
	S	0.261	0.185	0.131	0.107	0.092
6	A_0	1.2834	1.2834	1.2834	1.2834	1.2834
	μ	8.7666	15.249	28.212	41.174	54.137
	M	7.731	14.182	27.134	40.094	53.055
	μ_2	12.24	25.92	53.31	80.84	108.3
	S	0.296	0.210	0.148	0.120	0.104
7	A_0	1.2315	1.2315	1.2315	1.2315	1.2315
	μ	8.9704	15.452	28.416	41.380	54.343
	M	7.430	13.901	26.853	39.812	52.773
	μ_2	15.75	32.05	64.64	97.20	129.8
	S	0.388	0.274	0.194	0.159	0.138

TABLE III

MATRIX NOS. 8, 9 AND 10

D_2 = ∞, 10^{-6} and 10^{-7} $cm^2 \cdot sec^{-1}$, respectively
D_1 = 0
γ = 1

Matrix No.	*Parameter*	*Column number*				
		25	*50*	*100*	*150*	*200*
8	A_0	1.2963	1.2963	1.2963	1.2963	1.2963
	μ	7.4445	13.926	26.389	39.852	52.815
	M	7.180	13.681	26.646	39.609	52.572
	μ_2	4.166	8.97	18.57	28.19	37.78
	S	0.130	0.082	0.056	0.046	0.040
9	A_0	1.4236	1.2990	1.2963	1.2963	1.2963
	μ	16.090	22.826	35.770	48.734	61.698
	M	13.453	19.027	31.405	44.318	57.211
	μ_2	39.81	114.48	239.6	364.3	488.9
	S	0.418	0.355	0.282	0.231	0.203
10	A_0	3.9352	3.0909	2.1259	1.6794	1.4727
	μ	22.891	47.080	89.825	121.74	143.97

TABLE IV

MATRIX NOS. 11, 12, 13, 14, 15 AND 16
$D_1 = 10^{-5}$ cm^2·sec^{-1}
$D_2 = 5 \cdot 10^{-6}$ cm^2·sec^{-1}
γ = 0, 0.1, 0.2, 0.5, 2 and 5, respectively

Matrix No.	*Parameter*	*Column number*				
		25	*50*	*100*	*150*	*200*
11	A_0	4.9500	4.9500	4.9500	4.9500	3.4664
	μ	23.071	48.071	98.071	148.071	
	M	22.950	48.009	98.039	148.050	
	μ_2	4.13	6.55	11.6	16.7	
	S	0.059	0.023	0.009	0.005	
12	A_0	3.8540	3.8500	3.8500	3.8500	3.8489
	μ	19.892	39.358	78.247	117.135	156.013
	M	21.878	43.777	81.422	120.212	159.044
	μ_2	18.94	54.27	125.8	197.1	267.7
	S	—0.457	—0.600	—0.283	—0.219	—0.186
13	A_0	3.1519	3.1500	3.1500	3.1500	3.1500
	μ	17.385	33.302	65.121	96.937	128.756
	M	20.329	34.641	66.309	98.087	129.887
	μ_2	23.72	62.37	139.6	217.3	294.3
	S	—0.604	—0.170	—0.101	—0.078	—0.066
14	A_0	2.0383	2.0382	2.0382	2.0382	2.0382
	μ	12.581	22.875	43.463	64.052	84.638
	M	12.026	22.234	42.790	63.366	83.951
	μ_2	20.56	47.04	99.89	152.8	205.6
	S	0.122	0.093	0.067	0.056	0.048
15	A_0	0.73724	0.73724	0.73724	0.73724	0.73724
	μ	5.7741	9.4976	16.944	24.391	31.838
	M	4.842	8.789	15.986	23.424	30.876
	μ_2	5.602	11.38	22.95	34.52	46.10
	S	0.394	0.210	0.200	0.165	0.142
16	A_0	0.32386	0.32386	0.32386	0.32386	0.32386
	μ	3.5086	5.1442	8.4154	11.687	14.958
	M	2.913	4.404	7.695	10.966	14.228
	μ_2	1.874	3.717	7.403	11.10	14.78
	S	0.436	0.384	0.265	0.216	0.190

mobile (and stationary) phase of the chromatographic column. This value is independent of the diffusion coefficients D_1 and D_2 and, for a column of given geometry, depends only on the partition coefficient γ. The minor differences found in Tables II and III are due to end effects (diffusion out through the column ends). Under steady state conditions very simple rules exist concerning the translational velocity (peak velocity) and spreading of a concentration peak.

Peak velocity

The absolute peak velocity may be defined as the translational velocity of the center of mass of a concentration peak. A more convenient quantity is the relative

peak velocity, which will be designated by v and is defined as the ratio between the absolute peak velocity and the velocity of the mobile phase. It is obtained directly as the absolute velocity of the peak if the width of a cell and the equilibration time τ are used as length and time units respectively, as then the velocity of the mobile phase becomes unity.

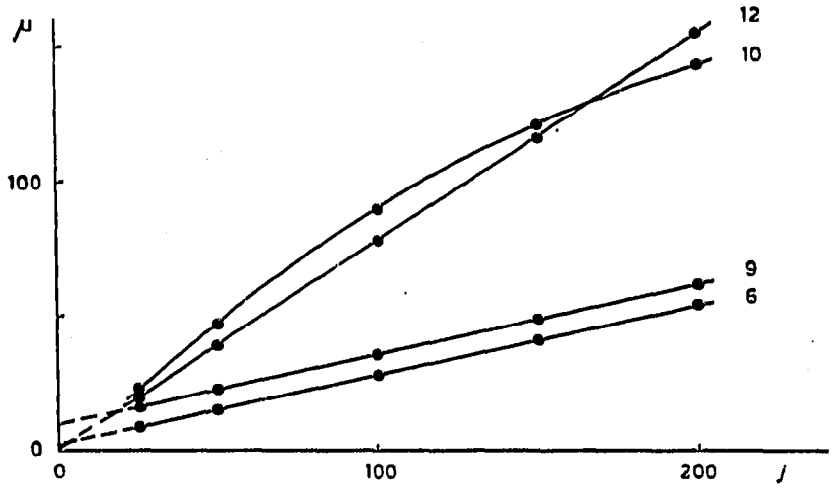

Fig. 2. Peak location as functions of time. Numbers in the figure indicate matrix numbers. For matrix No. 10 steady state is not established.

From the data in Tables II, III and IV it follows that under steady state conditions the peak velocity is constant. This is illustrated for some representative cases in Fig. 2, where plots of μ against time are shown. The calculated values of v are recorded in Table V. It is seen to be independent of the diffusion coefficients D_1 and D_2, but strongly dependent on the partition coefficient. The latter is illustrated in Fig. 3, where a plot of v against γ is shown.

Peak spreading

The breadth of a concentration peak is determined by its second moment around the mean μ_2. Under steady state conditions this is found to be a linear function of

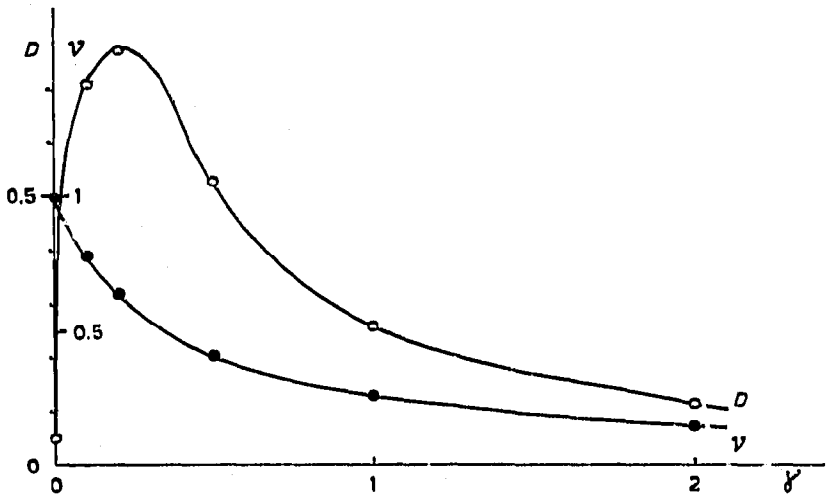

Fig. 3. Peak velocity and spreading coefficient as function of partition coefficient.

TABLE V

VALUES OF RELATIVE PEAK VELOCITIES AND SPREADING COEFFICIENTS

Matrix No.	*v*	*D* (*local units*)	$D \cdot 10^5$ (*c.g.s. units*)
5	0.2593	0.2610	5.220
6	0.2593	0.2745	5.489
7	0.2593	0.3260	6.519
8	0.2593	0.09605	1.921
9	0.2593	1.248	24.96
11	1.000	0.0503	1.006
12	0.7778	0.711	14.22
13	0.6364	0.773	15.46
14	0.4118	0.529	10.57
15	0.1489	0.1157	2.314
16	0.06543	0.03686	0.7372

time. This is seen from Fig. 4, where some representative plots of μ_2 against time are shown. It is thus possible to characterize the peak spreading by a spreading coefficient D, defined by:

$$\mu_2 = 2Dt + C \qquad (14)$$

where C is a constant, which takes care of the "end effect".

There is a close analogy between the present treatment of peak spreading and the spreading of concentration gradient curves in diffusion experiments[2]. Thus, the definition of the spreading coefficient is analogous to the definition of the diffusion coefficient in free diffusion experiments and the factor 2 in Eqn. (14) is included to make the correspondence complete. In the case of matrix No. 11, where the peak spreading is due only to longitudinal diffusion the value of D is $1.006 \cdot 10^{-5}$ cm$^2 \cdot$sec^{-1}, which is in good agreement with the longitudinal diffusion coefficient $D_1 = 10^{-5}$ cm$^2 \cdot$ sec^{-1}, used in these calculations. It is obvious that even other methods, *e.g.*, the area method may be used to determine the spreading coefficients.

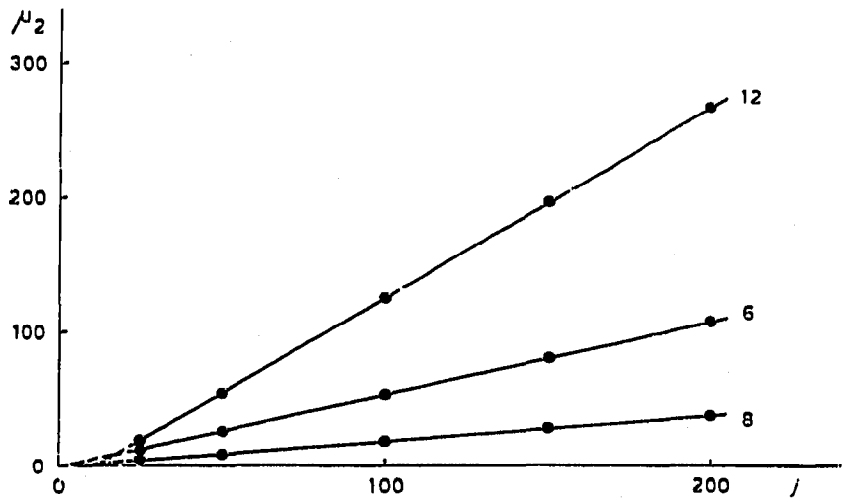

Fig. 4. Second moment as function of time. Numbers in the figure indicate matrix numbers.

The calculated values of D are listed in Table V. It is seen that longitudinal diffusion is of relatively minor importance as a cause for peak spreading. The major cause is the partition process, and its effect is considerable even at instantaneous equilibration ($D_2 = \infty$), and is greatly accentuated by local non-equilibrium. The influence of the partition coefficient is somewhat complicated, and is illustrated in Fig. 3. For $\gamma = 0$ the spreading coefficient equals the longitudinal diffusion coefficient; it rises steeply with increasing γ, passes through a maximum and then decreases monotonously with increasing γ.

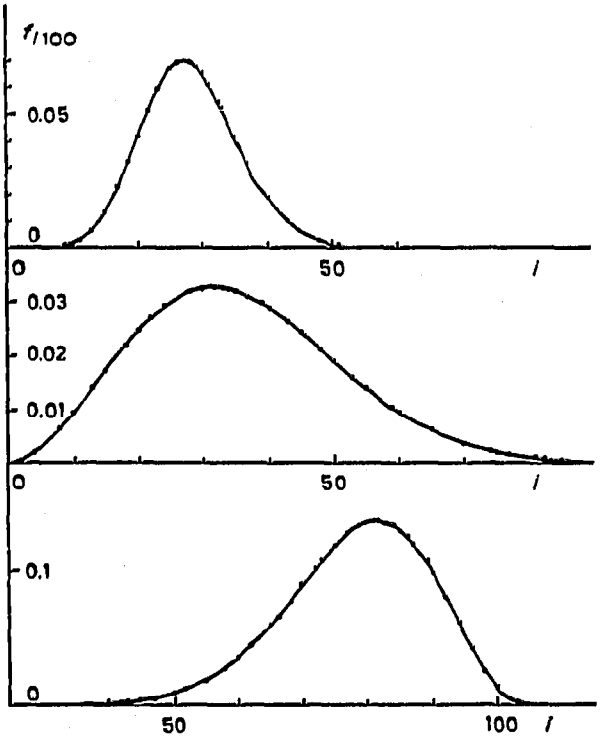

Fig. 5. Distribution curves for some peaks. Columns $j = 100$ for matrix Nos. 6, 9 and 12 from top to bottom.

Peak asymmetry

Besides the peak velocity and peak spreading, the asymmetry of a concentration peak is of fundamental importance in characterizing the chromatographic process. In the present treatment the asymmetry of the concentration distribution is described by the measure of skewness S, defined by Eqn. (7). As S admittedly gives a poor characterization of the form of a concentration peak, some typical peaks are reproduced in Fig. 5 for illustration purposes. It is seen from the S values in Tables II, III and IV that the peaks may exhibit both positive and negative skewness. It is also seen that the skewness invariably decreases with time. This indicates that the asymmetry is an "end effect", which is introduced into the distribution when the peak enters the chromatographic columns.

Peak exit from column

Hitherto the solute concentration distribution inside a chromatographic column has been considered. It is also of interest to examine the behaviour of a con-

centration peak at the exit from the column. From rather qualitative reasoning it can be induced that at exit a considerable spreading of the peak occurs. The reason for this is that the part of the peak which already has left the column has the same velocity as the mobile phase, whereas that part of the peaks which still is inside the column has a velocity very close to the peak velocity. Thus, the distortion is due to the difference in velocities of the peak and the mobile phase and is accentuated by low relative peak velocities. An illustration of the process is given in Fig. 6.

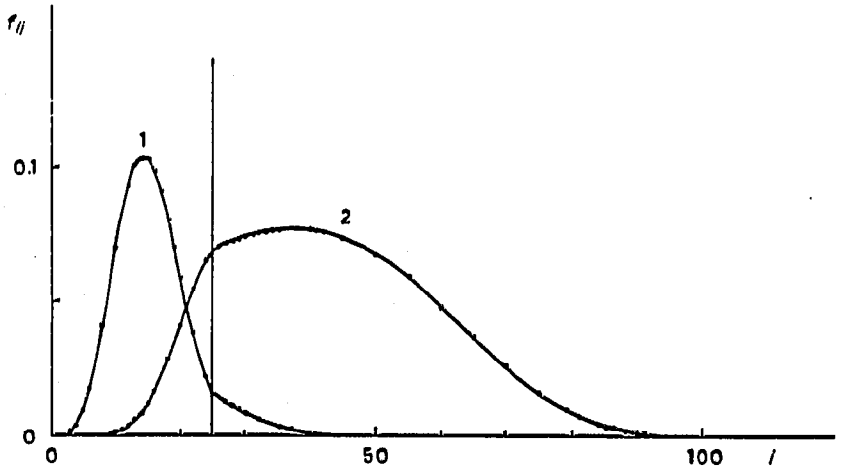

Fig. 6. Peak exit from column. Column end at cell No. 25. The data were obtained from matrix No. 5. Curve 1 refers to time $j = 50$, curve 2 to $j = 100$.

The present calculations represent "experiments" with the model column and, within this frame, constitute a complete study of the process of partition chromatography. They cover wide ranges of operational conditions and include all practical situations as to the magnitudes of the diffusion coefficients, the partition coefficient, etc. Although the model represents an idealization of a real chromatographic column it is felt that it brings out the pertinent features of the chromatographic process and, due to the high accuracy obtainable in the calculations, the significance of such characteristic quantities as peak velocity and the spreading coefficient of a peak are established. It thus makes a better understanding of the chromatographic process possible.

It should be mentioned here that, independent of the present work, the process of partition chromatography has been studied by LAURENT AND LAURENT[3] with the help of an electrical analogy computer. A comparison of the results will therefore be of interest.

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SUMMARY

The operation of a chromatographic column has been simulated by numerical calculations on a digital computer. The calculations cover wide ranges of operational conditions for a column and give a detailed characterization of the chromatographic process.

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