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Two-Dimensional Separation Processes

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Abstract

This paper reviews two-dimensional separation systems for both analysis and larger scale separations. The goals of this paper are to: (1) Delineate the three basic two-dimensional methods, (2) show various applications of these methods, and (3) develop new ideas for utilizing two-dimensional methods.

Most separations utilize a single spatial dimension to develop the desired separation. For example, in a chromatographic column the separation is developed along the column axis. The separation is also a function of time and, because of this, multicomponent mixtures can be separated. In a continuous, steady-state, staged distillation column the separation is again developed along the column axis. Any separation which occurs due to cross-flow on the stages is a secondary effect. This one-dimensional steady-state system can only do a binary separation between key components because there is no coordinate (time or spatial direction) available to separate additional components.

In a two-dimensional separation, two spatial directions are used to achieve the desired separation. This can be done in a sequential fashion using a time-dependent development (e.g., two-dimensional TLC or PC) or in a simultaneous fashion as a continuous steady-state system (e.g., rotating annulus chromatograph or 2-D electrophoresis) where one spatial direction replaces time. The sequential pattern has been used extensively for analysis while the simultaneous pattern has been used for preparative applications.

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Field-flow fractionation (*1*), where the second spatial direction is used to develop a polarization or concentration gradient which is then used to separate components by flow in the first direction, will not be reviewed here.

TWO-DIMENSIONAL PAPER AND THIN-LAYER CHROMATOGRAPHY

A common application of two-dimensional techniques is two-dimensional TLC and PC. This method was first used in 1944 (*2*) and was recently reviewed in great depth (*3*). The original idea was to place a single spot of the mixture to be analyzed in one corner of a sheet of paper. This spot is developed in direction 1 using solvent 1. The compounds will be partially separated as shown in Fig. 1(a). Then the sheet is removed from the solvent and dried. After rotating the paper by 90°, a second solvent with a different retention mechanism is used to develop the paper in direction 2 (see Fig. 1b). Now each separated component can be detected by the usual methods. The two-dimensional development method was quickly applied to thin-layer chromatography, and a large variety of stationary phases including inorganic, organic, polyamide, cellulose, reversed-phase, ion-exchange, and size-exclusion media has been used. Note that these are all sequential methods with time-dependent development.

Many modifications of the basic technique have been developed. Obviously, mixed solvents can be used. Two stationary phases can be employed. One way to do this is shown in Fig. 1(c) where the first development uses sorbent 1 and solvent 1 and the second development uses sorbent 2 and solvent 2. The sorbents can also be mixed together or spread in two separate layers. Alternatives are to modify the plate after the first development or to derivatize the solutes after the first development.

Compared to one-dimensional systems, the two-dimensional methods have the advantages of providing better resolution and higher spot capacity. The greater the differences in the retention mechanisms used in the two directions, the more improvement is possible. Between 150 and 300 peaks can be quantified in the two-dimensional systems. Unfortunately, the two-dimensional systems are slower, can handle fewer samples, and are more complex. In addition, the second development may have irregular ascent of the solvent and predicting the R_f values is often difficult. Both one- and two-dimensional systems can have detection problems and have nonconstant flow problems.

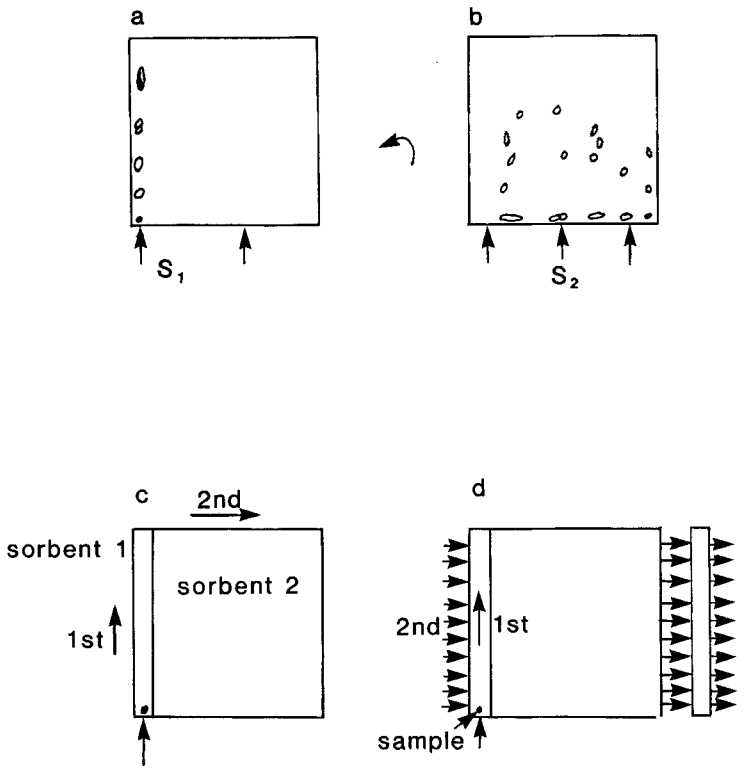

FIG. 1. Two-dimensional thin-layer chromatography. (a) First development, (b) second development, (c) first development for plate with two sorbents, (d) two-dimensional column.

The detection problems and nonconstant flow problem can be reduced by using overpressured development (*4, 5*). In this procedure a plastic plate is pressed against the surface of the TLC plate and the solvent is pumped through the system. Operation is in the elution mode with on-line detection. In applying this to two-dimensional systems, the solutes are retained in the system during the first development and eluted during the second development (*6, 7*). A two-dimensional column system using a 1024 pixel array of diodes as the detector is shown schematically in Fig. 1(d). Computer analysis of the data will be required. Up to 900 peaks should be separable with this apparatus, but no experimental results were presented (*6, 7*). A theoretical investigation of both two- and three-dimensional columns has been presented (*7*). Three-dimensional systems could have huge spot capacities, but the practical development of such systems will be difficult.

Two-dimensional PC and TLC will continue to be standard laboratory procedures for difficult analyses. The two-dimensional column chromatograph has the potential for being a very powerful tool for very complex mixtures. However, it will be a fairly complex and expensive apparatus.

CONTINUOUS, STEADY-STATE TWO-DIMENSIONAL CHROMATOGRAPHS

An alternate two-dimensional chromatographic system using simultaneous development was first suggested by Martin (*8*). In this system an annulus is packed with the sorbent and is then rotated. Feed is input at one point and solvent or carrier gas everywhere else. The apparatus is shown schematically in Fig. 2. Solutes which are not strongly sorbed spend more time in the carrier and are carried up the annulus with a high slope. These solutes will exit near the feed injection point. Solutes which are more strongly retained spend more time on the solid and thus are rotated through more of an angle ϑ. Thus a helical movement of solute is developed. The result is a steady-state,

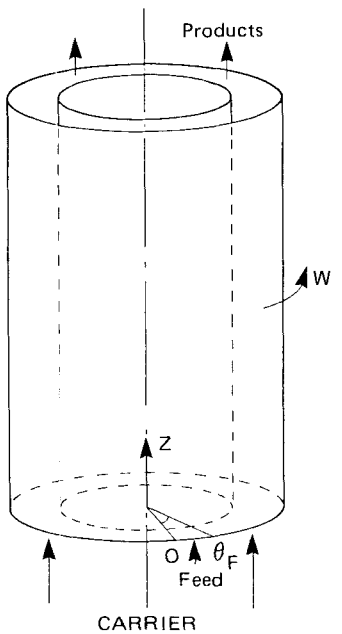

FIG. 2. Rotating annulus apparatus for continuous chromatography (*9*). Reprinted with permission from the *AIChE J., 23*, 859 (1977). Copyright 1977, AIChE.

multicomponent separation with simultaneous movement in the two spatial directions. The ϑ coordinate takes the place of time in a one-dimensional, time-dependent chromatograph. In fact, if diffusion in the ϑ direction can be ignored, the systems are completely analogous (*9*).

Many modifications of the basic device have been developed and extensively reviewed (*10–14*). Packed annulus systems for liquid chromatographs were first studied experimentally by Svensson and his co-workers (*10*). With an annulus packed with powder they had difficulties with lateral flow which decreased the separation obtained. To overcome this difficulty, they used a series of columns arranged in a circle as in a Gatling gun. Although this arrangement worked better and good continuous separations were obtained, they still had difficulty in obtaining equal flow rates in each column. Since equal column flow rates are essential to obtain a good separation, they controlled the liquid flow rate instead of the pressure drop.

A rotating annulus apparatus very similar to the earlier systems was used to study two-dimensional gel permeation chromatography (*15–17*). These researchers found that a uniform flow throughout the annulus was absolutely necessary to achieve successful separations. A similar system except with a stationary annulus and a rotating feed head and fraction collector has also been developed (*18, 19*). Since there was no way to pressurize these apparatus, flow rates were low.

Sison and his co-workers (*20–23*) developed a pressurized, rotating annulus system in which they were able to overcome the channeling and mechanical problems which plagued earlier devices. Both size-exclusion and ion-exchange separations were done. Gradient elution experiments were also done. The final device (*22*) is shown in Fig. 3. It is fairly large-scale with a bed length of 60 cm, an annulus with a width of 1.27 cm, and an o.d. of 27.9 cm which gives a cross-sectional area of 106 cm^2. The separations were analyzed with a two-dimensional staged model (*20*). Although this device does solve the problems observed with other rotating annulus systems, it is quite complex.

The same basic geometry was used for continuous paper chromatography but the annulus is replaced by a cylinder of filter paper (*24*). Note that this is very different from the paper chromatograph separations discussed previously since only one solvent is used and operation is simultaneous and continuous. Since only one retention mechanism is used, complex mixtures will not be completely separated.

The Gatling-gun-type system with a series of 100 columns replacing the packed annulus has been used for gas separations (*25–27*). The bundle of columns rotate at from 1 to 50 rph while feed and product receivers are stationary. Purities greater than 99.9% were obtained in steady-state

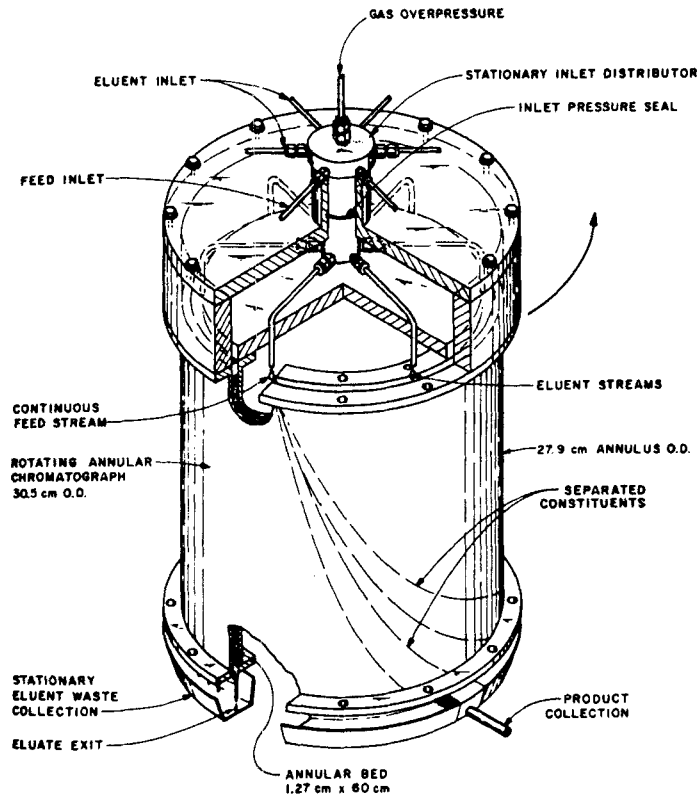

FIG. 3. Pressurized, rotating annulus chromatograph (*22*). Reprinted with permission from *Sep. Sci. Technol., 15*, 655 (1980). Copyright 1980, Marcel Dekker.

operation. A series of columns is easier to pack than an annulus, but each column must be matched to have the same residence times. Since each column behaves as a batch system, this type of two-dimensional apparatus does not appear to have an advantage compared to a single large column.

Other rotating two-dimensional geometries have been used. A rotating annulus device but with flow in a radial direction will produce continuous multicomponent separations if the feed injection is to only a portion of the circumference (*28, 29*). This equipment looks similar to, but is different from, the chromatofuge (*30, 31*) which is a one-dimensional (radial direction), time-dependent chromatograph.

A steady-state, two-dimensional chromatograph using a different approach is the "continuous surface chromatograph" developed by Sussman and his co-workers (*32–34*). Two flat plates are coated with the stationary phase and

held very close together (0.003 to 0.005 in.). The plates are slowly rotated (less than 10 rpm) which gives a helical pattern for each solute. This apparatus is shown in Fig. 4. The system is thus similar to the radial flow rotating annulus systems except this system acts as a gas capillary column instead of a packed column. At low rotational speeds excellent separations were obtained and agreement between theory and experiment was excellent. Since feed flow rates are low, this device was developed as a continuous analytical device.

Two-dimensional flow can be obtained without rotation in a rectangular box packed with adsorbent (*35*). Gas flow was horizontal while liquid flow was downward. By injecting feed into one corner of the apparatus, a continuous, two-dimensional gas–liquid chromatograph resulted. A simultaneous, continuous, two-dimensional, thin-layer chromatograph was developed (*36*) by flowing two solvents into different sides of a triangular TLC plate. This separation is quite different from the TLC separations discussed earlier since development is simultaneous, not sequential.

A variety of theoretical methods has been used to analyze two-dimensional chromatographic systems. The linear theory of chromatography has been applied to analyze the rotating annulus system (*37*). A similar theory was used to analyze continuous surface chromatography (*38*). Continuous surface chromatography was analyzed by superimposing the effects of zone

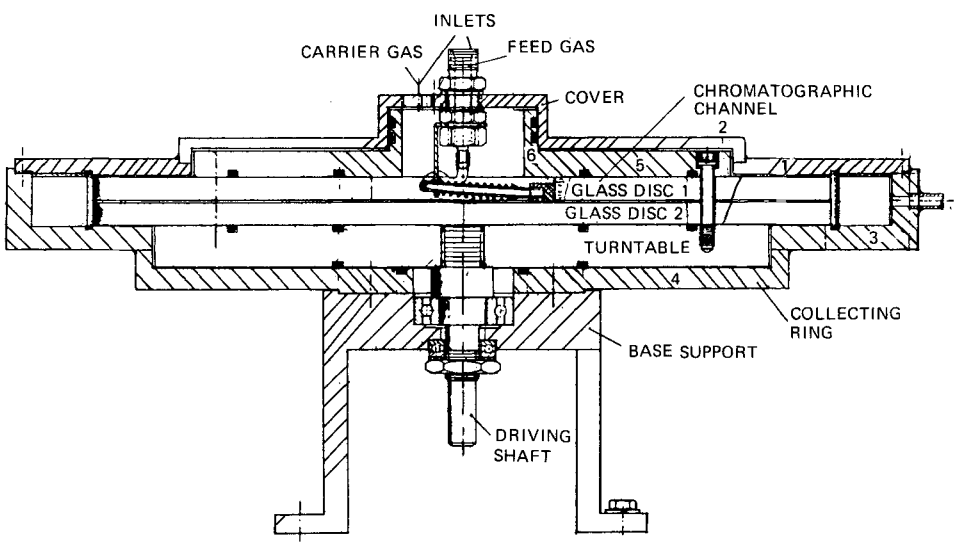

FIG. 4. Continuous surface chromatograph (*33*). Reprinted with permission from *Ind. Eng. Chem., Fundam., 11*, 181 (1972). Copyright 1972, American Chemical Society.

spreading caused by the increasing cross-sectional area of the flow channel, the effect of the rotation, and the effect of retention (*33, 34*). Staged models have also been used (*20, 39*). A retention argument was used to predict where solutes would exit in a Gatling-gun-type apparatus (*25*). Wankat (*40*) used both staged and local equilibrium theories to show that throughput could be increased by injecting feed along a sloped feed line. This last idea should be applicable to other continuous two-dimensional separators.

One-dimensional time-dependent columns and two-dimensional steady-state rotating annulus systems are analogous. Physically, the analogy is most obvious for the Gatling-gun-type systems with a bundle of columns rotating past a feed point. Each column in the bundle receives a pulse of feed and is then developed in exactly the same way as a single column. The mathematical analogy can be seen by comparing the mass balances in one-dimensional and two-dimensional systems (*9*). The column equation is

$$\varepsilon \frac{\partial c}{\partial t} + \varepsilon v \frac{\partial c}{\partial z} + (1 - \varepsilon)\rho_s \frac{\partial q}{\partial t} - D \frac{\partial^2 c}{\partial z^2} = 0 \qquad (1)$$

while the rotating annulus equation is

$$\varepsilon W \frac{\partial c}{\partial \vartheta} + \varepsilon v \frac{\partial c}{\partial z} + (1 - \varepsilon)\rho_s \frac{\partial q}{\partial \vartheta} - D \frac{\partial^2 c}{\partial z^2} - D_\vartheta \frac{1}{r^2} \frac{\partial^2}{\partial \vartheta^2} = 0 \qquad (2)$$

Note that there is a term-by-term equivalence except for diffusion in the ϑ direction. If diffusion and disperson in the ϑ direction can be neglected, then the mass and energy balances and the boundary conditions for the one-dimensional column system will be transformed into the equations for the two-dimensional rotating annulus system by using the transformation $t \rightarrow \vartheta / W$ (9). Thus the solutions obtained by a variety of methods for one-dimensional chromatography can be applied to rotating annulus systems with axial flow. One can, of course, go the other way and develop columnar systems based on two-dimensional systems. In addition to the analogy between time-dependent, one-dimensional systems and steady-state, two-dimensional systems, by using slanted feed and product lines the two-dimensional system becomes analogous to a steady-state, one-dimensional, countercurrent cascade (*41*). When this is done, only binary separations can be done and the ability to separate multicomponent mixtures is lost. Both these analogies can be extended to three-dimensional systems.

Naturally, this analogy needs to be modified for systems with changing cross-sectional areas since geometrically similar systems must be compared.

Thus the chromatofuge and the radial-flow, rotating-annulus systems are analogous. Physically, this makes sense since a segment cut like a piece of pie will have the same flow patterns in the one- and two-dimensional systems. The rotation provides a perpendicular shift which allows the ϑ direction to replace time.

Although extensively studied, including industrial prototypes and pilot-plant studies, the continuous two-dimensional chromatographs have not been accepted as standard separation methods. These devices do essentially the same separation as a column and have the disadvantages of being much more complex, harder to scale-up, harder to efficiently pack, require more maintenance, and are more expensive. The one advantage of the two-dimensional systems, their continuous steady-state behavior, has become less important as methods for control of cyclic systems have improved. Other continuous two-dimensional systems (e.g., electrophoresis and high gradient magnetic separation) have advantages compared to their one-dimensional analogs which the chromatographic systems do not have.

REGENERATED TWO-DIMENSIONAL ADSORPTION AND CHROMATOGRAPHY

The two-dimensional chromatographs discussed earlier have many of the same limitations as one-dimensional columns. Both systems require a lot of solvent or carrier gas, have low feed throughputs, and produce dilute products. To some extent these problems can be solved by operating at feed concentrations above the linear limit, accepting lower resolution, and recycling some of the product. Another alternative is to input energy to regenerate the adsorbent. This allows a larger portion of the adsorbent to be active and increases productivity. One common cycle is to adsorb solvent from an air stream and then regenerate the activated carbon adsorbent with a countercurrent flow of stream. This has also been done commercially in a rotating annulus system (*42*). This is illustrated in Fig. 5. Solvent-laden air flows radially inward while steam countercurrently regenerates the adsorbent. All solvents are recovered together by condensing the steam and solvent mixture. This device utilizes the ability of a two-dimensional apparatus to produce a steady-state separation, but not the multicomponent fractionation capability. A somewhat similar idea using axial flow with hot gases for regeneration has been proposed (*43*). A rotating ion-exchange system which replaces the steaming region of Fig. 5 with wash and regeneration sections has been proposed, but apparently was not commercialized (*44*).

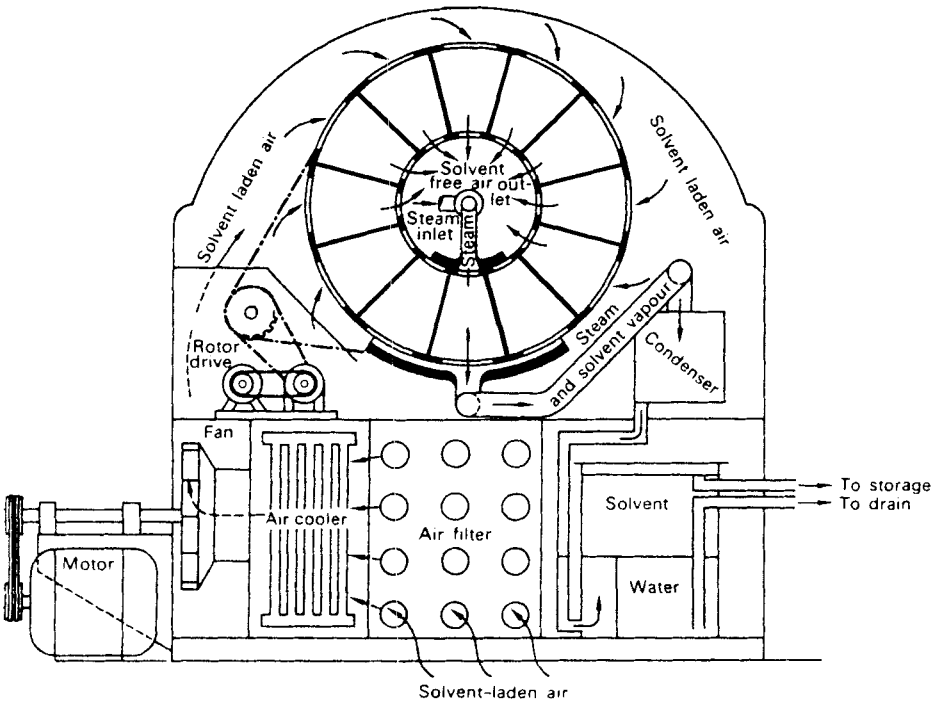

FIG. 5. Rotary bed activated carbon adsorber (*42*). Reprinted with permission from J. M. Coulson and J. F. Richardson, *Chemical Enginering*, Vol. 3, 2nd ed., Pergamon, New York, 1979. Copyright 1979, Pergamon Press.

Regenerated two-dimensional systems can be used for multicomponent separations (*39*). An apparatus similar to Fig. 2 was used with feed to all of the annulus. Each solute moves in the annulus at a slope, S_i, which can easily be calculated. For linear isotherms

$$q_i = k_i(T)c_i \tag{3}$$

the slope of the solute wave is

$$S_i = \frac{\varepsilon V}{\varepsilon\omega + (1 - \varepsilon)\rho_s k_i(T)\omega} \tag{4}$$

Equation (4) is the solution to Eqs. (2) and (3) when the local equilibrium assumptions are used. For most adsorbents $k_i(T)$ decreases as temperature increases. Thus S_i will increase as temperature increases. If the annulus

shown in Fig. 1 has fluid at different temperatures fed to it, the temperature waves will have a slope, S_{th}, of

$$S_{th} = \frac{V}{\omega}\left(\frac{\rho_L C_{P_L}}{\rho_L C_{P_L} + \left(\frac{1-\varepsilon}{\varepsilon}\right)\rho_S C_{P_S}}\right) \tag{5}$$

If the temperature can be adjusted so that

$$S_A(T_c) < S_{th} < S_A(T_1) \tag{6}$$

then solute A must concentrate at the temperature boundary between temperatures T_c and T_1. This is illustrated in Fig. 6. Note that the solute is fed to the entire annulus, but solute concentrates at two locations. With linear isotherms this theory (see Fig. 6) predicts infinite concentrations.

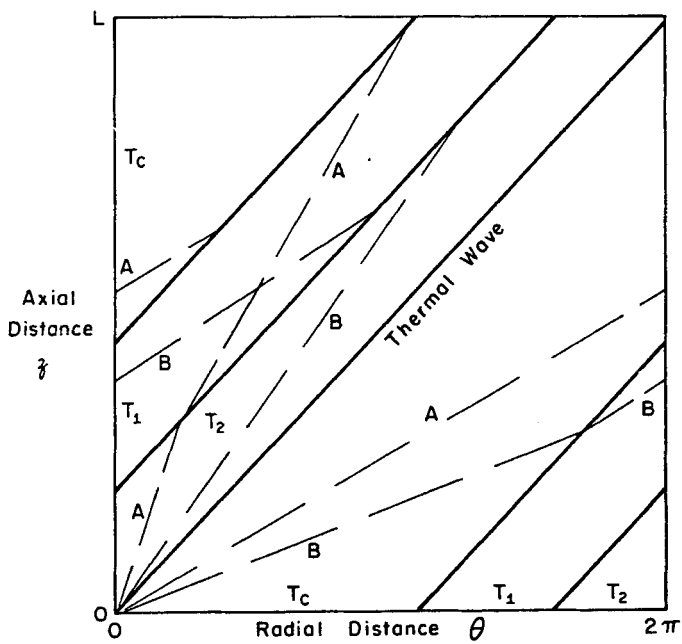

FIG. 6. Characteristic solution for regenerated rotating annulus system (*39*). Reprinted with permission from *Ind. Eng. Chem., Fundam., 15*, 309 (1976). Copyright 1976, American Chemical Society.

When more realistic nonlinear isotherms are used, infinite concentrations are not predicted. The naturally occurring slope of the thermal wave, S_{th}, given by Eq. (5) may be too high or too low to allow Eq. (6) to be satisfied. In this case external heaters and coolers could be used to obtain any slope desired for S_{th}. This regenerated, two-dimensional system can be considered the two-dimensional analog of chromatothermagraphy (*45*) or of multicomponent cycling zone adsorption (*46*). Equations (4) and (5) can also be used to predict the behavior of two-dimensional chromatographs. The experimental results obtained with this regenerated two-dimensional system (*39*) did not agree with the theory because of excessive channeling.

A variety of other regenerated systems such as parametric pumping, cycling zone adsorption, and pressure swing adsorption has been developed for one-dimensional, time-dependent columns. Steady-state, two-dimensional analogs for all of these systems can be developed in the rotating annulus system (*9*).

A flat plate with a stationary adsorbent can be used (*47*). Solvent at temperature T_1 flows for period t_1 in the x direction and is followed by solvent at temperature T_2 for period t_2 in the y direction. Because of the shift of the isotherm with temperature, solutes will follow different paths. Unfortunately, throughput will be low for this process since feed is input at only one point.

The regenerated, two-dimensional system for solvent recovery with activated carbon is a proven commercial device. More work is required to determine the potential of the multicomponent separators. These devices are interesting for large-scale separations since they have large throughputs of feed.

TWO-DIMENSIONAL ELECTROPHORETIC TECHNIQUE

A variety of two-dimensional electrophoretic techniques has been developed. These include batch sequential methods for analysis and continuous, simultaneous methods based on deflection of molecules or particles. First the two-dimensional analytical methods and then the continuous methods will be reviewed.

Several sequential, two-dimensional methods have been used for years (*48–51*). These methods involve electrophoresis in one direction followed by a second separation at right angles. The idea is the same as in two-dimensional TLC. Two independent retention mechanisms should be used to spread spots over the entire plane. Examples include electrophoresis followed by TLC, paper electrophoresis followed by paper chromatography either on the same sheet or a different sheet of paper, paper or cellulose

acetate electrophoresis followed by starch gel electrophoresis, and starch gel electrophoresis followed by TLC. The more independent the two methods, the more spots that can be observed. Immunoelectrophoresis (*48, 49, 52, 53*) can also be considered a sequential two-dimensional technique.

Interest in sequential two-dimensional methods boomed following O'Farrel's (*54*) development of isoelectric focusing (IEF) followed by sodium dodecyl sulfate (SDS) electrophoresis in a second direction. Since IEF separates on the basis of charge and SDS-electrophoresis on size, the two development directions are based on independent retention mechanisms. O'Farrel (*54*) first did IEF on a polyacrylamide gel in a narrow tube in 8 *M* urea. Then he extruded the gel and put it on top of a SDS polyacrylamide slab and did electrophoresis at right angles to the original development direction. Over 1100 spots were observed in the analysis of *E. coli* lysate. Since 1975 many variations of this basic method have appeared. Anderson and Anderson (*55*) developed the ISODALT method for doing multiple samples. This equipment is now commercially available. The SDS-electrophoresis can be done first and under some circumstances this is preferable. More recent developments have been reviewed elsewhere (*3, 52, 56–60*). Detection remains a major problem although computer imaging techniques (*58*) are rapidly improving. At least five other two-dimensional techniques using IEF have been used (*51*). Some of these were developed before O'Farrel's method, but they have not attracted the imagination of researchers as much as the IEF–SDS-electrophoresis method.

For preparative work, continuous, two-dimensional electrophoresis has advantages over its one-dimensional analog. The two-dimensional method is an elution method whereas the one-dimensional technique is not. This has obvious advantages for collecting samples. The free-flow two-dimensional methods can be used for particle separations while sedimentation would be a major problem with one-dimensional methods. Many of the basic ideas of continuous two-dimensional electrophoresis are evident in the early two-dimensional paper electrophoresis method (*49, 61, 62*), shown schematically in Fig. 7. In this process, solution flows down a sheet of paper between two electrodes. The charged molecules are deflected according to their mobility. If no chromatography or sieving occurs, all species will have the same vertical velocity, and the separation at any horizontal location will be analogous to the separation on a one-dimensional strip of paper at a time

$$t = z/v$$

where z is the axial distance from the feed point and v is the vertical velocity. If a chromatographic separation also occurs, then the exact analogy between one- and two-dimensional systems won't hold, but the separation may be

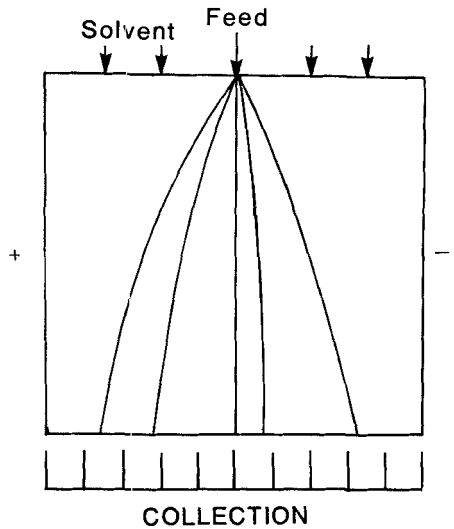

FIG. 7. Basis of two-dimensional electrophoresis.

improved. A gel can replace the paper in the two-dimensional system (*48*). The paper or gel serves to stabilize the flow and prevents convection currents from destroying the separation. The plates are often cooled to control temperature increases in the gel.

For larger-scale systems and for the separation of cells or other particles, two-dimensional, free-flow electrophoresis is employed. This process has been extensively reviewed (*63–69*). A large number of variations of the basic apparatus has been developed. The basic apparatus is also illustrated by Fig. 7. Since no stabilizing medium is used, both front and back of the flow chamber are cooled and the flow chamber is usually around 0.6 mm thick. Equipment very similar to this basic apparatus is available commercially and can be used for separation of either molecules or particles. Separation of species >0.1 μm is of greatest interest for free-flow electrophoresis since smaller materials can be electrophoresed in a gel. Free-flow electrophoresis has also been done in space to remove the detrimental effects of sedimentation and thermal convection (*64, 70*). These designs used special hydrophilic coatings of zero charge to prevent electroosmatic flow, and the experiments successfully demonstrated two-dimensional electrophoretic separation of cells in space.

Several clever methods have been used to stabilize the flow. Theoretically, flow will be stabilized if the chamber width is reduced to around 5 mm (*63*). In this case a special collector such as a fan collector (*71*) needs to be used.

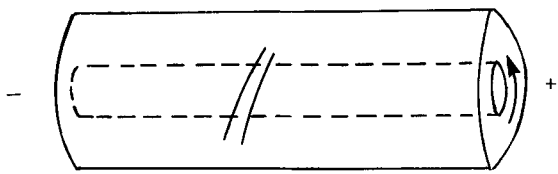

FIG. 8. Flow stabilization in two-dimensional electrophoresis by rotation.

Flow can also be stabilized by doing the electrophoresis in a horizontal annulus and rotating the inner cylinder as shown schematically in Fig. 8. The rotation causes secondary flows which stabilize the flow. Several different designs of this type have been developed and at least one is commercially available (*63, 66, 68, 69, 72*). Another scheme which does the same type of flow stabilization but without requiring rotating seals is endless belt continuous flow deviation electrophoresis (*66, 69*). In this method a magnet is used to induce the flow of the buffer. Kolin (*66*) found that the race-track geometry shown in Fig. 9 was advantageous because it minimized sedimentation problems. The pitch of the "helical" flow shown in Fig. 9 can be increased by imposing a uniform lateral flow in the direction of electrophoresis.

Continuous two-dimensional isoelectric focusing can utilize a free-flow electrophoresis system similar to Fig. 7 but with a continuous horizontal pH

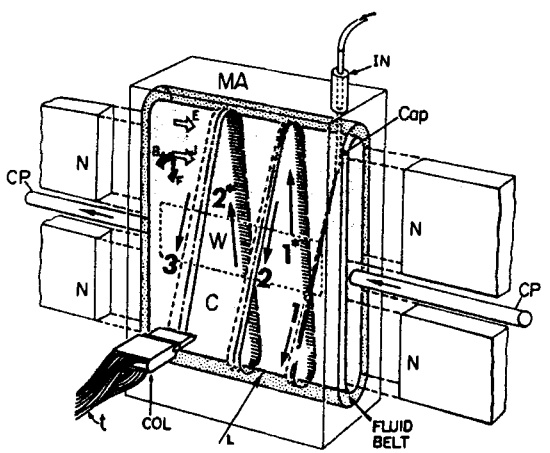

FIG. 9. Endless fluid belt electrophoresis (*66*). Reprinted with permission from P. G. Righetti, C. J. Van Oss, and J. W. Vanderhoff (eds.), *Electrokinetic Separation Methods*, Elsevier/North Holland Biomedical Press, Amsterdam, 1979. Copyright 1979, Elsevier/North Holland Biomedical Press.

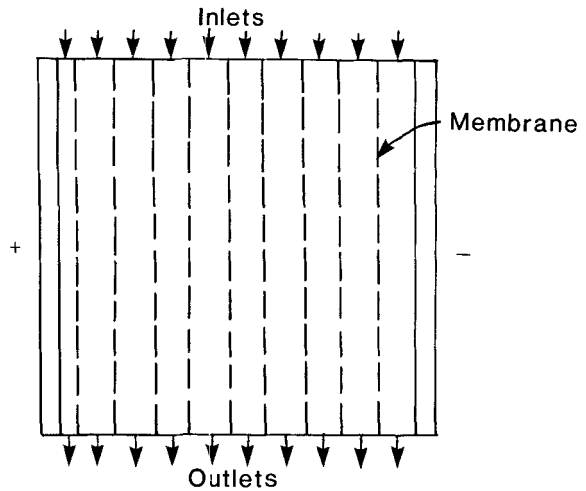

FIG. 10. Schematic of recycling isoelectric focusing.

gradient produced by adding carrier ampholytes (*57, 64, 73*). This system requires less current than continuous free-flow electrophoresis and gives a sharp separation since molecules or particles are focused at their isoelectric point. Compared to one-dimensional isoelectric focusing, elution is easier, particles spend a much shorter time in the separating chamber, and there is no need to support the pH gradient with a density gradient. Recycling isoelectric focusing is a variation which appears to have promise for scale-up (*57, 74, 75*). This system is shown schematically in Fig. 10. The outlet streams are cooled, passed through a UV monitor, pH adjusted, and recycled to the inlets. After some time a steady horizontal separation results and product can be withdrawn. The membranes serve to stabilize the flows.

TWO-DIMENSIONAL EXTRACTION AND DISTILLATION

Whereas two-dimensional electrophoresis has been accepted as a routine separation method, two-dimensional extraction and distillation are curiosities. Meltzer and his co-workers (*76–78*) developed a two-dimensional extractor with three liquid phases. The bottom phase was held stationary while the other two phases were transferred by a countercurrent distribution type of apparatus. A completely automated device was available commercially for awhile. Most of Meltzer's experiments were done with a heptane–water–nitromethane system for purification of strandin. Gradient elution by

varying pH could also be used. Since solutes have different distribution coefficients among the three phases, difficult separation could be achieved.

Since two phases move and one phase is stationary, the result is a two-dimensional, time-dependent, simultaneous development. This is thus a somewhat different development procedure from that used in sequential systems such as 2-D TLC. This discrete transfer, discrete equilibrium staged system was analyzed by an extension of the binomial distribution analysis used for countercurrent distribution (*77*). A similar analysis for sequential and simultaneous development has been published (*79*). This analysis also showed that the three-dimensional cross-flow system shown in Fig. 11 could produce a continuous, steady-state, two-dimensional development (*79*). All three phases move in the three-dimensional system. Either discrete transfer steps or continuous flow could be used.

Although working systems can and have been built, these two-dimensional batch extractors are complex, bulky, and expensive. Chromatographic systems can do many of the same separations and are usually much more convenient to use and are cheaper.

A steady-state, simultaneous, two-dimensional cross-flow (2DCF) system is the two-dimensional analog of countercurrent distribution (*80*). A model for nonideal partially miscible systems was in good agreement with test-tube experiments for steady-state separations (*81*).

The 2DCF system requires a large number of stages compared to the amount of feed which can be processed. The regenerated two-dimensional

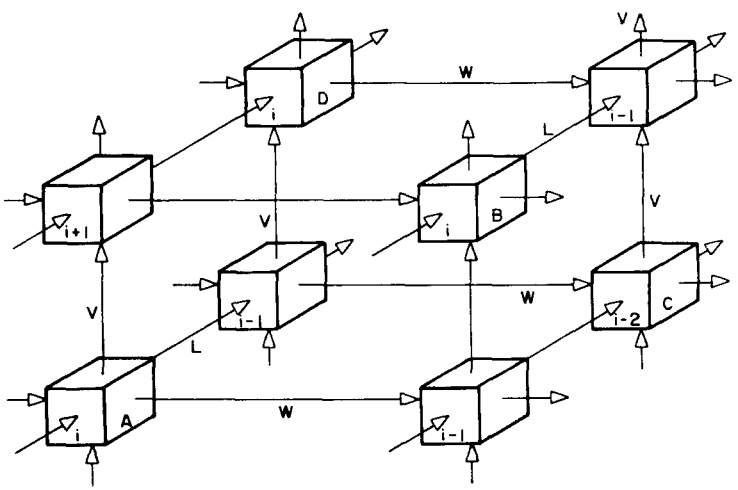

FIG. 11. Staged, three-dimensional cross-flow system (*79*). Reprinted with permission from *Sep. Sci.*, *7*, 345 (1972). Copyright 1972, Marcel Dekker.

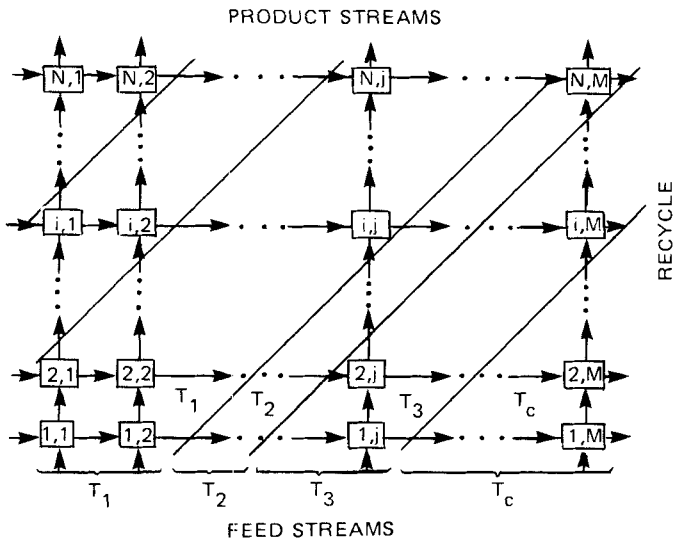

FIG. 12. Regenerated two-dimensional extraction (*39*). Reprinted with permission from *Ind. Eng. Chem., Fundam., 15*, 309 (1976). Copyright 1976, American Chemical Society.

system shown schematically in Fig. 12 was developed to increase the feed capacity greatly (*39*). This system uses the same principle of operation as the regenerated, rotating annulus chromatography system. Note that feed enters into the entire bottom of the cascade in Fig. 12, and that all solvent is recycled. Thus solvent regeneration is done within the cascade. Test-tube experiments were in good agreement with theory (*39*). Research on a regenerated two-dimensional extractor with continuous mixer-settlers is now in progress.

At this time two-dimensional distillation is only a theoretical construct. Kvaalen (*82*) considered a two-dimensional distillation system with horizontal liquid flow and vertical vapor flow. Part of the liquid is reboiled and part of the vapor refluxed. Analysis of a continuous contact device for a constant relative volatility system was mathematically similar to the analysis of a chromatograph for a system with interacting Langmuir equilibrium. Theoretically, all components could be obtained as pure products.

TWO-DIMENSIONAL PARTICLE SEPARATION METHODS

In addition to free-flow electrophoresis, a number of two-dimensional methods are used for particle separations. In this section these methods will be briefly reviewed. Some of these methods, such as filtration and magnetic

filtration, use the principle of holding the particle on an element while moving the element at right angles to fluid flow. These are thus similar to the rotating annulus, continuous chromatograph. Others, such as open gradient magnetic separators and eddy current separators, are deflection devices which impose a force on the particle which is perpendicular to the fluid flow. Thus these systems are similar to free-flow electrophoresis.

Continuous filtration of liquid slurries usually employs a two-dimensional filter of some type (*83–85*). The two-dimensional filters use the general scheme shown schematically in Fig. 13, although some of the elements shown may be missing in particular filters. Operation is continuous and the filter cake is carred at a right angle to the flow of slurry and wash water. Thus the second dimension results from a perpendicular shift. The method of moving the filter medium determines the actual geometry of the filter. Different types include horizontal belt filters (shown in Fig. 13), horizontal pan filters, rotating drums, rotating disks, and a variety of proprietary filters. Usually vacuum is used as the driving force. The two-dimensional filters are used for concentrated slurries. They have higher capacities and are much easier to automate than one-dimensional batch filters which do the same sequence of steps.

Since the concentration of particulates in gas streams is usually much lower than in liquids, the time for cleaning a batch filter is usually a small fraction of the total duty cycle. Thus continuous filters have less advantage. Continuous fibrous mat filters (*86*) are used in some cases. These filters automatically unroll a new filter surface when the pressure drop across the filter becomes too large. The old filter surface containing the dust is rolled away, perpendicular to the gas flow. Continuous electrostatic fibrous air filters using a similar two-dimensional arrangement are also in use (*86*). The

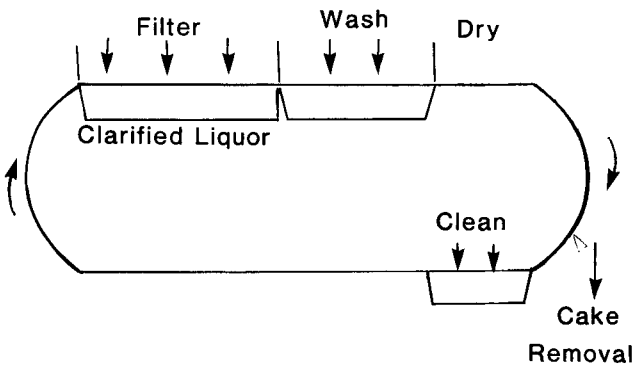

FIG. 13. Generalized two-dimensional filter.

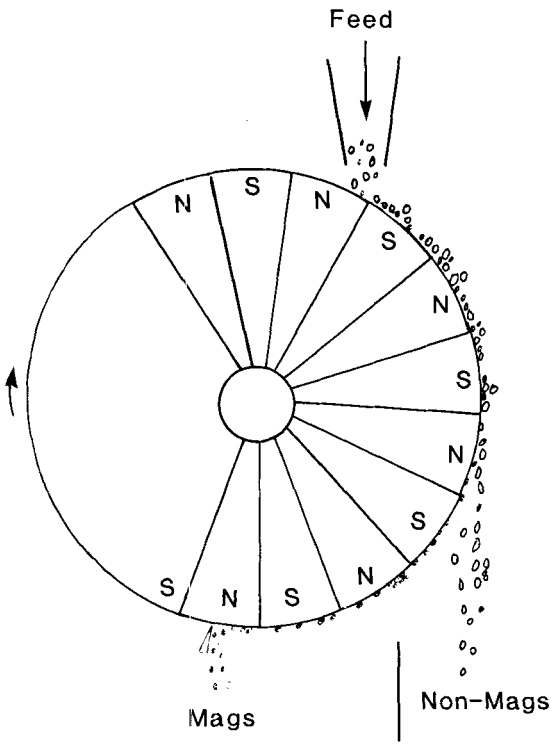

FIG. 14. Schematic of continuous rotary drum magnetic separator.

usual electrostatic precipitator (*87*) can also be considered a two-dimensional separator although it is not completely continuous.

A variety of continuous, two-dimensional magnetic separators are in use for particle separations (*84, 88, 89*). The simplest of these use a belt to carry nonmagnetic material past the magnet while magnetic materials are lifted off the belt. Since the magnet needs to be cleaned periodically, this is a batch operation. Continuous rotating drum separators are shown schematically in Fig. 14. The drum rotates past the permanent magnets. Magnetic materials adhere to the drum until carried past the magnetic region and thus are carried away from the nonmagnetic particles which drop due to gravity. Belt separators use similar principles. Rotating disk separators carry the magnetics sideways off a moving belt.

Rotating annulus or carousel systems (*88, 89*) are used with both Jones separators using grooved plates and high gradient magnetic separators (HGMS) using stainless steel wool packings to collect the particles. This is

illustrated in Fig. 15. The geometry is similar to Fig. 2. The annulus is packed with grooved plates or steel wool. A magnet is arranged around a fraction of the circumference. Feed and wash steps are done in the region of the magnet while magnetics are flushed out in the region away from the magnet. If one looks at the history of a particle or of the matrix, the one-dimensional, batch processes and the two-dimensional, continuous processes are analogous with $t \rightarrow \vartheta/\omega$. However, contrary to the case for two-dimensional chromatography, the two-dimensional carousel systems are preferred over the one-dimensional systems for feeds with high concentrations of magnetic particles. What is the difference between these two situations? In the magnetic separation the most expensive item is the magnet. In a batch separator the magnet must be turned off every time the magnetic solids are removed. If feed concentrations are high, the fraction of time the magnet is on may be quite low. With the two-dimensional system the magnet is always on and it is the much less expensive matrix which spends time out of the magnetic field.

Open-gradient magnetic separators which work by deflection of the particle (*88, 89*) are another type of steady-state, two-dimensional separator. In a nonuniform magnetic field, particles can be deflected at right angles to

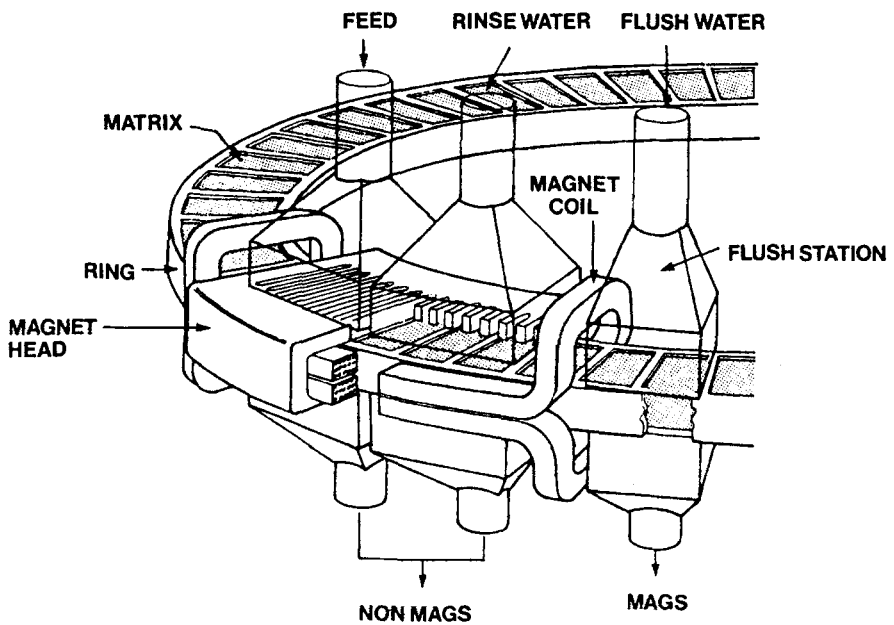

FIG. 15. Carousel separator for high gradient magnetic separation (courtesy of Sala Magnetics, Inc.).

the flow direction. Either conventional or superconducting magnets can be used. In theory, several different particles could be fractionated; however, in practice magnetic particles are separated from diamagnetic particles.

Another type of magnetic separator is magnetic density fractionation. Although this is usually a one-dimensional separator, two-dimensional magnetic density fractionation can have advantages (*90*). The second direction can be developed by imposing a flow perpendicular to gravity. Light particles which float are swept along with the flow while heavy particles sink. An alternative is to use a three-dimensional pole piece with flow perpendicular to gravity. Particles move horizontally until they reach the point that the maximum levitation force cannot hold them up. Then the particle sinks. Since each species has a different trajectory, continuous, multispecies separation with good resolution is possible. The very different approach of using a two-dimensional staged cascade for float–sink separation using ferromagnetic fluids has been proposed (*91*).

A different principle is used in eddy-current separators (*92*). Changes in a magnetic field will cause an electrical current in a conductor such as a metal. In a moving magnetic field the eddy current resists changes in the magnetic field strength and the metal is pushed to regions of weaker magnetic field. Separators using this principle were first patented by Thomas Edison (*93*), but they have only recently become practical. Since larger metal particles are more strongly deflected, the devices work well for removing aluminum cans from garbage. Ferromagnetic scrap is removed first in one of the magnetic separators discussed earlier. Three types of eddy-current separators have been used (*92*). In the "linear motor" separator a moving belt carries the scrap past an electromagnet energized by polyphase current (the linear motor) which pushes the metal pieces sideways off the belt. The "popper" or "pulse-sort" separator produces a very short but very strong magnetic field by discharging a condenser bank through a coil. This pulse pushes out the metals. The sliding ramp device shown in Fig. 16 can be constructed with permanent magnets which greatly lowers energy consumption. The rotary drum current separator is a different geometry for the sliding ramp system which can develop longer separation paths and achieve sharper separations. In all of these eddy-current systems the two-dimensional separation is produced by deflection.

Dielectrophoresis is based on the migration of particles with a dielectric constant different from the fluid in an inhomogeneous electric field. If $\varepsilon_{\text{particle}} > \varepsilon_{\text{fluid}}$, the particles migrate to the region of larger field gradient. Two-dimensional dielectrophoresis separations have been done (*94*) in an annulus where the inner and outer cylinders are electrodes. Fluid flows axially while particles move radially and concentrate at the inner cylinder at the bottom of

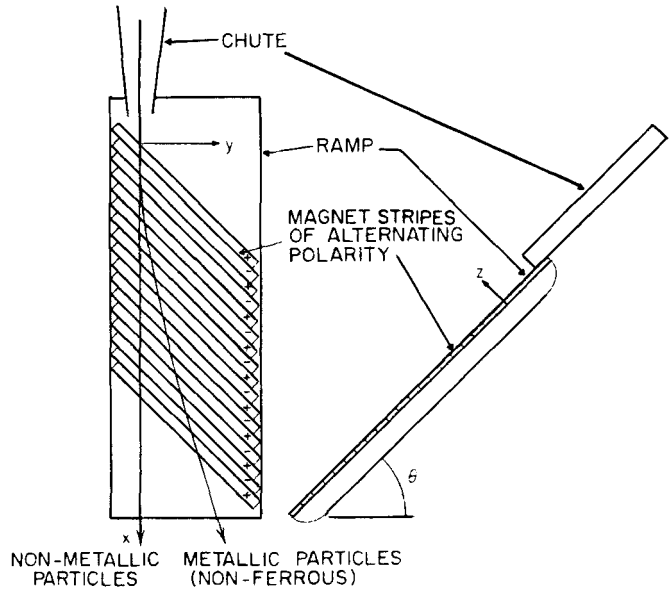

FIG. 16. Sliding ramp eddy-current separator (*92*). Reprinted with permission from R. J. Wakeman (ed.), *Progress in Filtration and Separation*, Vol. I, Elsevier, Amsterdam, 1979. Copyright 1979, Elsevier Publishing Co.

the column. This is a deflection-type system. A drum type of dielectric separator has been developed by the U.S. Bureau of Mines (*95*).

The Jeffrey-Galion shape sorting table (*96*) is used commercially to sort industrial diamonds by shape. In this two-dimensional device, feed enters one corner of a triangular-shaped sorting table. The table is tilted and vibrated. Spherical particles bounce on the table and spend little time in contact with the table. Thus the vibration has little effect on spherical particles and they concentrate at the low end of the table. Flat, flaky particles tend to shuffle along the table and are carried to the higher end. Particles of in-between shape concentrate at in-between locations. Thus this device is a continuous, multishape separator.

Other particle separation systems can also be adapted for steady-state, two-dimensional operation. While developing a morphological classification scheme for separations, Lightfoot and his co-workers (*97*) used two-dimensional settling as an example of perpendicular shifts. A steady horizontal flow of liquid is used to add the second dimension to a gravity settler.

Finally, to show that two-dimensional equipment is not limited to separators, Fig. 17 shows the thermal wheel (*98*). The thermal wheel was invented 80 years ago and is commercially available. Analogies between the thermal wheel and regenerated two-dimensional adsorbers are obvious.

SUMMARY AND POSSIBLE FUTURE RESEARCH

Sequential, two-dimensional development is a widely used method of analysis in TLC, PC, and electrophoresis. Although it is time consuming, this method is very powerful and can have a very high spot capacity. More research is required on detection and computer analysis procedures. One promising method is the two-dimensional column shown in Fig. 1(d). This technique could probably be extended to two-dimensional separations where the first dimension was isoelectric focusing and the second dimension was TLC, PC, or thin-layer, size-exclusion chromatography. This two-dimensionless column would probably simplify detection problems for the two-dimensional IEF–chromatographic system.

In three-phase liquid–liquid extraction a batch simultaneous development is preferable to sequential development. Although two-dimensional extraction is cumbersome, it might be possible to extend the idea of a simultaneous, two-dimensional development to TLC or PC.

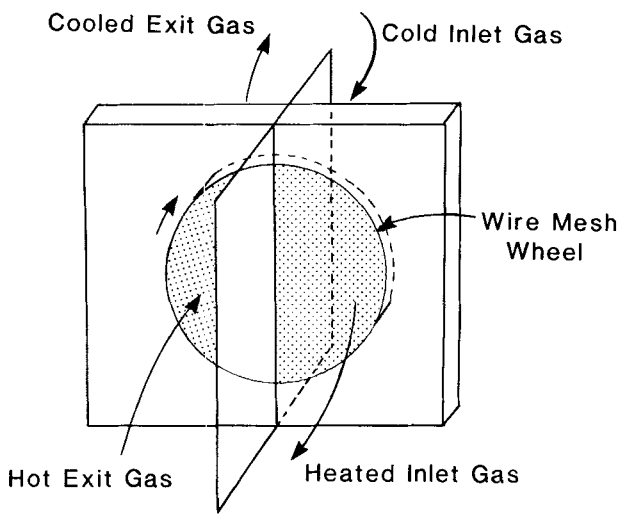

FIG. 17. Thermal wheel.

Another area in which research will undoubtedly occur is three-dimensional development. This could be done in a chromatographic system, in a combined IEF–SDS electrophoresis–chromatography, or in some other combination of three independent directions. I believe research will be done on 3-D systems because the spot capacities which could result are huge. However, the detection problems are also huge. One possible approach is to section the three-dimensional block into a series of slabs, each of which would be computer scanned. This is obviously laborious. An alternate would be to build the three-dimensional equivalent to a two-dimensional column. The first two developments would be done without eluting material. The last development would elute solutes past a planar array of detectors. If possible, all three developments should be independent. A complex but very powerful analytical separator would result.

Two types of continuous two-dimensional separators were reviewed. In one type a perpendicular shift was superimposed by moving a solid body or flowing a fluid at right angles to the direction of flow. This method was used for continuous chromatography, two-dimensional staged extraction, continuous filtration, and continuous magnetic separators where the magnetic particles are held by the matrix. These two-dimensional separators are preferred compared to their one-dimensional analogs if they have an inherent advantage and the feed is fairly concentrated. Since the number of possible geometries is quite large, one could search for alternate geometries. Comparing the geometries used in the different separations may be one fruitful approach. A second approach is to look for circumstances where the two-dimensional method gains an advantage. An example might be an adsorption system using microwave heating for regeneration. A two-dimensional system would allow continuous operation of the microwave oven. This might have both capital and operating advantages. A third area for future research would be to apply the perpendicular shift concept to other separation techniques. Distillation and sedementation were already mentioned as possibilities. Crystallization and precipitation are other examples. Before doing this, the researcher should try to determine what would be the possible advantages of a two-dimensional separation.

In the second type of continuous, two-dimensional separation an external force was used to deflect the solute or particles at right angles to the flow. This method was used in continuous electrophoresis, open-gradient magnetic separators, eddy-current separators, and dielectrophoresis. Extensive research is on-going on a variety of free-flow electrophoresis systems. For fairly large particles the other electromagnetic forces may have advantages and should also be explored. Perhaps some of the clever schemes developed for electrophoresis could be applied to the other separation methods. For example, the fan collector developed by Kolin (*71*) to multiply the collection

ability of electrophoresis could also be applied to the other separations. Perhaps techniques such as the slanted feed line (*40*) could be applied to electrophoresis. Could other forces be used to develop new two-dimensional deflection devices? Continuous flow isoelectric focusing uses a pH gradient. A similar idea might be useful in open gradient magnetic separators by using gradients of the magnetic susceptibility of the background fluid. A gradient in the dielectric constant of the fluid might also be useful in dielectrophoresis. Research in the area of two-dimensional deflection separators is likely to produce exciting new separators.

Acknowledgments

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