Separation Science and Technology
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713708471

Theoretical Plates, Resolution, and Peak Capacity in Countercurrent Distribution

Eli Grushka[a]
[a] DEPARTMENT OF CHEMISTRY STATE, UNIVERSITY OF NEW YORK AT BUFFALO BUFFALO, NEW YORK

To cite this Article Grushka, Eli(1971) 'Theoretical Plates, Resolution, and Peak Capacity in Countercurrent Distribution', Separation Science and Technology, 6: 3, 331 — 344

To link to this Article: DOI: 10.1080/00372367108055559

URL: http://dx.doi.org/10.1080/00372367108055559

SEPARATION SCIENCE, 6(3), pp. 331–344, June, 1971

Theoretical Plates, Resolution, and Peak Capacity in Countercurrent Distribution

ELI GRUSHKA
DEPARTMENT OF CHEMISTRY
STATE UNIVERSITY OF NEW YORK AT BUFFALO
BUFFALO, NEW YORK 14214

Summary

In countercurrent distribution, as in other methods of separation, a solute band broadens during the analysis. This allows the definition of theoretical plates, resolution, and peak capacities in terms of CCD parameters, namely, the number of transfers and the partition coefficients. The significance and the implication of the above quantities in evaluating CCD is discussed. When possible, comparisons with other methods of separation are made.

Countercurrent distribution (CCD) is now an established tool of analysis. Among its many uses are separation, purity analysis, and structure determination (*1*). As in other methods of separation, the solute band which is introduced to the CCD apparatus as a narrow zone at the beginning of the analysis is broadened during the separation process. In chromatography the width of a solute zone is characterized in terms of its variance or more frequently in terms of the height equivalent to theoretical plate. Either of these two quantities is a measure of the system's efficiency and both the resolution between two solutes and the peak capacity (*2*, *3*) of the system are dependent on it. Giddings (*2*) has recently demonstrated that the concepts of variance, HETP, resolution, and peak capacity can be extended to other methods of separation such as sedimentation and electrophoresis. In contrast to chromatography, sedimentation and electrophoresis CCD is not a continuous process. Nonetheless, the aforementioned parameters can be applied to analyze and characterize

CCD systems. This will allow direct comparison between CCD and other methods of separations.

PLATE NUMBER AND PLATE HEIGHT

It can be shown that after n extractions or transfers the tube $r_{\max}$ that contains the maximum amount of the solute is given by:

$$r_{\max} = np = \frac{nK}{1 + K} \tag{1}$$

Likewise the variance of the solute band is (*1*)

$$\sigma^2 = npq = \frac{nK}{(1 + K)^2} \tag{2}$$

K is the partition coefficient of the solute, p is the probability of finding a solute molecule in the upper or moving phase, and q is the probability of finding the solute molecule in the lower or stationary phase. In fact, p is equivalent to the chromatographic R parameter; that is, the ratio of the solute velocity to that of the mobile phase (*4*). In Eqs. (1) and (2), as in the rest of the paper, it is assumed that the volumes of the phases are equal. In the case where the two volumes are not equal, Eqs. (1) and (2) can be corrected by multiplying every K by the ratio of the moving phase volume to that of the stationary phase. In chromatography the variance of the zone is an important parameter since it is directly related to the chromatographic processes occurring and it is a measure of the efficiency of the system (*4*). Most frequently one talks about the plate number N or the height equivalent to theoretical plate H since both these quantities are related to the variance. Although the variance of a CCD peak has been previously studied (*5*), the generation of theoretical plates by a CCD train, to the knowledge of this author, has not been analyzed.

The number of plates N is defined as the ratio of the square of the length migrated to the variance. In the case of CCD this definition leads to

$$N = \frac{r_{\max}^2}{\sigma^2} = \frac{np}{q} \tag{3}$$

Since $q = 1 - p$, Eq. (3) becomes

$$N = \frac{np}{1 - p} = nK \tag{4}$$

The plate number is thus a linear function of the partition coefficient and of the number of transfers. Equation (4) has some interesting aspects. First, the number of plates will equal the number of tubes moved by the solute only in the case of $K = 1$. Depending on n and K the plate number can assume any value up to a certain upper limit and indeed it can be greater than the number of tubes moved by the solute. For example, if $K = 50$, then after 100 transfers the peak maximum will be at tube number 98, its width will be about 5 tubes, and the plate number is 5000—a surprisingly large number. The upper limit of the plate number is r_{max}^2 or n^2 and it occurs when K is of such a magnitude that the width of the peak is 1 tube. However when K is very large, Eqs. 1 and 2, and thus Eq. (4), are no longer good approximations. The second point of interest is that for a given number of transfers the plate number varies from one solute to another due to N dependence on K. It should be noted that while the peak width has a maximum at $K = 1$, the plate number has no such maximum and it increases continuously with increasing K. Finally, Eq. (4) indicates the benefits of a large number of transfers. A large n will increase the plate number, which means a relative sharpening of the zone as it moves down the CCD train.

The height equivalent to theoretical plate H is given by

$$H = \frac{\sigma^2}{r_{\max}} = q = \frac{1}{1 + K} \tag{5}$$

The plate height is a function of the partition coefficient and it is independent of the number of transfers. It should be stressed that H can vary between $1/n$ and unity only. Although one might expect that H should equal 1 tube, Eq. (5) shows that it is almost always less than unity. The expression for H in Eq. (5) is much simpler than its equivalent in chromatography where the plate height depends on many factors besides K.

Until now the discussion was centered on the so-called fundamental process (*1*); that is, the number of transfers is equal to the number of tubes in the train. Another method of CCD is the single withdrawal procedure (*1*) in which the mobile phase is withdrawn off the last tube in the train. In this case the shape of the concentration profile can still be considered as Gaussian and the transfer number that contains the peak maximum is given by (*6*)

$$n_{\max} = \frac{R}{p} = \frac{R(1 + K)}{K} \tag{6}$$

where R is the number of tubes in the train minus 1 for the zeroth tube. The variance of the peak is given by

$$\sigma^2 = \frac{n_{\max}}{K} \tag{7}$$

The plate number, then, is given by

$$N = \frac{n_{\max}^2}{\sigma^2} = n_{\max}K = R(1 + K) \tag{8}$$

Equation (8) is similar to Eq. (4) in its dependence on K and on the number of transfers. Here, however, the way to increase the relative sharpness of the peaks is to increase the number of stages in the train or to change K by changing the nature of the two phases. Equation (8) indicates that the lower limit of N is just the number of stages in the train. As before, the upper limit of N is $n_{\max}^2$.

The plate height is given by

$$H = \frac{\sigma^2}{n_{\max}} = \frac{1}{K} \tag{9}$$

Similarly to the fundamental process, H depends solely on the partition coefficient. A comparison between Eqs. (9) and (5) or (7) and (2) indicates that, under the condition that $n_{\max}$ is equal to n in the fundamental process, the latter yields narrower peaks. The HETP values of the two techniques becomes equal at high values of K. However, at very large partition coefficients Eqs. (6) and (7) are not entirely valid and should be used with caution.

The fact that for a given CCD system N depends only on the number of transfers and on the partition coefficient means that N can be reproduced from one laboratory to another provided that the systems are identical in composition and temperature. This is an advantage over chromatographic techniques where the reproducibility of N can be a challenging problem. H or N can be of great value in determining partition coefficients and compound purity. Moreover, as will be shown in the next section, N is related to the resolution between two components and hence to the required number of transfers that will resolve two solutes.

RESOLUTION IN CCD

In chromatography the resolution Rs is defined as (*4*, *7*)

$$Rs = \frac{\Delta t_R}{\bar{W}} \tag{10}$$

where Δt_R is the difference between the two peaks maxima and $\bar{W}$ is the average width of the two concentration profiles. In a similar manner the resolution between two peaks in the fundamental procedure can be written as

$$Rs = \frac{r_2 - r_1}{1/2(4\sigma_1 + 4\sigma_2)} \tag{11}$$

where the subscripts 1 and 2 refer to the first and second peaks, respectively, and 4σ is defined as the peak width. We now assume that the widths of the two peaks are equal. Equation (2) indicates that the variances of two peaks are never the same, but if K_1 is close in value to K_2 this approximation is not a bad one. Using Eq. (3) we can obtain

$$Rs = \frac{\sqrt{N}}{4}\left(\frac{r_2 - r_1}{r_2}\right) \tag{12}$$

Finally, from Eq. (1) we obtain

$$Rs = \frac{\sqrt{N}}{4}\left(\frac{p_2 - p_1}{p_2}\right) = \frac{\sqrt{N}}{4}\frac{\Delta p}{p_2} \tag{13}$$

which is the analog of the chromatographic resolution equation (7). Here N is the plate number of the peak with the highest K value. The resolution depends implicitly on the number of transfers via its dependence on the plate number. Thus in order to double the resolution, the number of transfers done should be quadrupled. The resemblance to the resolution dependence on the column length in chromatography is striking.

Following a similar line of reasoning for the case of single withdrawal one obtains a resolution equation which is identical to that in Eq. (13). The resolution here is proportional to the square root of the number of tubes in the train.

In chromatography the number of plates that are required to yield a resolution of unity is frequently a sought after quantity. While in CCD the required plate number can be calculated from Eq. (13), a more important parameter is the required number of transfers that must be carried out to achieve unit resolution. A few workers have already dealt with various aspects of the required number of transfers (8–14). To a first approximation we can start with Eq. (13) by rearranging it and by solving for the required number of transfers n_{req} which will yield $Rs = 1$

$$n_{\mathrm{req}} = \frac{16p_2(1 - p_2)}{(p_2 - p_1)^2} \tag{14}$$

or in terms of the K's

$$n_{\mathrm{req}} = \frac{16K_2(1 + K_1)^2}{(K_2 - K_1)^2} \tag{15}$$

Here $K_2 > K_1$. Equation (15), except for the numerical constant, is identical to the required number of transfers expression given by Nichols (*9*, Eq. 19) although it was derived here from a different point of view. Equation (15) has reasonable limits; i.e.

$$\begin{aligned} &\lim_{K_2 \to K_1} n_{\mathrm{req}} \to \infty \\ &\lim_{K_2 \to 0} n_{\mathrm{req}} \to \infty \end{aligned} \tag{16}$$

When K_2 is very large compared to K_1, n_{req} should approach the limit of unity and not zero as predicted by Eq. (15). The reason for this discrepancy lies in the nature of the approximation made; i.e., similar K values of the two solutes.

A more rigorous method of approach lies in Eq. (11). Unit resolution means that

$$r_2 - r_1 = 2(\sigma_1 + \sigma_2) \tag{17}$$

By substituting for r_1, r_2, σ_1, and σ_2 and solving for the required number of transfers to achieve unit resolution, one obtains the following equation which is a modification of some previously derived expressions (*6*, *9*, *12*, *14*)

$$n_{\mathrm{req}} = 4\left[\frac{\sqrt{K_1}(K_2 + 1) + \sqrt{K_2}(K_1 + 1)}{K_2 - K_1}\right]^2 \tag{18}$$

This equation has the same limits previously shown in Eq. (16). When K_2 is very large and much greater than K_1, then n_{req} approaches the limit of $4K_1$. Equation (18) has three variables and when plotted in three-dimensional space a curved surface is obtained which has no maximum or minimum. The surface can be represented in two-dimensional plots in terms of contour lines of constant n_{req}. In Table 1 the entries at each crossing of a K_1 column with a K_2 row is n_{req} as calculated from Eq. (18). The table was arbitrarily limited to K value of 0.1 to 1 with increments of 0.05 K units. Since $K_2 > K_1$, the only relevant values are those to the left of the diagonal line which

TABLE 1

The Required Number of Transfers as a Function of K_1 and K_2

	K_1																		
K_2	0.1	0.15	0.2	.25	.3	.35	.4	.45	.5	.55	.6	.65	.7	.75	.8	.85	.9	.95	1
0.1																			
0.15	998																		
0.2	304	1534																	
0.25	159	449	2149																
0.3	103	228	614	2850															
0.35	74	145	307	800	3641														
0.4	58	103	192	395	1010	4527													
0.45	47	79	135	244	494	1244	5513												
0.5	39	63	103	171	303	603	1503	6603											
0.55	34	53	82	129	210	368	724	1789	7804										
0.6	30	45	68	102	158	254	439	858	2104	9118									
0.65	26	39	57	84	124	189	302	518	1004	2447	10552								
0.7	24	35	50	71	102	149	224	355	604	1163	2821	12109							
0.75	21	31	44	61	86	121	176	262	412	697	1336	3226	13796						
0.8	20	28	39	54	74	102	143	205	304	474	798	1523	3664	15616					
0.85	18	26	35	48	65	88	120	166	236	349	541	908	1725	4136	17574				
0.9	16	24	32	43	57	76	102	139	191	271	397	614	1026	1942	4643	19676			
0.95	16	22	30	39	52	68	89	118	159	219	308	450	692	1152	2176	5187	21926		
1	15	21	27	36	47	61	79	103	136	182	248	348	506	776	1288	2426	5768	24328	

represent the contour line of $n_{req} = \infty$. An inspection of the entries in the table reveals the various lines of constant required number of transfers. For example n_{req} is 39 for the following sets of the partition coefficients: $K_2 = 0.5, K_1 = 0.1$; $K_2 = 0.65, K_1 = 0.15$; $K_2 = 0.8, K_1 = 0.2$; $K_2 = 0.95$, $K_1 = 0.25$. Table 1 and its extension to higher K's can be very useful in determining the capabilities of any CCD train and in allowing the resolution of two components in the shortest possible time.

Three comments can be made about Eq. (18); (a) when K_2 is close in value to K_1, Eq. (18) can be reduced to Eq. (15). This is to be expected since the expression for n_{req} given in Eq. (15) was derived with the approximation that the two partition coefficients are close in their magnitude. (b) When expressed in terms of $\beta = K_2/K_1$, the required number of transfers is given by

$$n_{req} = 4\left[\frac{\sqrt{K_1}(K_1\beta + 1) + \sqrt{\beta K_1}(K_1 + 1)}{K_1(\beta - 1)}\right]^2 \tag{19}$$

At constant β values Eq. (19) has a minimum which occurs at

$$K_1 = \frac{1 + \sqrt{\beta}}{\beta + \sqrt{\beta}} = \frac{1}{K_2} \tag{20}$$

This is in agreement with the results of Bush and Densen (*15*). It should be noted that the above minimum occurs only under the condition of constant β. The general expression of n_{req}, i.e., Eq. (18), does not predict a minimum. Wolf's (*14*) statement that the minimum number of transfers occurs when $K_1K_2 = 1$ is correct only at constant β. Since Eq. (18) does not predict a minimum of n_{req}, Eq. (20) means that under the constraint of constant β a path is traced on the n-K_1-K_2 surface as K_1 is changed and this path will have a minimum. (c) In the case when $K_1K_2 = 1$, Eq. (18) becomes

$$n_{req} = \frac{16K_2}{(1 - K_2)^2} \tag{21}$$

which, except for a numerical constant, is similar to the expression obtained by Gregory and Craig (*10*).

PEAK CAPACITY OF A CCD TRAIN

Giddings (*2*, *16*) and more recently Grushka (*3*) have shown that the peak capacity is an important efficiency parameter in many separation methods. Briefly the peak capacity is the theoretical maximum number of component that can be separated, with the resolution of unity between two consecutive solutes, between the fastest moving component and the slowest. In chromatography the peak capacity is proportional to the square root of the plate number of the column and to the logarithm of the ratio of the retention time of the last solute to that of an inert one. In CCD, the plate number cannot be assumed constant for all solutes, and the peak capacity cannot be expressed in a simple analytical equation. A generating equation, however, can be set up which will allow the determination of the peak capacity. This can be done as follows.

The condition of unit resolution means that for the fundamental process the following equation can be set up.

$$np_i - np_{i-1} = 2[\sqrt{np_iq_i} + \sqrt{np_{i-1}q_{i-1}}] \tag{22}$$

where n is the number of transfers and is equal to the number of tubes in the train. Subscript i represents the ith solute and $i - 1$ the slower solute; i.e., $p_i > p_{i-1}$. This equation can be rearranged to give

$$np_i - 2\sqrt{np_i(1 - p_i)} = np_{i-1} + 2\sqrt{np_{i-1}(1 - p_{i-1})} \tag{23}$$

We can arbitrarily choose the highest K to be 100. This solute will have a p value of 0.9901 and it will move as fast as the upper phase does. Thus for a given number of tubes in a CCD train and for a solute with p given as above, the left-hand side of Eq. (23) is known quantity which we call T. Equation (22) has now only one unknown, namely p_{i-1}, which can be easily computed

$$p_{i-1} = \frac{2nT + 4n \pm [(2nT + 4n)^2 - 4T^2(n^2 + 4n)]^{1/2}}{2(n^2 + 4n)} \tag{24}$$

Only the negative root has physical significance. p_{i-1} is the p value of the solute following the ith one and subject to the constraint of unit resolution between the two peaks. Once p_{i-1} is known it is substituted for p_i in the left-hand side of Eq. (23). A new T value is obtained and Eq. (24) is then used for the computation of p_{i-2}. This generation of p values is continued until such a small p value is obtained that the position of its maximum is around the second tube in the train. The number of p values generated is the total number of peaks that can be resolved; i.e., the peak capacity of the instrument.

Equations (23) and (24) indicate that for a given solvent system the peak capacity depends only on the number of tubes in the train. Figure 1 shows that the dependence is not linear. In fact Fig. 1

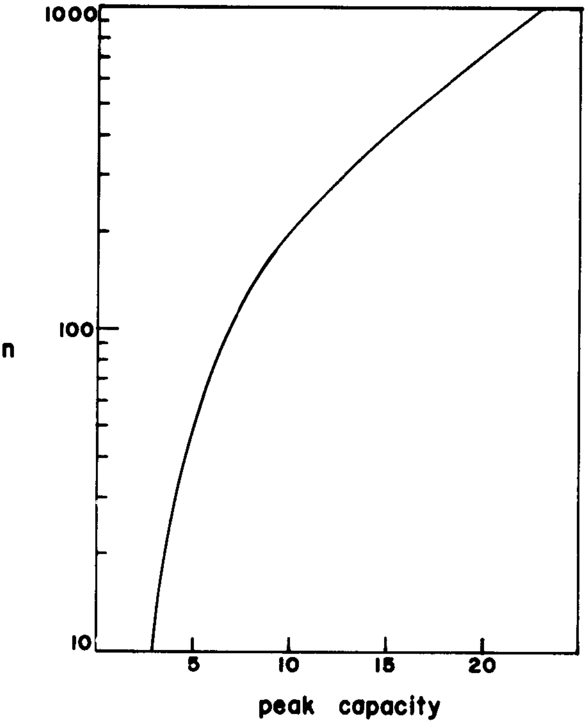

FIG. 1. Peak capacity vs. number of tubes. Fundamental process.

shows that to a first approximation the peak capacity is roughly equal to $n^{0.45}$.

The peak capacity can be increased if by some mechanism, such as a continuous change in the nature of the moving upper phase, one can maintain constant peak width. In this case it can be shown that after n transfers (n being equal to the number of tubes in the apparatus) the following relation holds

$$n = 2\sqrt{np(1-p)} + 4(C-1)\sqrt{np(1-p)} \tag{25}$$

where p is determined from the fastest moving component and C is the peak capacity. Rearranging

$$C = 1/2 + 1/4\left[\frac{n}{p(1-p)}\right]^{1/2} \tag{26}$$

If we choose $K = 100$, i.e., $p = 0.9901$, then the dependence of C on the number of tubes is shown in Fig. 2. For the sake of comparison

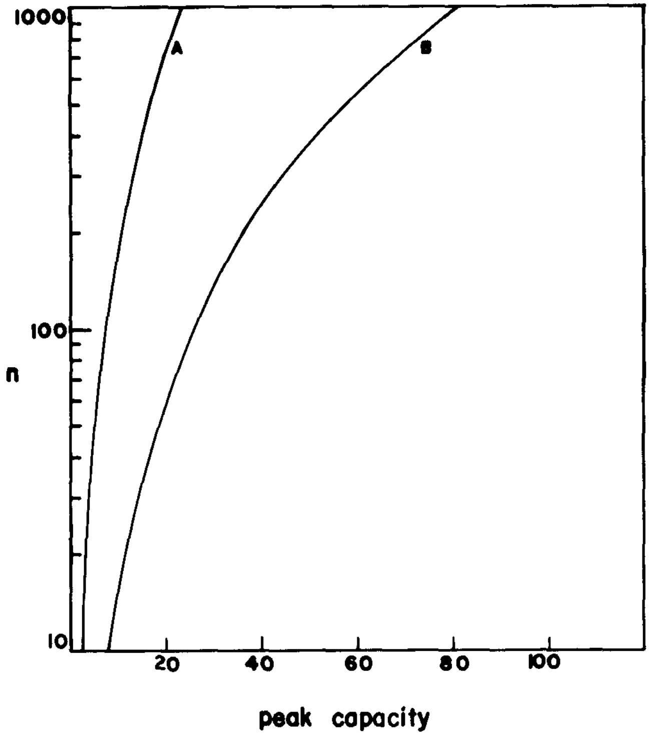

FIG. 2. Peak capacity vs. number of tubes. A: Fundamental process. B: Constant peak width.

Fig. 1 is included in Fig. 2. While Eq. (26) predicts ∞ as the upper limit of C, in actual practice that limit is, of course, equal to the number of tubes in the train.

The peak capacity of CCD system can also be increased by using the single withdrawal procedure. Here again a generating equation can be set up both for the withdrawal material and for the remainder in the train. Following a similar line of argument as in the case of the fundamental process, it can be shown that

$$p_{i-1} = \frac{-(4R - 2RT) \pm [(4R - 2RT)^2 - 4T^2(R^2 - 4R)]^{1/2}}{2T^2} \tag{27}$$

where

$$T = \frac{R}{p_i} + \frac{2[R(1 - p_i)]^{1/2}}{p_i}$$

and R is the number of tubes minus 1. In Eq. (27) only the negative root has a physical significance. As before, the generation of the p values begins by assuming that the fastest moving peak has a partition coefficient of 100. Once p_{i-1} is found it is used to obtain T which in turn is used to obtain p_{i-2}. This process stops when the p value is such that for n transfers the solute having that p value begins to emerge from the train. As an example, assume that the train has 100 tubes and 1000 transfers were applied. When calculating the peak capacity for the withdrawn portion, the generating of p should be stopped at $p = 0.1$. Again the number of generations is the peak capacity. The peak capacity, for a given solvent system, depends on the number of transfers performed. Figure 3 shows the dependence

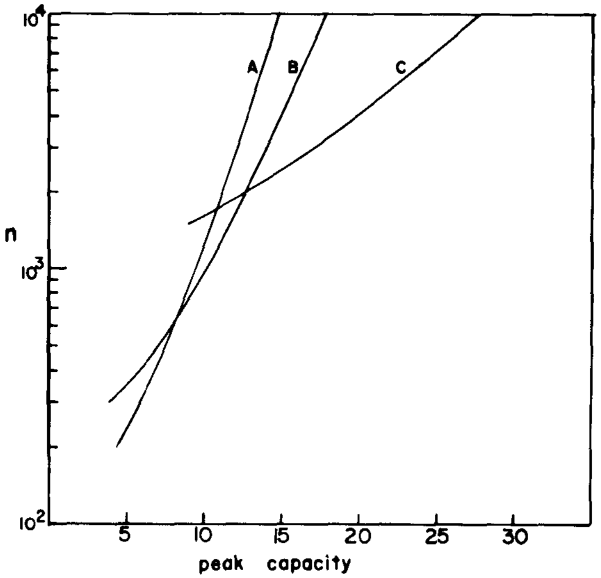

FIG. 3. Peak capacity vs. number of transfers. Withdrawn part. A: 100 tube train. B: 200 tube train. C: 1000 tube train.

for three CCD trains of different lengths. It is interesting to note that, in certain cases, for an equal number of transfers a shorter train is slightly more efficient in terms of the number of resolvable peaks than a longer one.

In order to obtain the total peak capacity of the single withdrawal technique, the number of components left in the train must be taken into account. This can be easily accomplished with the aid of Eqs. (23) and (24) because we have essentially a fundamental process. The only alteration that one must make is in the value of the first p_i in the generation, which is dictated by the number of transfers done. The p_i value should be such that for n transfers the peak maximum is at the last tube of the train. When the number of resolved component left in the train is determined, one finds the following. In the case of the 100 tube train the peak capacity is 6 for the 200 transfers and 5 for all other n up to 10,000. In the case of the 200 tube train, for n up to 10,000 the number of resolved peaks left will be 8. Finally, with the 1000 tube unit at 1500 transfers, 19 resolved peaks will be left, at 2000 transfers 18 peaks, at 3000 and 5000 transfers 17 peaks, and at 10,000 transfers the train will contain 16 resolved peaks. Our theoretical results can be compared with Craig's (*17*) work. He showed a CCD pattern for 1000 tube unit with 4000 transfers. The withdrawn portion showed 17 resolved peaks and the train had 11 additional solutes in it. From Fig. 3 our treatment predicts about 20 peaks withdrawn after 4000 transfers with about 17 left in the train. Craig did not indicate his criterion of unit resolutions. Therein might lie the cause for the small discrepancy between his and our results. Our results also indicate that the fundamental process is the more efficient of the two techniques. For example, the peak capacity in a 1000 tube train after 1000 transfers is larger than in a 200 tube unit after 1000 transfers.

To increase the efficiency of a CCD train in term of resolvable peaks the following recommendation can be made. (a) When possible, increase the number of transfers; (b) when possible, carry out the separation only in the fundamental process manner; and (c) when possible, program the moving phase in such a manner as to increase the partition coefficient of slow moving solutes.

In summary it can be said that the knowledge of such parameters as the plate height, plate number, resolution, and peak capacity allows a direct comparison of CCD with other methods of separation. For example, in terms of peak capacity CCD compares favorably with gel permeation and liquid chromatography but not with gas chromatography. The parameters can facilitate the optimization of CCD runs both in terms of the analysis time and of the number of tubes in the train.

Acknowledgment

The author wishes to thank Dr. Garry Rechnitz for the use of his Hewlett-Packard model 9100A calculator.

REFERENCES

1. L. C. Craig and D. Craig in *Technique of Organic Chemistry*, Vol. 3 (A. Weissberger, ed.), Wiley (Interscience), New York, 1956, pp. 149–332.
2. J. C. Giddings, *Separ. Sci.*, **4**, 181 (1969).
3. E. Grushka, *Anal. Chem.*, **42**, 1142 (1970).
4. J. C. Giddings, *Dynamics of Chromatography, Part I: Principles and Theory*, Dekker, New York, 1965.
5. N. C. Saha, *Indian J. Technol.*, **2**, 153 (1964).
6. J. R. Weisiger, in *Organic Analysis*, Vol. 2 (J. Mitchell, Jr., et al., eds.), Interscience, New York, 1954, p. 277.
7. B. L. Karger, in *Advances in Gas Chromatography, 1967* (A. Zlatkis, ed.), Preston Technical Abstracts Co., Evanston, Ill., 1967, p. 1.
8. C. R. Lancaster, E. B. Lancaster, and H. J. Dutton, *J. Amer. Oil Chem. Soc.*, **27**, 386 (1950).
9. P. L. Nichols, *Anal. Chem.*, **22**, 915 (1950).
10. J. D. Gregory and L. C. Craig, *Ann. N. Y. Acad. Sci.*, **53**, 1015 (1951).
11. E. Hecker, *Z. Naturforsch.*, **8b**, 77 (1953).
12. C. A. Hollingsworth, J. J. Taber, and B. F. Daubert. *Anal. Chem.*, **28**, 1901 (1956).
13. E. Nelson, *Anal. Chem.*, **28**, 1998 (1956).
14. F. J. Wolf, *Separation Methods in Organic Chemistry and Biochemistry*, Academic, New York, 1969.
15. M. T. Bush and P. M. Densen, *Anal. Chem.*, **20**, 121 (1948).
16. J. C. Giddings, *Anal. Chem.*, **39**, 1027 (1967).
17. L. C. Craig, *Bull. N. Y. Acad. Med.*, **39**, 686 (1963).

Received by editor July 6, 1970