Alternative Separation Processes

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CRYSTALLIZATION FROM THE MELT

SUPERCRITICAL FLUID SEPARATION PROCESSES

ALTERNATIVE SOLID/LIQUID SEPARATIONS

MEMBRANE SEPARATION PROCESSES

SELECTION OF BIOCHEMICAL SEPARATION PROCESSES

CRYSTALLIZATION FROM THE MELT

General References: Mullin, *Crystallization, 3d ed.,* Butterworth-Heinemann, 1993. Myerson, *Handbook of Industrial Crystallization,* Butterworth-Heinemann, 1993. Pfann, *Zone Melting, 2d ed.,* Wiley, New York, 1966. U.S. Patents 3,621,664 and 3,796,060. Zief and Wilcox, *Fractional Solidification,* Marcel Dekker, New York, 1967.

INTRODUCTION

Purification of a chemical species by solidification from a liquid mixture can be termed either **solution** crystallization or crystallization from the **melt.** The distinction between these two operations is somewhat subtle. The term **melt crystallization** has been defined as the separation of components of a binary mixture without addition of solvent, but this definition is somewhat restrictive. In **solution crystallization** a diluent solvent is added to the mixture; the solution is then directly or indirectly cooled, and/or solvent is evaporated to effect crystallization. The solid phase is formed and maintained somewhat below its pure-component freezing-point temperature. In melt crystallization no diluent solvent is added to the reaction mixture, and the solid phase is formed by cooling of the melt. Product is frequently maintained near or above its pure-component freezing point in the refining section of the apparatus.

A large number of techniques are available for carrying out crystallization from the melt. An abbreviated list includes partial freezing and solids recovery in cooling crystallizer-centrifuge systems, partial melting (e.g., sweating), staircase freezing, normal freezing, zone melting, and column crystallization. A description of all these methods is not within the scope of this discussion. Zief and Wilcox (op. cit.) and Myerson (op. cit.) describe many of these processes. Three of the more common methods—progressive freezing from a falling film, zone melting, and melt crystallization from the bulk—are discussed here to illustrate the techniques used for practicing crystallization from the melt.

High or ultrahigh product purity is obtained with many of the melt-purification processes. Table 22-1 compares the product quality and product form that are produced from several of these operations. Zone refining can produce very pure material when operated in a batch mode; however, other melt crystallization techniques also provide high purity and become attractive if continuous high-capacity processing is desired. Comparison of the features of melt crystallization and distillation are shown on Table 22-2.

A brief discussion of solid-liquid phase equilibrium is presented prior to discussing specific crystallization methods. Figures 22-1 and 22-2 illustrate the phase diagrams for binary solid-solution and eutectic systems respectively. In the case of binary solid-solution systems, illustrated in Fig. 22-1, the liquid and solid phases contain equilibrium quantities of both components in a manner similar to vapor-liquid phase behavior. This type of behavior causes separation difficulties since multiple stages are required. In principle, however, high purity and yields of both components can be achieved since no eutectic is present.

TABLE 22-1 Comparison of Processes Involving Crystallization from the Melt

Processes	Approximate upper melting point, °C	Materials tested	Minimum purity level obtained, ppm, weight	Product form
Progressive freezing	1500	All types	1	Ingot
Zone melting				
Batch	3500	All types	0.01	Ingot
Continuous	500	SiI_4	100	Melt
Melt crystallization				
Continuous	300	Organic	10	Melt
Cyclic	300	Organic	10	Melt

Abbreviated from Zief and Wilcox, *Fractional Solidification,* Marcel Dekker, New York, 1967, p. 7.

TABLE 22-2 Comparison of Features of Melt Crystallization and Distillation

Distillation	Melt crystallization
Phase equilibria	
Both liquid and vapor phases are totally miscible.	Liquid phases are totally miscible; solid phases are not.
Conventional vapor/liquid equilibrium.	Eutectic system.
Neither phase is pure.	Solid phase is pure, except at eutectic point.
Separation factors are moderate and decrease as purity increases.	Partition coefficients are very high (theoretically, they can be infinite).
Ultrahigh purity is difficult to achieve.	Ultrahigh purity is easy to achieve.
No theoretical limit on recovery.	Recovery is limited by eutectic composition.
Mass-transfer kinetics	
High mass-transfer rates in both vapor and liquid phases.	Only moderate mass-transfer rate in liquid phase, zero in solid.
Close approach to equilibrium.	Slow approach to equilibrium; achieved in brief contact time. Included impurities cannot diffuse out of solid.
Adiabatic contact assures phase equilibrium.	Solid phase must be remelted and refrozen to allow phase equilibrium.
Phase separability	
Phase densities differ by a factor of 100–10,000:1.	Phase densities differ by only about 10%.
Viscosity in both phases is low.	Liquid phase viscosity moderate, solid phase rigid.
Phase separation is rapid and complete.	Phase separation is slow; surface-tension effects prevent completion.
Countercurrent contacting is quick and efficient.	Countercurrent contacting is slow and imperfect.

If the impurity or minor component is completely or partially soluble in the solid phase of the component being purified, it is convenient to define a distribution coefficient k, defined by Eq. (22-1):

$$k = C_s/C_\ell \qquad (22\text{-}1)$$

C_s is the concentration of impurity or minor component in the solid phase, and C_ℓ is the impurity concentration in the liquid phase. The distribution coefficient generally varies with composition. The value of k is greater than 1 when the solute raises the melting point and less than 1 when the melting point is depressed. In the regions near pure *A* or *B* the liquidus and solidus lines become linear; i.e., the distribution coefficient becomes constant. This is the basis for the common assumption of constant k in many mathematical treatments of fractional solidification in which ultrapure materials are obtained.

In the case of a simple eutectic system shown in Fig. 22-2, a pure solid phase is obtained by cooling if the composition of the feed mix-

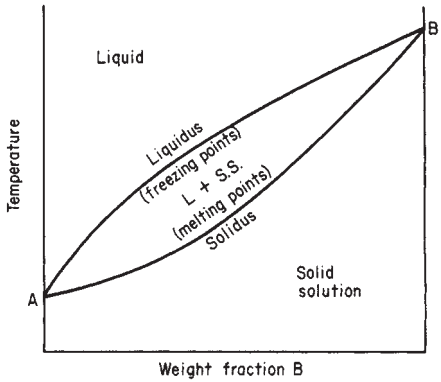


FIG. 22-1 Phase diagram for components exhibiting complete solid solution. (*Zief and Wilcox,* Fractional Solidification, *vol. 1, Marcel Dekker, New York, 1967, p. 31.*)

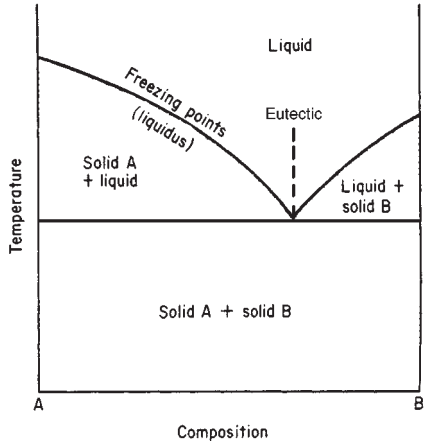


FIG. 22-2 Simple eutectic-phase diagram at constant pressure. (*Zief and Wilcox,* Fractional Solidification, *vol. 1, Marcel Dekker, New York, 1967, p. 24.*)

ture is not at the eutectic composition. If liquid composition is eutectic, then separate crystals of both species will form. In practice it is difficult to attain perfect separation of one component by crystallization of a eutectic mixture. The solid phase will always contain trace amounts of impurity because of incomplete solid-liquid separation, slight solubility of the impurity in the solid phase, or volumetric inclusions. It is difficult to generalize on which of these mechanisms is the major cause of contamination because of analytical difficulties in the ultrahigh-purity range.

The distribution-coefficient concept is commonly applied to fractional solidification of eutectic systems in the ultrapure portion of the phase diagram. If the quantity of impurity entrapped in the solid phase for whatever reason is proportional to that contained in the melt, then assumption of a constant k is valid. It should be noted that the theoretical yield of a component exhibiting binary eutectic behavior is fixed by the feed composition and position of the eutectic. Also, in contrast to the case of a solid solution, only one component can be obtained in a pure form.

There are many types of phase diagrams in addition to the two cases presented here; these are summarized in detail by Zief and Wilcox (op. cit., p. 21). Solid-liquid phase equilibria must be determined experimentally for most binary and multicomponent systems. Predictive methods are based mostly on ideal phase behavior and have limited accuracy near eutectics. A predictive technique based on extracting liquid-phase activity coefficients from *vapor-liquid* equilibria that is useful for estimating nonideal binary or multicomponent *solid-liquid* phase behavior has been reported by Muir (Pap. 71f, 73d ann. meet., AIChE, Chicago, 1980).

PROGRESSIVE FREEZING

Progressive freezing, sometimes called *normal* freezing, is the slow, directional solidification of a melt. Basically, this involves slow solidification at the bottom or sides of a vessel or tube by indirect cooling. The impurity is rejected into the liquid phase by the advancing solid interface. This technique can be employed to concentrate an impurity or, by repeated solidifications and liquid rejections, to produce a very pure ingot. Figure 22-3 illustrates a progressive freezing apparatus. The solidification rate and interface position are controlled by the rate of movement of the tube and the temperature of the cooling medium. There are many variations of the apparatus; e.g., the residual-liquid portion can be agitated and the directional freezing can be carried out vertically as shown in Fig. 22-3 or horizontally (see Richman et al., in Zief and Wilcox, op. cit., p. 259). In general, there is a solute redistribution when a mixture of two or more components is directionally frozen.

Component Separation by Progressive Freezing When the distribution coefficient is less than 1, the first solid which crystallizes contains less solute than the liquid from which it was formed. As the fraction which is frozen increases, the concentration of the impurity in the remaining liquid is increased and hence the concentration of impurity in the solid phase increases (for $k < 1$). The concentration gradient is reversed for $k > 1$. Consequently, in the absence of diffusion in the solid phase a concentration gradient is established in the frozen ingot.

One extreme of progressive freezing is equilibrium freezing. In this case the freezing rate must be slow enough to permit diffusion in the solid phase to eliminate the concentration gradient. When this occurs, there is no separation if the entire tube is solidified. Separation can be achieved, however, by terminating the freezing before all the liquid has been solidified. Equilibrium freezing is rarely achieved in practice because the diffusion rates in the solid phase are usually negligible (Pfann, op. cit., p. 10).

If the bulk-liquid phase is well mixed and no diffusion occurs in the solid phase, a simple expression relating the solid-phase composition to the fraction frozen can be obtained for the case in which the distribution coefficient is independent of composition and fraction frozen [Pfann, *Trans. Am. Inst. Mech. Eng.*, **194,** 747 (1952)].

$$C_s = kC_0(1 - X)^{k-1} \qquad (22\text{-}2)$$

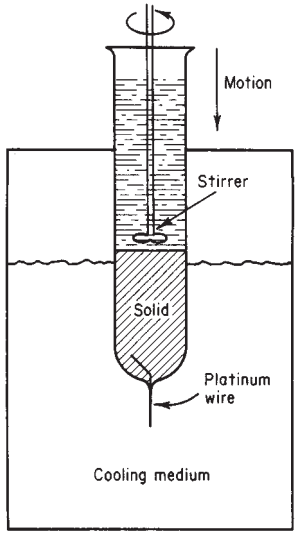


FIG. 22-3 Progressive freezing apparatus.

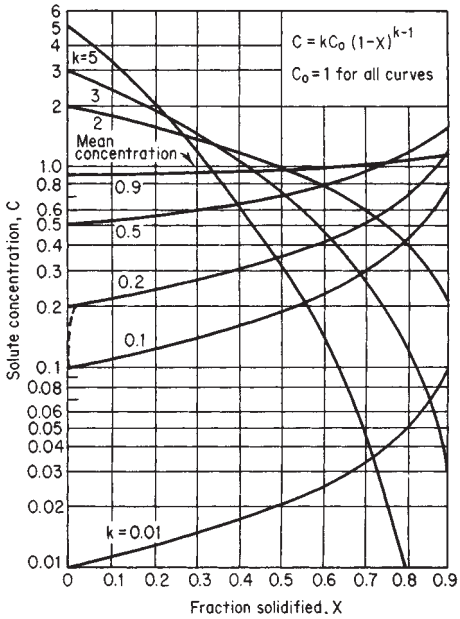


FIG. 22-4 Curves for progressive freezing, showing solute concentration C in the solid versus fraction-solidified X. (*Pfann,* Zone Melting, *2d ed., Wiley, New York, 1966, p. 12.*)

C_0 is the solution concentration of the initial charge, and X is the fraction frozen. Figure 22-4 illustrates the solute redistribution predicted by Eq. (22-2) for various values of the distribution coefficient.

There have been many modifications of this idealized model to account for variables such as the freezing rate and the degree of mixing in the liquid phase. For example, Burton et al. [*J. Chem. Phys.,* **21,** 1987 (1953)] reasoned that the solid rejects solute faster than it can diffuse into the bulk liquid. They proposed that the effect of the freezing rate and stirring could be explained by the diffusion of solute through a stagnant film next to the solid interface. Their theory resulted in an expression for an effective distribution coefficient k_{eff} which could be used in Eq. (22-2) instead of k.

$$k_{\text{eff}} = \frac{1}{1 + (1/k - 1)e^{-f\delta/D}} \tag{22-3}$$

where f = crystal growth rate, cm/s; δ = stagnant film thickness, cm; and D = diffusivity, cm^2/s. No further attempt is made here to summarize the various refinements of Eq. (22-2). Zief and Wilcox (op. cit., p. 69) have summarized several of these models.

Pertinent Variables in Progressive Freezing The dominant variables which affect solute redistribution are the degree of mixing in the liquid phase and the rate of solidification. It is important to attain sufficient mixing to facilitate diffusion of the solute away from the solid-liquid interface to the bulk liquid. The film thickness δ decreases as the level of agitation increases. Cases have been reported in which essentially no separation occurred when the liquid was not stirred. The freezing rate which is controlled largely by the lowering rate of the tube (see Fig. 22-3) has a pronounced effect on the separation achieved. The separation is diminished as the freezing rate is increased. Also fluctuations in the freezing rate caused by mechanical vibrations and variations in the temperature of the cooling medium can decrease the separation.

Applications Progressive freezing has been applied to both solid solution and eutectic systems. As Fig. 22-4 illustrates, large separation factors can be attained when the distribution coefficient is favorable. Relatively pure materials can be obtained by removing the desired portion of the ingot. Also in some cases progressive freezing provides a convenient method of concentrating the impurities; e.g., in the case of $k < 1$ the last portion of the liquid that is frozen is enriched in the distributing solute.

Progressive freezing has been applied on the commercial scale. For example, aluminum has been purified by continuous progressive freezing [Dewey, *J. Metals,* **17,** 940 (1965)]. The Proabd refiner described by Molinari (Zief and Wilcox, op. cit., p. 393) is also a commercial example of progressive freezing. In this apparatus the mixture is directionally solidified on cooling tubes. Purification is achieved because the impure fraction melts first; this process is called sweating. This technique has been applied to the purification of naphthalene and *p*-dichlorobenzene and commercial equipment is available from BEFS PROKEM, Houston, Tx.

ZONE MELTING

Zone melting also relies on the distribution of solute between the liquid and solid phases to effect a separation. In this case, however, one or more liquid zones are passed through the ingot. This extremely versatile technique, which was invented by W. G. Pfann, has been used to purify hundreds of materials. Zone melting in its simplest form is illustrated in Fig. 22-5. A molten zone can be passed through an ingot from one end to the other by either a moving heater or by slowly drawing the material to be purified through a stationary heating zone.

Progressive freezing can be viewed as a special case of zone melting. If the zone length were equal to the ingot length and if only one pass were used, the operation would become progressive freezing. In general, however, when the zone length is only a fraction of the ingot length, zone melting possesses the advantage that a portion of the ingot does not have to be discarded after each solidification. The last portion of the ingot which is frozen in progressive freezing must be discarded before a second freezing.

Component Separation by Zone Melting The degree of solute redistribution achieved by zone melting is determined by the zone length l, ingot length L, number of passes n, the degree of mixing in the liquid zone, and the distribution coefficient of the materials being purified. The distribution of solute after one pass can be obtained by material-balance considerations. This is a two-domain problem; i.e., in the major portion of the ingot of length $L - l$ zone melting occurs in the conventional sense. The trailing end of the ingot of length l undergoes progressive freezing. For the case of constant-distribution coefficient, perfect mixing in the liquid phase, and negligible diffusion in the solid phase, the solute distribution for a single pass is given by Eq. (22-4) [Pfann, *Trans. Am. Inst. Mech. Eng.,* **194,** 747 (1952)].

$$C_s = C_0[1 - (1 - k)e^{-kx/\ell}] \tag{22-4}$$

The position of the zone x is measured from the leading edge of the ingot. The distribution for multiple passes can also be calculated from a material balance, but in this case the leading edge of the zone encounters solid corresponding to the composition at the point in question for the previous pass. The multiple-pass distribution has been numerically calculated (Pfann, *Zone Melting,* 2d ed., Wiley, New York, 1966, p. 285) for many combinations of k, L/l, and n. Typical solute-composition profiles are shown in Fig. 22-6 for various numbers of passes.

The ultimate distribution after an infinite number of passes is also shown in Fig. 22-6 and can be calculated for $x < (L - l)$ from the following equation (Pfann, op. cit., p. 42):

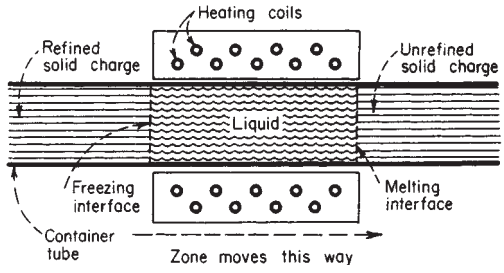


FIG. 22-5 Diagram of zone refining.

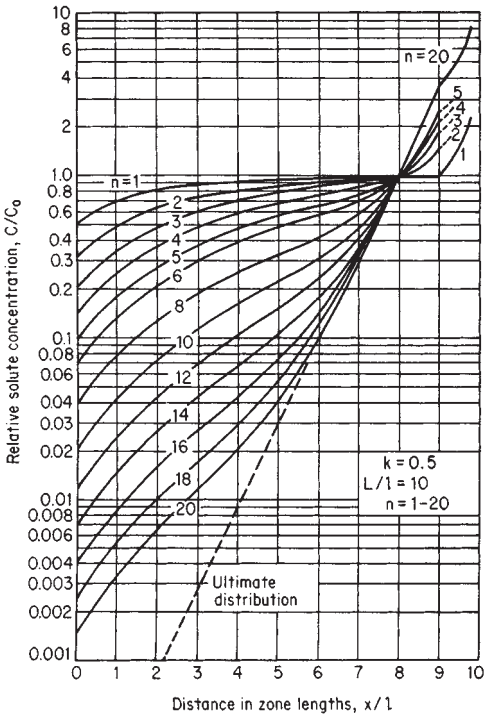


FIG. 22-6 Relative solute concentration C/C_o (logarithmic scale) versus distance in zone lengths x/ℓ from beginning of charge, for various numbers of passes n. L denotes charge length. (*Pfann,* Zone Melting, *2d ed., Wiley, New York, 1966, p. 290.*)

$$C_s = Ae^{BX} \tag{22-5}$$

where A and B can be determined from the following relations:

$$k = B\ell/(e^{B\ell} - 1) \tag{22-6}$$

$$A = C_0BL/(e^{BL} - 1) \tag{22-7}$$

The ultimate distribution represents the maximum separation that can be attained without cropping the ingot. Equation (22-5) is approximate because it does not include the effect of progressive freezing in the last zone length.

As in progressive freezing, many refinements of these models have been developed. Corrections for partial liquid mixing and a variable distribution coefficient have been summarized in detail (Zief and Wilcox, op. cit., p. 47).

Pertinent Variables in Zone Melting The dominant variables in zone melting are the number of passes, ingot-length–zone-length ratio, freezing rate, and degree of mixing in the liquid phase. Figure 22-6 illustrates the increased solute redistribution that occurs as the number of passes increases. Ingot-length–zone-length ratios of 4 to 10 are commonly used (Zief and Wilcox, op. cit., p. 624). An exception is encountered when one pass is used. In this case the zone length should be equal to the ingot length; i.e., progressive freezing provides the maximum separation when only one pass is used.

The freezing rate and degree of mixing have effects in solute redistribution similar to those discussed for progressive freezing. Zone travel rates of 1 cm/h for organic systems, 2.5 cm/h for metals, and 20 cm/h for semiconductors are common. In addition to the zone-travel rate the heating conditions affect the freezing rate. A detailed summary of heating and cooling methods for zone melting has been outlined by Zief and Wilcox (op. cit., p. 192). Direct mixing of the liquid region is more difficult for zone melting than progressive freezing. Mechanical stirring complicates the apparatus and increases the probability of contamination from an outside source. Some mixing occurs because of natural convection. Methods have been developed to stir the zone magnetically by utilizing the interaction of a current and magnetic field (Pfann, op. cit., p. 104) for cases in which the charge material is a reasonably good conductor.

Applications Zone melting has been used to purify hundreds of inorganic and organic materials. Many classes of inorganic compounds including semiconductors, intermetallic compounds, ionic salts, and oxides have been purified by zone melting. Organic materials of many types have been zone-melted. Zief and Wilcox (op. cit., p. 624) have compiled tables which give operating conditions and references for both inorganic and organic materials with melting points ranging from −115°C to over 3000°C.

Some materials are so reactive that they cannot be zone-melted to a high degree of purity in a container. Floating-zone techniques in which the molten zone is held in place by its own surface tension have been developed by Keck et al. [*Phys. Rev.,* **89,** 1297 (1953)].

Continuous-zone-melting apparatus has been described by Pfann (op. cit., p. 171). This technique offers the advantage of a close approach to the ultimate distribution, which is usually impractical for batch operation.

Performance data have been reported by Kennedy et al. (*The Purification of Inorganic and Organic Materials,* Marcel Dekker, New York, 1969, p. 261) for continuous-zone refining of benzoic acid.

MELT CRYSTALLIZATION FROM THE BULK

Conducting crystallization inside a vertical or horizontal column with a countercurrent flow of crystals and liquid can produce a higher product purity than conventional crystallization or distillation. The working concept is to form a crystal phase from the bulk liquid, either internally or externally, and then transport the solids through a countercurrent stream of enriched reflux liquid obtained from melted product. The problem in practicing this technology is the difficulty of controlling solid-phase movement. Unlike distillation, which exploits the specific-gravity differences between liquid and vapor phases, melt crystallization involves the contacting of liquid and solid phases that have nearly identical physical properties. Phase densities are frequently very close, and gravitational settling of the solid phase may be slow and ineffective. The challenge of designing equipment to accomplish crystallization in a column has resulted in a myriad of configurations to achieve reliable solid-phase movement, high product yield and purity, and efficient heat addition and removal.

Investigations Crystallization conducted inside a column is categorized as either **end-fed** or **center-fed** depending on whether the feed location is upstream or downstream of the crystal forming section. Figure 22-7 depicts the features of an end-fed commercial column described by McKay et al. [*Chem. Eng. Prog. Symp. Ser.,* no. 25, 55, 163 (1969)] for the separation of xylenes. Crystals of *p*-xylene are formed by indirect cooling of the melt in scraped-surface heat exchangers, and the resultant slurry is introduced into the column at

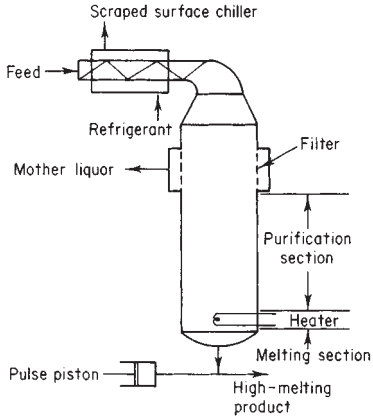


FIG. 22-7 End-fed column crystallizer. (*Phillips Petroleum Co.*)

the top. This type of column has no mechanical internals to transport solids and instead relies upon an imposed hydraulic gradient to force the solids through the column into the melting zone. Residue liquid is removed through a filter directly above the melter. A pulse piston in the product discharge improves washing efficiency and column reliability.

Figure 22-8 shows the features of a horizontal center-fed column [Brodie, *Aust. Mech. Chem. Eng. Trans.*, **37** (May 1979)] which has been commercialized for continuous purification of naphthalene and *p*-dichlorobenzene. Liquid feed enters the column *between* the hot purifying section and the cold freezing or recovery zone. Crystals are formed internally by indirect cooling of the melt through the walls of the refining and recovery zones. Residue liquid that has been depleted of product exits from the coldest section of the column. A spiral conveyor controls the transport of solids through the unit.

Another center-fed design that has only been used on a preparative scale is the vertical spiral conveyor column reported by Schildknecht [*Angew. Chem.*, **73,** 612 (1961)]. In this device, a version of which is shown on Fig. 22-9, the dispersed-crystal phase is formed in the freezing section and conveyed downward in a controlled manner by a rotating spiral with or without a vertical oscillation.

Differences have been observed in the performance of end- and center-fed column configurations. Consequently, discussions of center- and end-fed column crystallizers are presented separately. The design and operation of both columns are reviewed by Powers (Zief and Wilcox, op. cit., p. 343). A comparison of these devices is shown on Table 22-3.

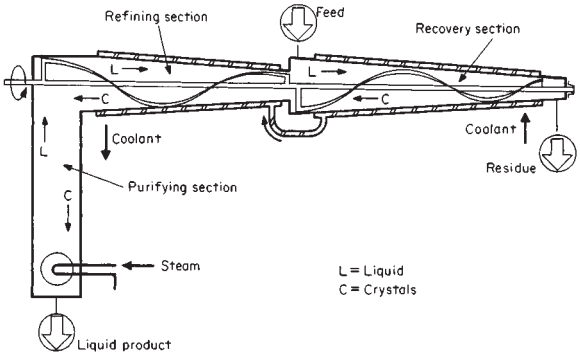


FIG. 22-8 Horizontal center-fed column crystallizer. (*The C. W. Nofsinger Co.*)

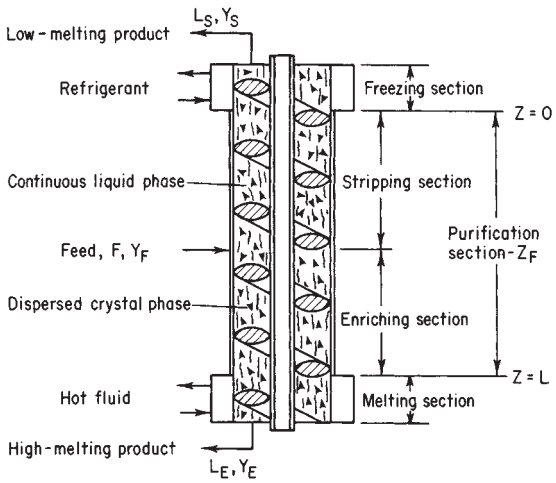


FIG. 22-9 Center-fed column crystallizer with a spiral-type conveyor.

TABLE 22-3 Comparison of Melt-Crystallizer Performance

Center-fed column	End-fed column
Solid phase is formed internally; thus, only liquid streams enter and exit the column.	Solid phase is formed in external equipment and fed as slurry into the purifier.
Internal reflux can be controlled without affecting product yield.	The maximum internal liquid reflux is fixed by the thermodynamic state of the feed relative to the product stream. Excessive reflux will diminish product yield.
Operation can be continuous or batchwise at total reflux.	Total reflux operation is not feasible.
Center-fed columns can be adapted for both eutectic and solid-solution systems.	End-fed columns are inefficient for separation of solid-solution systems.
Either low- or high-porosity-solids-phase concentrations can be formed in the purification and melting zones.	End-fed units are characterized by low-porosity-solids packing in the purification and melting zones.
Scale-up depends on the mechanical complexity of the crystal-transport system and techniques for removing heat. Vertical oscillating spiral columns are likely limited to about 0.2 m in diameter, whereas horizontal columns of several meters are possible.	Scale-up is limited by design of melter and/or crystal-washing section. Vertical or horizontal columns of several meters in diameter are possible.

Center-Fed Column Crystallizers Two types of center-fed column crystallizers are illustrated on Figs. 22-8 and 22-9. As in a simple distillation column, these devices are composed of three distinct sections: a freezing or recovery section, where solute is frozen from the impure liquor; the purification zone, where countercurrent contacting of solids and liquid occurs; and the crystal-melting and -refluxing section. Feed position separates the refining and recovery portions of the purification zone. The section between feed location and melter is referred to as the refining or enrichment section, whereas the section between feed addition and freezing is called the recovery section. The refining section may have provisions for sidewall cooling. The published literature on column crystallizers connotes stripping and refining in a reverse sense to distillation terminology, since refined product from a melt crystallizer exits at the hot section of the column rather than at the cold end as in a distillation column.

Rate processes that describe the purification mechanisms in a column crystallizer are highly complex since phase transition and heat- and mass-transfer processes occur simultaneously. Nucleation and growth of a crystalline solid phase along with crystal washing and crystal melting are occurring in various zones of the apparatus. Column hydrodynamics are also difficult to describe. Liquid- and solid-phase mixing patterns are influenced by factors such as solids-transport mechanism, column orientation, and, particularly for dilute slurries, the settling characteristics of the solids.

Most investigators have focused their attention on a differential segment of the zone between the feed injection and the crystal melter. Analysis of crystal formation and growth in the recovery section has received scant attention. Table 22-4 summarizes the scope of the literature treatment for center-fed columns for both solid-solution and eutectic forming systems.

The dominant mechanism of purification for column crystallization of solid-solution systems is recrystallization. The rate of mass transfer resulting from recrystallization is related to the concentrations of the solid phase and free liquid which are in intimate contact. A model based on height-of-transfer-unit (HTU) concepts representing the composition profile in the purification section for the high-melting component of a binary solid-solution system has been reported by Powers et al. (in Zief and Wilcox, op. cit., p. 363) for total-reflux operation. Typical data for the purification of a solid-solution system, azobenzene-stilbene, are shown in Fig. 22-10. The column crystallizer was operated

TABLE 22-4 Column-Crystallizer Investigations

	Treatments	
	Theoretical	Experimental
Solid solutions		
Total reflux—steady state	1, 2, 4, 6	1, 4, 6
Total reflux—dynamic	2	
Continuous—steady state	1, 4	4, 8, 9
Continuous—dynamic		
Eutectic systems		
Total reflux—steady state	1, 3, 4, 7	1, 3, 6
Total reflux—dynamic		
Continuous—steady state	1, 5, 10, 11, 12	5, 8, 9, 10, 11, 13
Continuous—dynamic		

1. Powers, *Symposium on Zone Melting and Column Crystallization,* Karlsruhe, 1963.
2. Anikin, *Dokl. Akad. Nauk SSSR,* **151,** 1139 (1969).
3. Albertins et al., *Am. Inst. Chem. Eng. J.,* **15,** 554 (1969).
4. Gates et al., *Am. Inst. Chem. Eng. J.,* **16,** 648 (1970).
5. Henry et al., *Am. Inst. Chem. Eng. J.,* **16,** 1055 (1970).
6. Schildknecht et al., *Angew. Chem.,* **73,** 612 (1961).
7. Arkenbout et al., *Sep. Sci.,* **3,** 501 (1968).
8. Betts et al., *Appl. Chem.,* **17,** 180 (1968).
9. McKay et al., *Chem. Eng. Prog. Symp. Ser.,* no. 25, 55, 163 (1959).
10. Bolsaitis, *Chem. Eng. Sci.,* **24,** 1813 (1969).
11. Moyers et al., *Am. Inst. Chem. Eng. J.,* **20,** 1119 (1974).
12. Griffin, M.S. thesis in chemical engineering, University of Delaware, 1975.
13. Brodie, *Aust. Mech. Chem. Eng. Trans.,* 37 (1971).

at total reflux. The solid line through the data was computed by Powers et al. (op. cit., p. 364) by using an experimental HTU value of 3.3 cm.

Most of the analytical treatments of center-fed columns describe the purification mechanism in an adiabatic oscillating spiral column (Fig. 22-9). However, the analyses by Moyers (op. cit.) and Griffin (op. cit.) are for a nonadiabatic dense-bed column. Differential treatment of the horizontal-purifier (Fig. 22-8) performance has not been reported; however, overall material and enthalpy balances have been described by Brodie (op. cit.) and apply equally well to other designs.

A dense-bed center-fed column (Fig. 22-11) having provision for internal crystal formation and variable reflux was tested by Moyers et al. (op. cit.). In the theoretical development (ibid.) a nonadiabatic, plug-flow axial-dispersion model was employed to describe the performance of the entire column. Terms describing interphase transport of impurity between adhering and free liquid are not considered.

A comparison of the axial-dispersion coefficients obtained in oscillating-spiral and dense-bed crystallizers is given in Table 22-5. The dense-bed column approaches axial-dispersion coefficients similar to those of densely packed ice-washing columns.

The concept of minimum reflux as related to column-crystallizer operation is presented by Brodie (op. cit.) and is applicable to all types of column crystallizers, including end-fed units. In order to stabilize column operation the sensible heat of subcooled solids entering the melting zone should be balanced or exceeded by the heat of fusion of the refluxed melt. The relationship in Eq. (22-8) describes the minimum reflux requirement for proper column operation.

$$R = (T_P - T_F)\, C_P/\lambda \qquad (22\text{-}8)$$

R = reflux ratio, g reflux/g product; T_P = product temperature, °C; T_F = saturated-feed temperature, °C; C_P = specific heat of solid crystals, cal/(g·°C); and λ = heat of fusion, cal/g.

All refluxed melt will refreeze if reflux supplied equals that computed by Eq. (22-8). When reflux supplied is greater than the minimum, jacket cooling in the refining zone or additional cooling in the recovery zone is required to maintain product recovery. Since high-

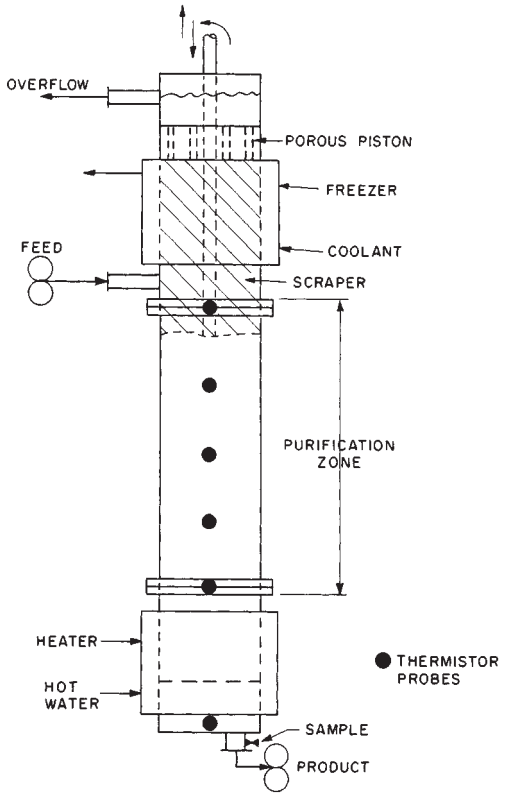


FIG. 22-11 Dense-bed center-fed column crystallizer. [*Moyers et al.,* Am. Inst. Chem. Eng. J., ***20,*** *1121 (1974).*]

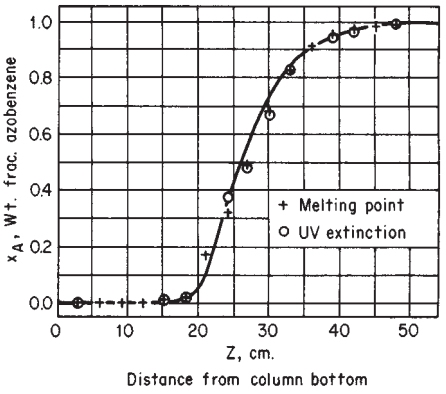


FIG. 22-10 Steady-state separation of azobenzene and stilbene in a center-fed column crystallizer with total-reflux operation. To convert centimeters to inches, multiply by 0.3937. (*Zief and Wilcox,* Fractional Solidification, *vol. 1, Marcel Dekker, New York, 1967, p. 356.*)

TABLE 22-5 Comparison of Axial-Dispersion Coefficients for Several Liquid-Solid Contactors

Column type	Dispersion coefficient, cm^2/s	Reference
Center-fed crystallizer (oscillating spiral)	1.6–3.5	1
Center-fed crystallizer (oscillating spiral)	1.3–1.7	2
Countercurrent ice-washing column	0.025–0.17	3
Center-fed crystallizer	0.12–0.30	4

References:
1. Albertins et al., *Am. Inst. Chem. Eng. J.,* **15,** 554 (1969).
2. Gates et al., *Am. Inst. Chem. Eng. J.,* **16,** 648 (1970).
3. Ritter, Ph.D. thesis, Massachusetts Institute of Technology, 1969.
4. Moyers et al., *Am. Inst. Chem. Eng. J.,* **20,** 1119 (1974).

purity melts are fed near their pure-component freezing temperatures, little refreezing takes place unless jacket cooling is added.

To utilize a column-crystallizer design or rating model, a large number of parameters must be identified. Many of these are empirical in nature and must be determined experimentally in equipment identical to the specific device being evaluated. Hence macroscopic evaluation of systems by large-scale piloting is the rule rather than the exception. Included in this rather long list of critical parameters are factors such as impurity level trapped in the solid phase, product quality as a function of reflux ratio, degree of liquid and solids axial mixing in the equipment as a function of solids-conveyor design, size and shape of crystals produced, and ease of solids handling in the column. Heat is normally removed through metal surfaces; thus, the stability of the solution to subcooling can also be a major factor in design.

End-Fed Column Crystallizer End-fed columns were developed and successfully commercialized by the Phillips Petroleum Company in the 1950s. The sections of a typical end-fed column, often referred to as a Phillips column, are shown on Fig. 22-7. Impure liquor is removed through filters located between the product-freezing zone and the melter rather than at the end of the freezing zone, as occurs in center-fed units. The purification mechanism for end-fed units is basically the same as for center-fed devices. However, there are reflux restrictions in an end-fed column, and a high degree of solids compaction exists near the melter of an end-fed device. It has been observed that the free-liquid composition and the fraction of solids are relatively constant throughout most of the purification section but exhibit a sharp discontinuity near the melting section [McKay et al., *Ind. Eng. Chem.*, **52,** 197 (1969)]. Investigators of end-fed column behavior are listed in Table 22-6. Note that end-fed columns are adaptable only for eutectic-system purification and cannot be operated at total reflux.

Performance information for the purification of *p*-xylene indicates that nearly 100 percent of the crystals in the feed stream are removed as product. This suggests that the liquid which is refluxed from the melting section is effectively refrozen by the countercurrent stream of subcooled crystals. A high-melting product of 99.0 to 99.8 weight percent *p*-xylene has been obtained from a 65 weight percent *p*-xylene feed. The major impurity was *m*-xylene. Figure 22-12 illustrates the column-cross-section-area–capacity relationship for various product purities.

Column crystallizers of the end-fed type can be used for purification of many eutectic-type systems and for aqueous as well as organic systems (McKay, loc. cit.). Column crystallizers have been used for xylene isomer separation, but recently other separation technologies including more efficient melt crystallization equipment have tended to supplant the Phillips style crystallizer.

Commercial Equipment and Applications In the last two decades the practice of melt crystallization techniques for purification of certain organic materials has made significant commercial progress. The concept of refining certain products by countercurrent staging of crystallization in a column has completed the transition from laboratory and pilot equipment to large-scale industrial configurations. Chemicals which have been purified by suspension crystallization-purifier column techniques are listed on Table 22-7. The practice of crystal formation and growth from the bulk liquid (as is practiced in suspension crystallization techniques described in Sec. 18 of this handbook) and subsequent crystal melting and refluxing in a purifier column has evolved into two slightly different concepts: (1) the horizontal continuous crystallization technique with vertical purifier invented by Brodie (op. cit.) and (2) the continuous multistage or stepwise system with vertical purifier developed by Tsukishima Kikai Co., Ltd. (TSK). A recent description of these processes has been published by Meyer [*Chem. Proc.*, **53,** 50 (1990)].

TABLE 22-6 End-Fed-Crystallizer Investigations

Eutectic systems	Treatments	
	Theoretical	Experimental
Continuous—steady state	1, 2, 4	1, 4
Batch	3	3

1. McKay et al., *Ind. Eng. Chem. Process Des. Dev.*, **6,** 16 (1967).
2. Player, *Ind. Eng. Chem. Process Des. Dev.*, **8,** 210 (1969).
3. Yagi et al., *Kagaku Kogaku*, **72,** 415 (1963).
4. Shen and Meyer, Prepr. 19F, AIChE Symp., Chicago, 1970.

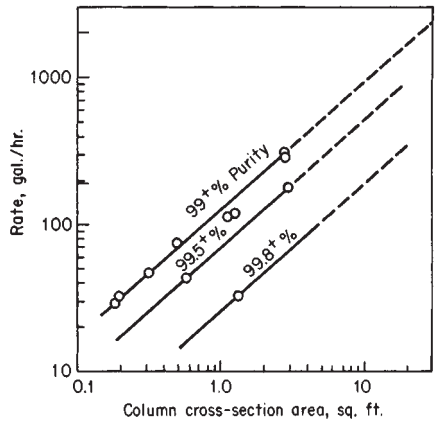


FIG. 22-12 Pulsed-column capacity versus column size for 65 percent *p*-xylene feed. To convert gallons per hour to cubic meters per hour, multiply by 0.9396; to convert square feet to square meters, multiply by 0.0929. (*McKay et al., prepr., 59th nat. meet. AIChE, East Columbus, Ohio.*)

The horizontal continuous Brodie melt crystallizer is basically an indirectly cooled crystallizer with an internal ribbon conveyor to transport crystals countercurrent to the liquid and a vertical purifier for final refining. Figure 22-8 describes the operation of a single tube unit and Fig. 22-13 depicts a multitube unit. The multitube design has been successfully commercialized for a number of organic chemicals. The Brodie purifier configuration requires careful control of process and equipment temperature differences to eliminate internal encrustations and is limited by the inherent equipment geometry to capacities of less than 15,000 tons per year per module.

In the multistage process described on Fig. 22-14 feed enters one of several crystallizers installed in series. Crystals formed in each crystallizer are transferred to a hotter stage and the liquid collected in the clarified zone of the crystallizer is transferred to a colder stage and eventually discharged as residue. At the hot end, crystals are transferred to a vertical purifier where countercurrent washing is performed by pure, hot-product reflux. TSK refers to this multistage process as the countercurrent cooling crystallization (CCCC) process. In principle any suitable type of crystallizer can be used in the stages

TABLE 22-7 Chemicals Purified by TSK CCCC Process (The C. W. Nofsinger Co.)

Acetic acid	Isophthaloyl chloride
Acrylic acid	Isopregol
Adipic acid	Lutidine
Benzene	Maleic anhydride
Biphenyl	Naphthalene
Bisphenol-A	*p*-Nitrochloro benzene
Caprolactam	*p*-Nitrotoluene
Chloroacetic acid	Phenol
p-Chloro toluene	*b*-Picoline
p-Cresol	*g*-Picoline
Combat (proprietary)	Pyridine
Dibutyl hydroxy toluene (BHT)	Stilbene
p-Dichloro benzene	Terephthaloyl chloride
2,5 Dichlorophenol	Tertiary butyl phenol
Dicumyl peroxide	Toluene diisocyanate
Diene	Trioxane
Heliotropin	*p*-Xylene
Hexachloro cyclo butene	3,4 Xylidine
Hexamethylene diamine	

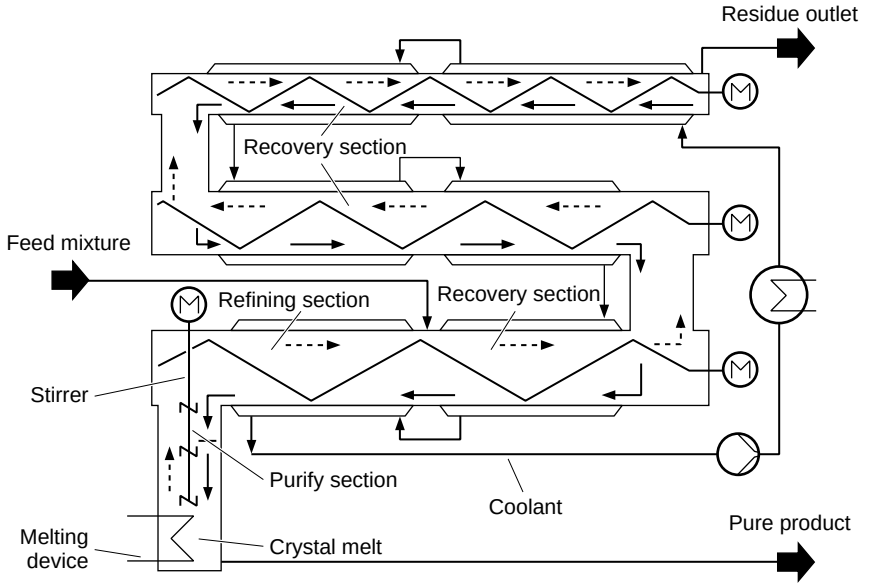


FIG. 22-13 Horizontal continuous Brodie melt crystallizer—multitube unit. (*The C. W. Nofisinger Co.*)

TABLE 22-8 Commercial TSK Crystallization Operating Plants

	Capacity MM lbs/yr	Company	Date & location
Countercurrent Cooling Crystallization (CCCC) Process			
Nofsinger license			
Nofsinger design & construct			
p-Dichlorobenzene	Confidential	Monsanto Co.	1989—Sauget, IL
TSK license			
TSK design & construct			
Confidential[1]	Confidential	Confidential	1988—Japan
p-Xylene	137	MGC	1986—Mizushima, Japan
Confidential[2]	Confidential	Confidential	1985—Japan
p-Xylene	132	MGC	1983—Mizushima, Japan
	expanded to 160		1984—Japan
p-Xylene	26.5	MGC	1981—Mizushima, Japan
Brodie			
TSK license			
TSK design & construct			
Naphthalene	8	SHSM	1985—China
p-DCB	13	Hodogaya	1981—Japan
p-DCB	5.5	Sumitomo	1978—Japan
UCAL license & design			
TSK hardware			
Naphthalene	16	Nippon Steel	1974—Japan
p-DCB	13	Hodogaya	1974—Japan
UCAL license & design			
Naphthalene	10	British Tar	1972—U.K.
p-DCB	3	UCAL	1969—Australia

ABBREVIATIONS:
Nofsinger The C. W. Nofsinger Company
TSK Tsukishima Kikai Co., Ltd.
SHSM Shanghai Hozan Steel Mill
UCAL Union Carbide Australia, Ltd.
MGC Mitsubishi Gas Chemical Co., co-developer with TSK of the application for *p*-Xylene

1. Commercial scale plant started up in the spring of 1988 purifying a bulk chemical. This is the first application of the CCCC process on this bulk chemical.
2. This small unit is operating in Japan with an 800 mm crystallizer and 300 mm purifier. Because of confidentiality, we cannot disclose the company, capacity, or product.

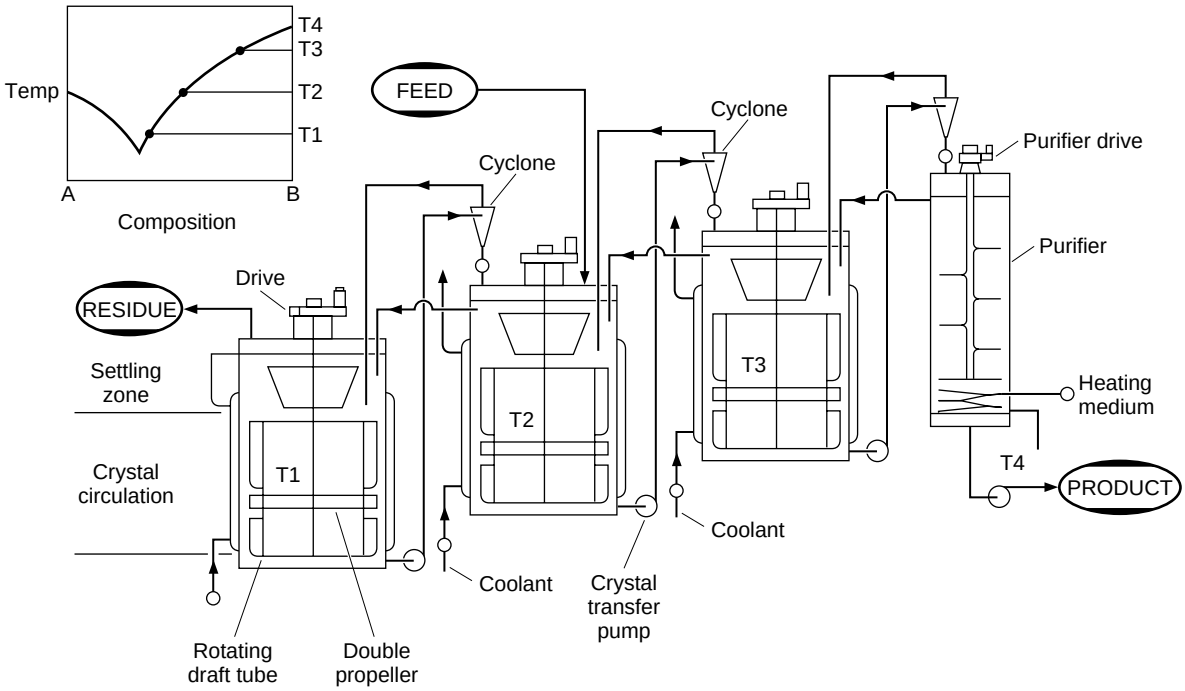


FIG. 22-14 Crystallizer—multistage process. (*The C. W. Nofisinger Co.*)

as long as the crystals formed can be separated from the crystallizer liquid and settled and melted in the purifier.

Commercial applications for both the Brodie and CCCC process are indicated on Table 22-8. Both the Brodie Purifier and the CCCC processes are available from The C. W. Nofsinger Company, PO Box 419173, Kansas City, MO 64141-0173.

FALLING-FILM CRYSTALLIZATION

Falling-film crystallization utilizes progressive freezing principles to purify melts and solutions. The technique established to practice the process is inherently cyclic. Figure 22-15 depicts the basic working concept. First a crystalline layer is formed by subcooling a liquid film

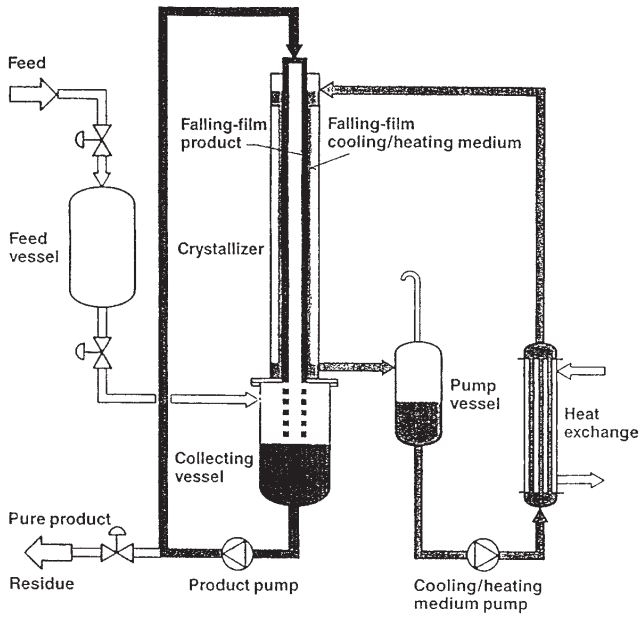
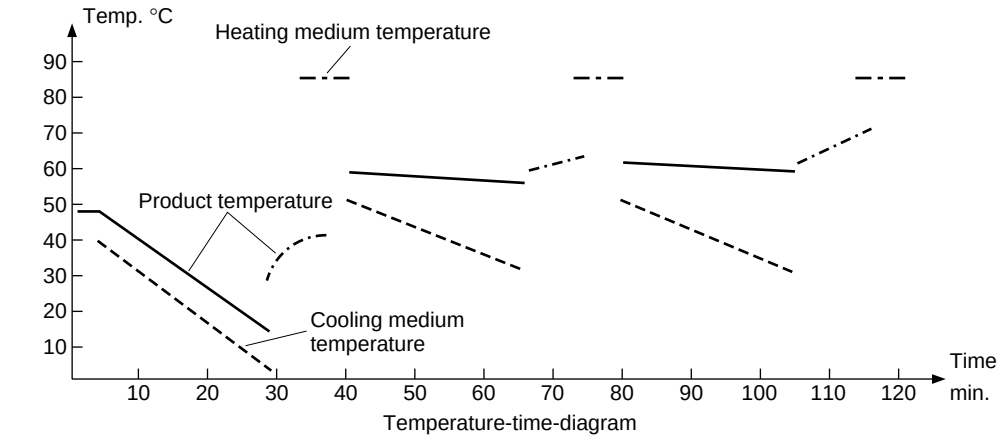
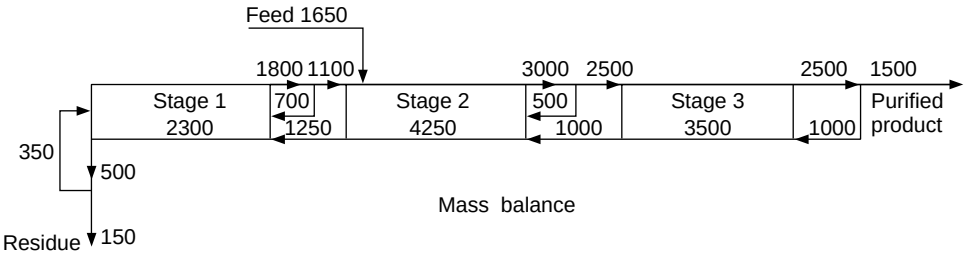
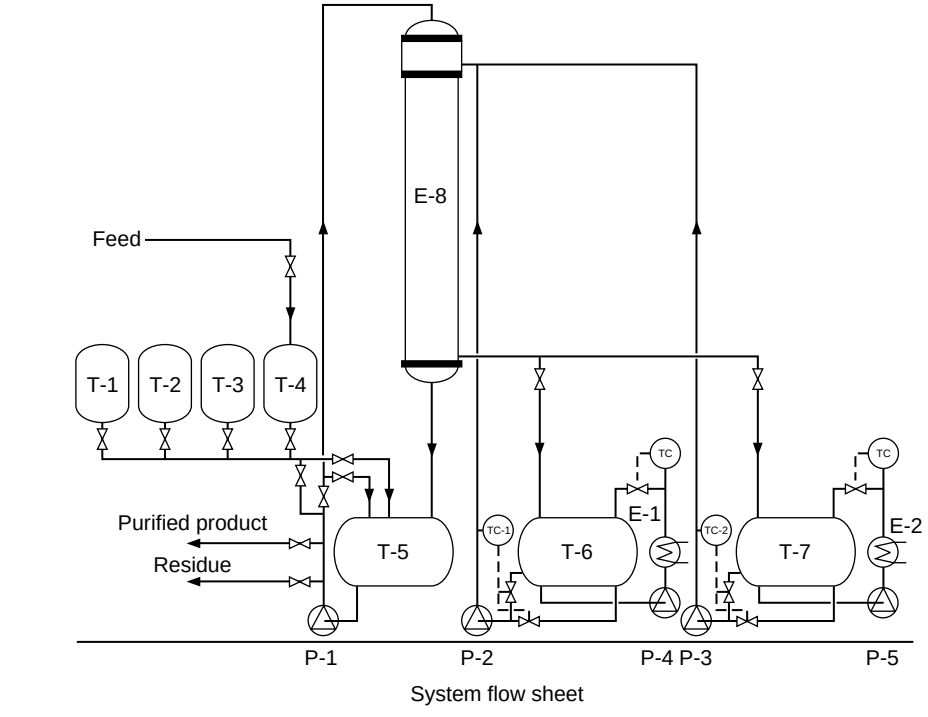


FIG. 22-15 Dynamic crystallization system. (*Sulzer Chemtech*)





(a)



(b)

FIG. 22-16 Sulzer MWB-crystallization process. (*a*) Stepwise operation of the process. (*b*) System flow sheet. (*Sulzer Chemtech*)

on a vertical surface inside a tube. This coating is then grown by extracting heat from a falling film of melt (or solution) through a heat transfer surface. Impure liquid is then drained from the crystal layer and the product is reclaimed by melting. Variants of this technique have been perfected and are used commercially for many types of organic materials. Both static and falling-film techniques have been described by Wynn [*Chem. Eng. Progr.,* (1992)]. Mathematical models for both static and dynamic operations have been presented by Gilbert [*AIChE J.,* **37,** 1205 (1991)].

Principles of Operation Figure 22-16 describes a typical three-stage falling-film crystallization process for purification of MCA (monochloro acetic acid). Crystallizer E-8 consists of a number of vertical tubular elements working in parallel enclosed in a shell. Normal tube length is 12 meters with a 50- to 75-millimeter tube inside diameter. Feed enters stage two of the sequential operation, is added to the kettle (T-5), and is then circulated to the top of the crystallizer and distributed as a falling film inside the tubes. Nucleation is induced at the inside walls and a crystal layer starts to grow. Temperature of the coolant is progressively lowered to compensate for reduced heat transfer and lower melt freezing point until the thickness inside the tube is between 5 and 20 millimeters depending on the product. Kettle liquid is evactuated to the first-stage holding tank (T-3) for eventual recrystallization at a lower temperature to maximize product yield and to strip product from the final liquid residue. Semirefined product frozen to the inside of the tube during operation of stage two is first heated above its melting point and slightly melted (sweated). This semipurified melted material (sweat) is removed from the crystallizer kettle, stored in a stage tank (T-4), and then added to the next batch of fresh feed. The remaining material inside the crystallizer is then melted, mixed with product sweat from stage three, recrystallized, and sweated to upgrade the purity even further (stage 3).

Commercial Equipment and Applications The falling-film crystallization process was invented by the MWB company in Switzerland. The process is now marketed by Sulzer Chemtech. Products successfully processed in the falling-film crystallizer are listed on Table 22-9. The falling-film crystallization process is available from the Chemtech Div. of Sulzer Canada Inc., 60 Worcester Rd., Rexdale, Ontario N9W 5X2 Canada.

TABLE 22-9 Fractional Crystallization Reference List

Product	Main characteristics	Capacity, tons/year	Purity	Type of plant	Country	Client
Acrylic acid	Very low aldehyde content, no undesired polymerization in the plant	Undisclosed Undisclosed	99.95% 99.9%	Falling film Falling film	Undisclosed Undisclosed	Undisclosed Undisclosed
Benzoic acid	Pharmaceutical grade, odor- and color free	4,500	99.97%	Falling film	Italy	Chimica del Friuli
Bisphenol A	Polycarbonate grade, no solvent required	150,000	Undisclosed	Falling film	USA	General Electric
Carbonic acid		1,200	Undisclosed	Falling film	Germany	Undisclosed
Fatty acid	Separation of tallow fatty acid into saturated and unsaturated fractions	20,000	Stearic acid: Iodine no. 2 Oleic acid: Cloud pt 5°C	Falling film	Japan	Undisclosed
Fine chemicals		<1,000 <1,000 <1,000 <1,000 <1,000 <1,000 <1,000	Undisclosed Undisclosed Undisclosed Undisclosed Undisclosed Undisclosed Undisclosed	Falling film Static Falling film Falling film Falling film Falling film Falling film	GUS Switzerland Switzerland Switzerland USA Germany Japan	Undisclosed Undisclosed Undisclosed Undisclosed Undisclosed Undisclosed Undisclosed
Hydrazine	Satellite grade	3	>99.9%	Falling film	Germany	ESA
Monochloro acetic acid (MCA)	Low DCA content	6,000	>99.2%	Falling film	USA	Undisclosed
Multipurpose	Separation or purification of two or more chemicals, alternatively	1,000 1,000	Various grades Undisclosed	Falling film Falling film	Belgium Belgium	UCB Reibelco
Naphthalene	Color free and color stable with low thionaphthene content	60,000 20,000 10,000 12,000	99.5% 99.5% 99.8% Various grades	Falling film Falling film/static Falling film/static Falling film	Germany P.R. China P.R. China The Netherlands	Rütgers-Werke Anshan Jining Cindu Chemicals
p-Dichlorobenzene	No solvent washing required	40,000 5,000 4,000 3,000 3,000	99.95% 99.98% 99.8% 99.95% >97%	Falling film Falling film Falling film/distillation Falling film Static	USA Japan Brazil P.R. China P.R. China	Standard Chlorine Toa Gosei Nitroclor Fuyang Shandong
p-Nitrochlorobenzene		18,000 10,000	99.3% 99.5%	Falling film/distillation Static	P.R. China India	Jilin Chemical Mardia
Toluene diisocyanate (TDI)	Separation of TDI 80 into TDI 100 & TDI 65	22,000	Undisclosed	Falling film	Undisclosed	Undisclosed
Trioxan		<1,000	99.97%	Falling film	Undisclosed	Undisclosed

SUPERCRITICAL FLUID SEPARATION PROCESSES

General References: Bruno and Ely, *Supercritical Fluid Technology: Reviews in Modern Theory and Applications,* CRC Press, Boca Raton, 1991. Brunner, *Gas Extraction: An Introduction to Fundamentals of Supercritical Fluids and the Application to Separation Processes,* Springer, New York, 1994. Gloyna and Li, *Waste Management,* **13,** 379 (1993). Johnston and Penninger, *Supercritical Fluid Science and Technology,* Am. Chem. Soc. Symp. Series, **406**, 1989. Kiran and Brennecke, *Am. Chem. Soc. Symp. Ser.,* **512**, 1993. Kiran and Sengers, *Supercritical Fluids: Fundamentals for Application;* NATO Adv. Study Inst. Series E, 1994, Kluwer, Boston, 1994, p. 273. McHugh and Krukonis, *Supercritical Fluid Extraction: Principles and Practice, 2d ed.*. Butterworth-Heinemann, Boston, 1994. Paulaitis, Krukonis, Kurnik, and Reid, *Rev. Chem. Eng.,* **1,** 179 (1983). Savage, Gopalan, Mizan, Martino, and Brock, *AIChE J.,* **41,** 1723 (1995). Shaw, Brill, Clifford, Eckert, and Franck, *Chem. Eng. News,* **69,** 26 (1991). Stahl, Quirin, and Gerard, *Dense Gases for Extraction and Refining,* Springer-Verlag, Berlin, 1988. Tester, Holgate, Armellini, Webley, Killilea, Hong, and Barnes, *Am. Chem. Soc. Symp. Ser.,* **518,** 1993, p. 35.

INTRODUCTION

Fluids above their critical temperatures and pressures, called supercritical fluids (SCFs), exhibit properties intermediate between those of gases and liquids. Consequently, each of these two boundary conditions shed insight into the nature of these fluids. Unlike gases, SCFs possess a considerable solvent strength, transport properties are more favorable (e.g., lower viscosities and higher diffusion coefficients, than in liquid solvents). In regions where a SCF is highly compressible, its density and hence its solvent strength may be adjusted over a wide range with modest variations in temperature and pressure. This tunability may be used to control phase behavior, separation processes (e.g., SCF extraction), rates and selectivities of chemical reactions, and morphologies in materials processing. A variety of advantages of SCF separation processes are given in Table 22-10. In some cases these advantages compensate for the disadvantage of the need for elevated pressure. Despite the diversity of SCF separation processes (see Table 22-11), an attempt will be made to identify unifying themes.

TABLE 22-10 Advantages of Supercritical Fluid Separations

Adjustable solvent strength to tailor selectivities and yields.
Higher diffusion coefficients and lower viscosities compared with liquids.
Rapid diffusion of CO_2 through condensed phases, e.g. polymers.
Solvent recovery is fast and complete, with minimal residue in product.
Properties of CO_2 as a solvent:
Environmentally acceptable solvent for waste minimization, nontoxic, nonflammable, inexpensive, usable at mild temperatures.
Properties of water as a solvent:
Nontoxic, nonflammable substitute for organic solvents.
Extremely wide variation in solvent strength with temperature and pressure.
Collapse of structure due to capillary forces is prevented during solvent removal.

TABLE 22-11 Commercial Applications of Supercritical Fluid Separations Technology

Extraction of foods and pharmaceuticals
Coffee and tea decaffeination
Flavors from hops
Cholesterol and fat from eggs
Nicotine from tobacco
Acetone from antibiotics
Extraction of organics from water
Extraction of volatile substances from substrates
Drying and aerogel formation
Cleaning, e.g. quartz rods for light guide fibers
Removal of monomers, oligomers, and solvent from polymers
Fractionation
Residuum oil supercritical extraction-petroleum deasphalting
Polymer fractionation
Edible oils fractionation
Analytical SCF extraction and chromatography
Reactive separations
Extraction of sec-butanol from isobutene
Hydrothermal oxidation of organic wastes in water

The two fluids most often studied in supercritical fluid technology, carbon dioxide and water, are the two least expensive of all solvents. Carbon dioxide is nontoxic, nonflammable, and has a near-ambient critical temperature of 31.1°C. CO_2 is an environmentally friendly substitute for organic solvents including chlorocarbons and chlorofluorocarbons. Supercritical water (T_c = 374°C) is of interest as a substitute for organic solvents to minimize waste in extraction and reaction processes. Additionally, it is used for hydrothermal oxidation of hazardous organic wastes (also called supercritical water oxidation) and hydrothermal synthesis.

PHYSICAL PROPERTIES OF PURE SUPERCRITICAL FLUIDS

Thermodynamic Properties The variation in solvent strength of a supercritical fluid from gaslike to liquidlike values may be described qualitatively in terms of the density, ρ, or the solubility parameter, δ (square root of the cohesive energy density). It is shown for gaseous, liquid, and SCF CO_2 as a function of pressure in Fig. 22-17 according to the rigorous thermodynamic definition:

$$\delta = \left(\frac{u^{ig} - u}{v}\right)^{1/2} = \left(\frac{h^{ig} - RT - h + Pv}{v}\right)^{1/2} \qquad (22\text{-}9)$$

where u is the internal energy, v is the molar volume, h is the enthalpy, and the superscript ig refers to the ideal gas. Similar characteristics are observed for a plot of other density-dependent variables versus pressure, e.g., density, enthalpy, entropy, viscosity, and diffusion coefficient. However, unlike δ, some of these properties decrease with density. The δ for gaseous carbon dioxide is essentially zero; whereas, the value for liquid carbon dioxide is like that of a hydrocarbon. At –30°C there is a large increase in δ upon condensation from vapor to liquid. Above the critical temperature, it is possible to tune the solubility parameter continuously over a wide range with either a small isothermal pressure change or a small isobaric temperature change. This ability to tune the solvent strength of a supercritical fluid is its

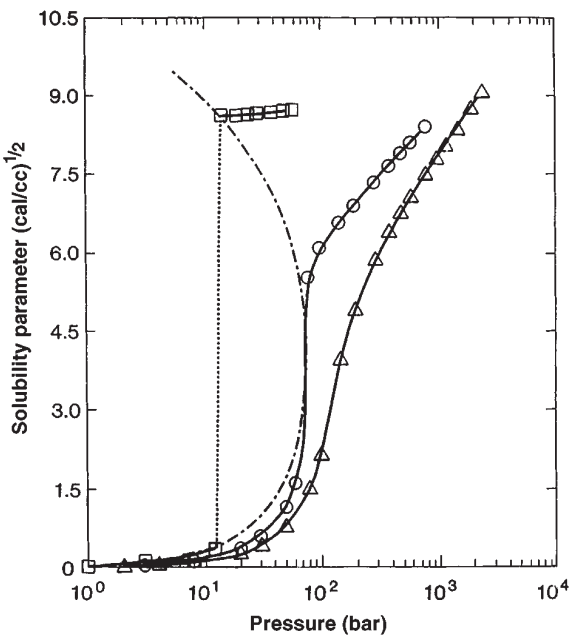


FIG. 22-17 Solubility parameter of CO_2 as a function of pressure in the gas, liquid, and supercritical states (⋯: –30°C; ○: 31°C; Δ: 70°C).

unique feature, and it can be used to extract and then recover selected products. Note that density and δ are more direct measures of the solvent strength of a SCF than pressure.

Although density (either mass or molar) is a good indicator of solvent strength for a single SCF, it is not a useful indicator for comparing different fluids. For example, CF_3Cl at 40°C and 1300 bar has a mass density of 1.95 g/cm^3, yet it is a weaker solvent than the much less dense fluid SCF CO_2 or liquid hexane. The same argument applies for SF_6. A better indicator of the van der Waals forces contributed by a SCF is obtained by multiplying ρ by the molecular polarizability, α, which is a constant for a given molecule. The solubility parameter δ of CO_2 can be misleading. It is larger than ethane's even though ethane has a larger value of αρ. However about 20 percent of δ for CO_2 may be attributed to its large quadrupole moment. For nonpolar solutes, where this quadrupole moment is unimportant, CO_2 is a much weaker solvent than *n*-hexane, and is more like fluorocarbons, which also have small values of αρ.

Water, a key SCF, undergoes profound changes upon heating to the critical point. It expands by a factor of 3 destroying about ⅔ of the hydrogen bonds, and the dielectric constant drops from 80 to 5 (Shaw et al., op. cit.). (See Fig. 22-18.) *Supercritical water* (SCW) therefore behaves like a "nonaqueous" solvent, and it dissolves many organics and even gases such as O_2. At 400°C and 350 bar, the density of water is 0.47 g/mL, the dielectric constant, ε, is 10, and the ion product, K_w, is 7×10^{-14} compared with 10^{-14} at room temperature. Here, water behaves as a dense fluid which can dissolve electrolytes, with high diffusion coefficients and ion mobilities. At 500°C and the same pressure, the density of water is only 0.144 g/mL, ε is 2, and K_w is 2×10^{-20}. At these conditions, water is a high-temperature gas which does not solvate ions significantly.

Transport Properties Although the densities of supercritical fluids approach those of conventional liquids, their transport properties are closer to those of gases, as shown for a typical SCF such as CO_2 in Table 22-12. For example, the viscosity is several orders of magnitude lower than at liquidlike conditions. The self-diffusion coefficient ranges between 10^{-3} and 10^{-5} cm^2/s, and binary-diffusion coefficients are similar [Liong, Wells, and Foster, *J. Supercritical Fluids* **4,** 91 (1991); Catchpole and King, *Ind. Eng. Chem. Research,* **33,** 1828 (1994)]. These values are as much as one hundred times larger than those typically observed in conventional liquids. The improved transport rates in SCFs versus liquid solvents are important in practical applications including supercritical extraction. Furthermore, carbon dioxide diffuses through condensed-liquid phases (e.g., adsorbents and polymers) faster than do typical solvents which have larger molecular sizes.

TABLE 22-12 Density and Transport Properties of a Gas, Supercritical Fluid, and a Liquid

State	ρ (g/cm^3)	μ (g/cm·s)	D (cm^2/s)
Gas, 1 bar	10^{-3}	10^{-4}	0.2
SCF (T_c, P_c)	0.3	10^{-4}	10^{-3}
Liquid	1	10^{-2}	10^{-5}

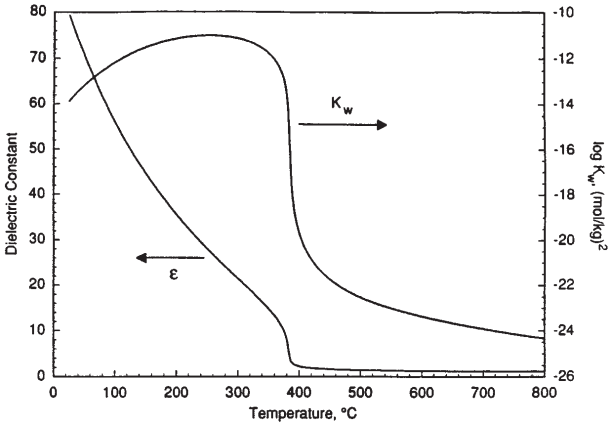


FIG. 22-18 Dielectric constant and dissociation constant, K_w, of water at 250 bar (*Tester et al., op. cit.*).

PROCESS CONCEPTS IN SUPERCRITICAL FLUID EXTRACTION

Figure 22-19 shows a one-stage extraction process that utilizes the adjustability of the solvent strength with pressure in a separation process. The solvent flows through the extraction chamber at a relatively high pressure to extract the components of interest from the feed. The products are then recovered in the separator by depressurization, and the solvent is recompressed and recycled. The products can also be precipitated from the extract phase by raising the temperature after the extraction to lower the solvent density. In the increasing pressure profiling approach, conditions are set so that only the lightest components in the feed are extracted in the first fraction. The recovery vessel is then replaced, and the pressure is increased to collect the next heavier fraction. In the multistage isothermal decreasing pressure profiling process, all but the heaviest fraction are extracted in the first vessel. The extract then passes through a series of recovery vessels held at successively lower pressures, each of which precipitates the next lower molecular-weight fraction in the raffinate. A new process, critical isobaric temperature-rising elution fractionation, is a supercritical variation on temperature-rising elution fractionation in a liquid solvent (McHugh and Krukonis, op. cit.).

Solids may be processed continuously or semicontinuously by pumping slurries or by using lock hoppers. An example is the separation of insoluble polymers by floatation with a variable-density SCF. For liquid feeds, multistage separation may be achieved by continuous counter-current extraction, much like conventional liquid-liquid extraction. The final products may be recovered from the extract phase by a depressurization, a temperature change, or by conventional distillation.

PHASE EQUILIBRIA

Liquid-Fluid Equilibria Nearly all binary liquid-fluid phase diagrams can be conveniently placed in one of six classes (Fig. 22-20). Two-phase regions are represented by an area and three-phase regions by a line. In Class I, the two components are completely miscible, and a single critical mixture curve connects their critical points. Class II behavior is similar, except that a region of liquid-liquid immiscibility is found at lower temperatures. As the two components become increasingly dissimilar, the *upper critical solution temperature* (UCST) line merges with the branch of the critical mixture curve that begins at the heavier component's critical point, and Class III

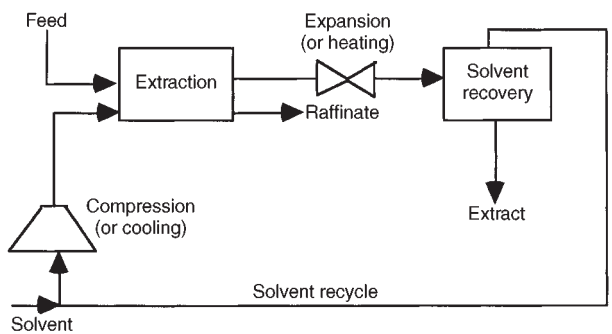


FIG. 22-19 Schematic diagram of a typical supercritical fluid-extraction process.

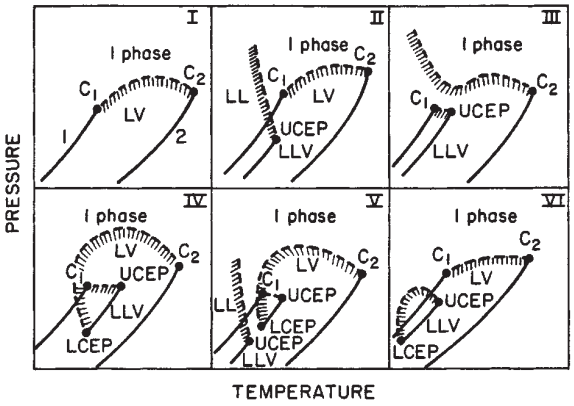


FIG. 22-20 Six classes of binary liquid-fluid phase diagrams (*Prausnitz et al.*, Molecular Thermodynamics of Fluid-Phase Equilibria, © *1986. Reprinted by permission of Prentice-Hall, Inc.*).

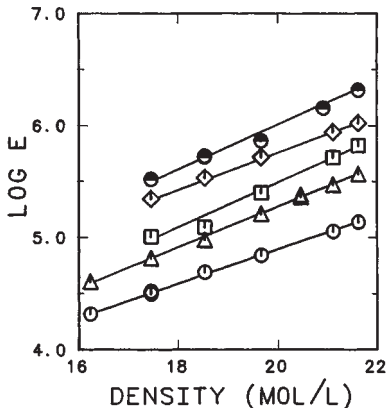


FIG. 22-21 Enhancement factor for solids with a variety of polar functionalities in CO_2 at 35°C (from bottom to top: hexamethylbenzene, 2-naphthol, phthalic anhydride, anthracene, acridine).

behavior is observed. In Class IV behavior, the mixture critical curve bends down to low pressures and intercepts the three-phase *liquid-liquid-vapor* (LLV) line at the lower critical end point. Class V resembles Class IV except it includes an additional LL critical curve. Class VI has features of Class II except that the critical curve intersects the LLV line twice.

For a ternary system, the phase diagram appears much like that in conventional liquid-liquid equilibrium. However, because a SCF solvent is compressible, the slopes of the tie lines (distribution coefficients) and the size of the two-phase region can vary significantly with pressure as well as temperature. Furthermore, at lower pressures, LLV tie-triangles appear upon the ternary diagrams and can become quite large.

Solid-Fluid Equilibria The phase diagrams of binary mixtures in which the heavier component (the solute) is normally a solid at the critical temperature of the light component (the solvent) include *solid-liquid-vapor* (SLV) curves which may or may not intersect the LV critical curve. The solubility of the solid is very sensitive to pressure and temperature in compressible regions where the solvent's density and solubility parameter are highly variable. In contrast, plots of the log of the solubility versus density at constant temperature exhibit fairly simple linear behavior.

To understand the role of solute-solvent interactions on solubilities and selectivities, it is instructive to define an enhancement factor, E, as the actual solubility, y_2, divided by the solubility in an ideal gas, so that $E = y_2P/P_2^{sat}$, where P_2^{sat} is the vapor pressure. This factor is a normalized solubility because it removes the effect of the vapor pressure, providing a means to focus on interactions in the SCF phase. For a given fluid at a particular temperature and pressure, enhancement factors do not vary much for many types of organic solids of similar molecular weight. As shown in Fig. 22-21, Es fall within a range of only about 1.5 orders of magnitude for substances with a variety of polar functional groups, even though the actual solubilities (not shown) vary by many orders of magnitude. This means that solubilities, and also selectivities, in carbon dioxide are governed primarily by vapor pressures and only secondarily by solute-solvent interactions in the SCF phase. However, fluid-phase interactions can be especially important if cosolvents are added which are strong Lewis acids or bases.

Polymer-Fluid Equilibria and the Glass Transition Most polymer systems fall in the Class III or Class V phase diagrams, and the same system can often change from one class into the other as the polymer's molecular weight changes. Most polymers are insoluble in CO_2 below 100°C, yet CO_2 can be quite soluble in the polymer. For example, the sorption of CO_2 into silicone rubber is highly dependent upon temperature and pressure, since these properties have a large influence on the density and activity of CO_2.

For glassy polymers, sorption isotherms are more complex and hysteresis between the pressurization and depressurization steps may appear. CO_2 adds free volume to the polymer that can relax very slowly. Furthermore, CO_2 can act as a plasticizer and depress the glass transition temperature by 100°C or even more. Not only do the mechanical properties change as the polymer is plasticized, but the diffusion coefficient of CO_2 and other solutes can increase by orders of magnitude. In PMMA, for instance, carbon dioxide's diffusion coefficient increases by as much as two orders-of-magnitude as the pressure is increased by 75 bar at 35°C.

Cosolvents and Surfactants Many nonvolatile polar substances cannot be dissolved at moderate temperatures in nonpolar fluids such as CO_2. Cosolvents (also called entrainers, modifiers, moderators) such as alcohols and acetone have been added to fluids to raise the solvent strength. The addition of only 2 mol % of the complexing agent tri-*n*-butyl phosphate (TBP) to CO_2 increases the solubility of hydroquinone by a factor of 250 due to Lewis acid-base interactions. Very recently, surfactants have been used to form reverse micelles, microemulsions, and polymeric latexes in SCFs including CO_2. These organized molecular assemblies can dissolve hydrophilic solutes and ionic species such as amino acids and even proteins. Examples of surfactant tails which interact favorably with CO_2 include fluoroethers, fluoroacrylates, fluoroalkanes, propylene oxides, and siloxanes.

Phase Equilibria Models Two approaches are available for modeling the fugacity of a solute, f_i, in a supercritical fluid solution. The compressed gas approach is the most common where:

$$f_i^G = y_i \phi_i P \tag{22-10}$$

and ϕ_i is the fugacity coefficient of component i. The "expanded liquid" approach is given as:

$$f_i^L = x_i \gamma_i (P^0, x_i) f_i^{0L}(P^0) \exp\left\{ \int_{P^0}^{P} \frac{\bar{v}_i}{RT}\, dP \right\} \tag{22-11}$$

where x_i is the mole fraction, γ_i is the activity coefficient, P^0 and f_i^0 are the reference pressure and fugacity, respectively, and $\bar{v}_i$ is the partial molar volume of component i. In principle this approach has an advantage in that γ_i can be chosen to give exact results at a pressure in the near-critical region, but the use of γ_i introduces an additional parameter.

A variety of equations-of-state have been applied to supercritical fluids, ranging from simple cubic equations like the Peng-Robinson equation-of-state to the Statistical Associating Fluid Theory. All are able to model nonpolar systems fairly successfully, but most are increasingly challenged as the polarity of the components increases. The key is to calculate the solute-fluid molecular interaction parameter from the pure-component properties. Often the standard approach (i.e. corresponding states based on critical properties) is of limited accuracy due to the vastly different critical temperatures of the solutes (if known) and the solvents; other properties of the solute

are more appropriate [Johnston et al., *Ind. Eng. Chem. Research.*, **28,** 1115 (1989)].

MASS TRANSFER

Experimental gas-solid mass-transfer data have been obtained for naphthalene in CO_2 to develop correlations for mass-transfer coefficients [Lim et al., *Am. Chem. Soc. Symp. Ser.*, **406,** 379 (1989)]. The data were correlated over a wide range of conditions with the following equation for combined natural and forced convection:

$$\mathrm{Sh}/(\mathrm{Sc}\cdot\mathrm{Gr})^{1/4} = e(\mathrm{Re}/\mathrm{Gr}^{1/2})^{f} \qquad (22\text{-}12)$$

where Sh, Sc, Gr, and Re are the Sherwood, Schmidt, Grashof, and Reynolds numbers, respectively, and e and f are constants. The mass-transfer coefficient increases dramatically near the critical point, goes through a maximum and then decreases gradually. The strong natural convection at SCF conditions leads to higher mass-transfer rates than in liquid solvents.

A comprehensive mass-transfer model has been developed for SCF extraction from an aqueous phase to CO_2 in countercurrent sieve tray and packed columns [Seibert and Moosberg, *Sep. Sci. Technol.*, **23,** 2049 (1988)]. Both the hydraulics and mass-transfer coefficients were obtained from models developed for conventional liquid extraction, and the results were in good agreement with experiment for a 10-cm diameter column either with sieve trays or packing. If interfacial tensions are comparable, mass-transfer rates for extraction of organics from aqueous solutions are higher for CO_2 than hydrocarbon solvents. For this type of extraction, it was found that CO_2 preferentially wets ceramic and metal packings; consequently, trays are more efficient than packings.

APPLICATIONS

Food and Pharmaceutical Applications These applications are driven by the environmental acceptability of CO_2, as well as by the ability to tailor the extraction with the adjustable solvent strength. The General Foods coffee decaffeination plant in Houston, Texas is designed to process between 15,000 and 30,000 pounds of coffee beans per hour (McHugh and Krukonis, op. cit.). See Fig. 22-22. The moist, green coffee beans are charged to an extraction vessel approximately 7 ft diameter by 70 ft high, and carbon dioxide is used to extract the caffeine from the beans. Various methods have been proposed for recovery of the caffeine including washing with water and adsorption. Often the recovery of a particular component of an extract is the key challenge in SCF extraction. Thus, SCF extraction is frequently combined with another process such as distillation, absorption, or adsorption.

Temperature-Controlled Residuum Oil Supercritical Extraction (ROSE) The Kerr-McGee ROSE process has been licensed by over a dozen companies worldwide. The extraction step uses a liquid solvent, and the solvent is recovered at supercritical conditions to save energy as shown in Fig. 22-23. The residuum is contacted with butane or pentane to precipitate the heavy asphaltene fraction. The extract is then passed through a series of heaters, where it goes from the liquid state to a lower-density supercritical fluid state. Because the entire process is carried out at conditions near the critical point, a relatively small temperature change is required to produce a fairly large density change. After the light oils have been removed, the solvent is cooled back to the liquid state and recycled.

Extraction from Aqueous Solutions Critical Fluid Technologies, Inc. has developed a continuous countercurrent extraction process based on a 0.5- by 10-m column to extract residual organic solvents such as trichloroethylene, methylene chloride, benzene, and chloroform from industrial wastewater streams. Typical solvents include supercritical CO_2 and near-critical propane. The economics of these processes are largely driven by the hydrophilicity of the product, which has a large influence on the distribution coefficient. For example, at 16°C, the partition coefficient between liquid CO_2 and water is 0.4 for methanol, 1.8 for *n*-butanol, and 31 for *n*-heptanol.

Adsorption and Desorption Adsorbents may be used to recover solutes from supercritical fluid extracts; for example, activated carbon and polymeric sorbents may be used to recover caffeine from CO_2. This approach may be used to improve the selectivity of a supercritical fluid extraction process. SCF extraction may be used to regenerate adsorbents such as activated carbon and to remove contaminants from soil. In many cases the chemisorption is sufficiently strong that regeneration with CO_2 is limited, even if the pure solute is quite soluble in CO_2. In some cases a cosolvent can be added to the SCF to displace the sorbate from the sorbent. Another approach is to use water at elevated or even supercritical temperatures to facilitate desorption. Many of the principles for desorption are also relevant to extraction of substances from other substrates such as natural products and polymers.

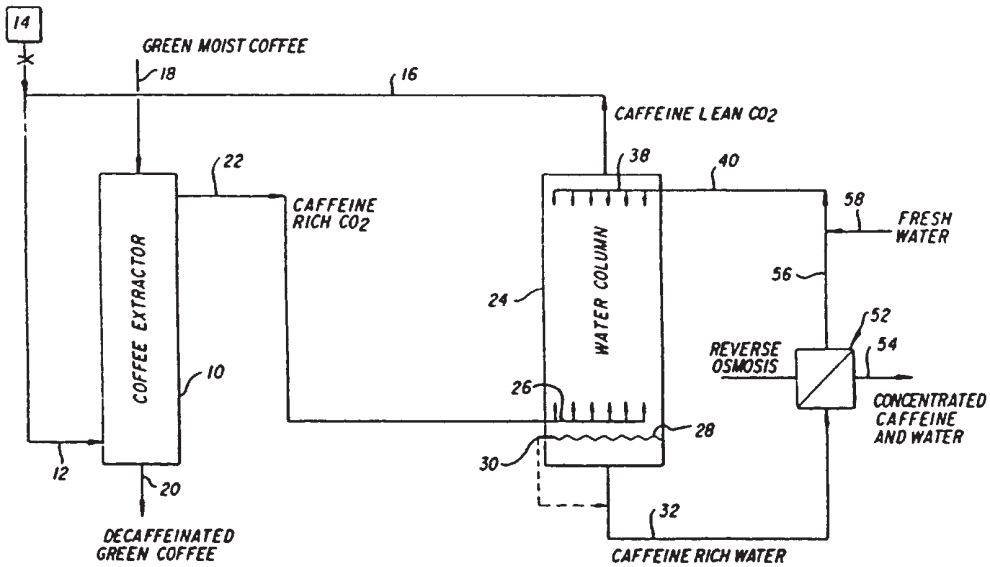


FIG. 22-22 Schematic diagram of the Kraft process for producing decaffeinated coffee using supercritical carbon dioxide (*McHugh and Krukonis, op. cit.*).

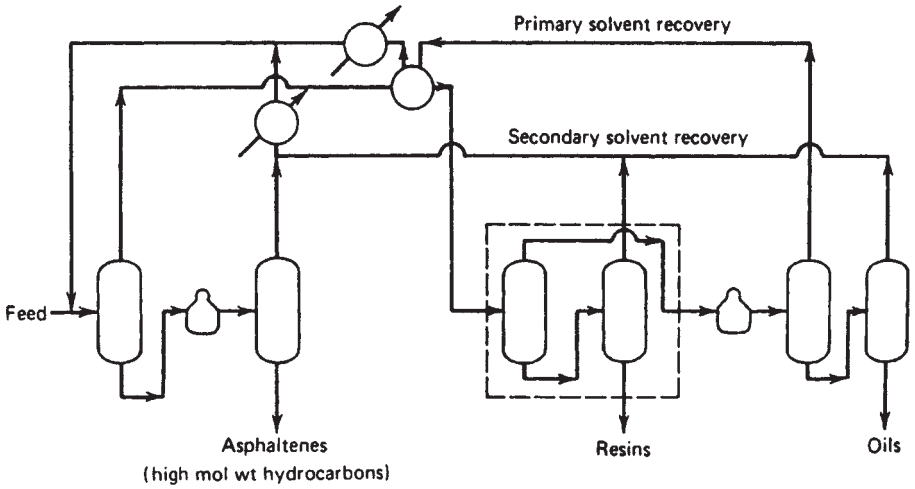


FIG. 22-23 Schematic diagram of the Kerr-McGee ROSE process.

Polymer Devolatilization and Fractionation Supercritical fluids may be used to extract solvent, monomers, and oligomers from polymers. After extraction the pressure is reduced to atmospheric leaving little residue in the substrate; furthermore, the extracted impurities are easily recovered from the SCF. To aid process design, partition coefficients of various solutes between polymers and CO_2 have been measured with static and dynamic techniques such as inverse supercritical fluid chromatography. The swelling and lowering of the glass transition temperature of the polymer by the SCF can increase mass-transfer rates markedly. The polymer may or may not return to its original dimensions, depending upon factors such as the glass transition properties and crystallinity.

Supercritical fluids may be used to fractionate polymers on the basis of molecular weight and/or composition. The most common techniques are isothermal increasing-pressure profiling and isothermal decreasing-pressure profiling as discussed in the above section on process concepts. The critical isobaric temperature rising elution fractionation process can be used to fractionate polymers as a function of crystallinity (e.g., due to branching), based on the melting points in the presence of the fluid (McHugh and Krukonis, op. cit.).

Drying and Aerogel Formation One of the oldest practical applications of supercritical fluids, developed in 1932, is supercritical fluid drying. Here the solvent is extracted from a porous solid with a SCF fluid, and then the fluid is depressurized. Because the fluid expands from the solid without crossing a liquid-vapor phase boundary, capillary forces are not present which would otherwise collapse the structure. Using supercritical fluid drying, aerogels have been prepared with densities so low that they essentially float in air and look like a cloud of smoke. The process is used in a commercial instrument to dry samples for electron microscopy without perturbing the structure.

Cleaning Supercritical fluids such as CO_2 are being used to clean and degrease quartz rods used to produce optical fibers, products used in the fabrication of printed circuit boards, oily chips from machining operations, and precision bearings in military applications, and so on. Here, CO_2 replaces conventional chlorocarbon or chlorofluorocarbon solvents.

Analytical Supercritical Fluid Extraction and Chromatography Supercritical fluids, especially CO_2, are used widely to extract a wide variety of solid and liquid matrices to obtain samples for analysis. Benefits compared with conventional Soxhlet extraction include minimization of solvent waste, faster extraction, tunability of solvent strength, and simple solvent removal with minimal solvent contamination in the sample. Compared with high-performance liquid chromatography, the number of theoretical stages is higher in SCF chromatography due to the more favorable transport rates. A limitation in each of these applications is the low solvent strength of CO_2; often cosolvents are required.

Precipitation with a Compressed Fluid Antisolvent (PCA) Because fluids such as CO_2 are weak solvents, they are often more effective as antisolvents. In this process, the antisolvent may be a compressed gas, pressurized liquid, or a supercritical fluid. Mixing of a solution with the antisolvent leads to a precipitated product. There are two primary process configurations for this mixing: (1) a pure, compressed fluid may be added to a liquid solution or (2) a liquid solution may be sprayed through a nozzle into a pure, compressed fluid. Gaseous CO_2 is quite soluble in a number of organic solvents such as methanol, toluene, dimethylformamide, and tetrahydrofuran, at pressures from 10 to 100 bar. As CO_2 mixes with the liquid phase, it decreases the cohesive energy density (solvent strength) substantially, leading to precipitation of dissolved solutes (e.g., crystals of progesterone). It has been demonstrated that the rate of addition of a fluid antisolvent or the liquid solvent may be programmed to control crystal morphology, size, and size distribution over a wide range from 1 to 100 μm. The high-diffusion rates of the organic solvent into CO_2 and vice-versa can lead to rapid-phase separation. This process may be used to precipitate a solute from a solvent or for separation of solutes.

Crystallization Solutes may be crystallized from supercritical fluids by temperature and/or pressure changes, and by the PCA process described above. In the *rapid expansion from supercritical solution* (RESS) process, a SCF containing a dissolved solute is expanded through a nozzle or orifice in less than 1 ms to form small particles or fibers. A variety of inorganic crystals have been formed naturally and synthetically in SCF water.

Reactive Separations Reactions may be integrated with SCF separation processes to achieve a large degree of control for producing a highly purified product. Reaction products may be recovered by volatilization into, or precipitation from, a SCF phase. A classic example is the high-pressure production of polyethylene in the reacting solvent SCF ethylene. The molecular-weight distribution may be controlled by choosing the temperature and pressure for precipitating the polymer from the SCF phase.

In the last few years, Idemitsu commercialized a 5000 metric ton/year integrated reaction and separation process in SCF isobutene, as shown in Fig. 22-24. The reaction of isobutene and water takes place in the water phase and is acid catalyzed. The product, *sec*-butanol, is extracted into the isobutene phase to drive the reversible reaction to the right. The *sec*-butanol is then recovered from the isobutene by depressurizing the SCF phase, and the isobutene is recompressed and recycled.

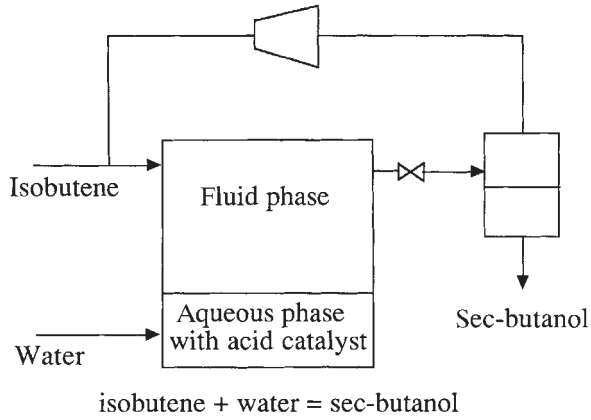


FIG. 22-24 Process for the integrated reaction and separation of *sec*-butanol from isobutene.

Supercritical fluid solvents have been tested for reactive extractions of liquid and gaseous fuels from heavy oils, coal, oil shale, and biomass. In some cases the solvent participates in the reactions, as in the hydrolysis of coal and heavy oils with water. Related applications include conversion of cellulose to glucose in water, delignification of wood with ammonia, and liquefaction of lignin in water.

Hydrothermal oxidation (HO) (also called supercritical water oxidation) is a reactive process to separate aqueous wastes into water, CO_2, nitrogen, salts, and other byproducts. It is an enclosed and complete water-treatment process making it more desirable to the public than incineration (Fig. 22-25) (Tester et al., op. cit.; Gloyna and Li, op. cit.; Shaw et al., op. cit.). As mentioned above, organics and oxygen mix in a single phase in SCW due the low dielectric constant. Oxidation is rapid and efficient in this one-phase solution, so that wastewater containing 1 to 20 wt % organics may be oxidized rapidly in SCW with higher energy efficiency and much less air pollution than in conventional incineration. Temperatures range from about 375 to 650°C and pressures from 3000 to about 5000 psia. Conversions can be greater than 99.99 percent for reactor residence times of a minute or less. Organics are oxidized to CO_2, H_2O, and molecular nitrogen with little NO_x. A commercial plant designed by Eco-Waste Technology appeared in Austin, Texas in 1994.

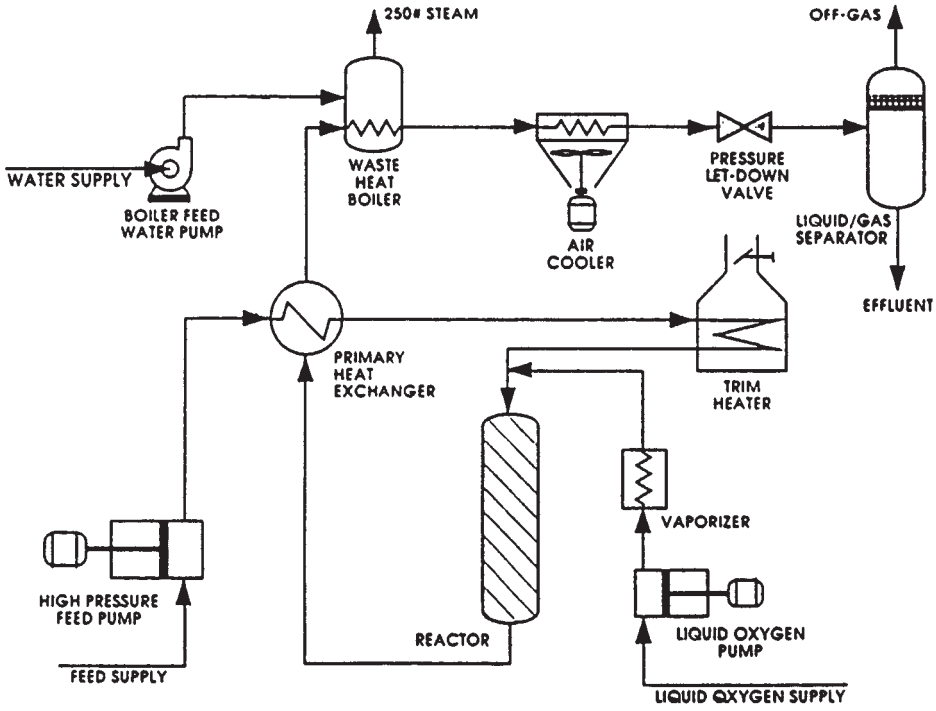


FIG. 22-25 Hydrothermal-oxidation process (also called supercritical water oxidation) for wastewater purification. *(Courtesy Eco-Waste Technologies.)*

ALTERNATIVE SOLID/LIQUID SEPARATIONS

SEPARATION PROCESSES BASED PRIMARILY ON ACTION IN AN ELECTRIC FIELD

Differences in mobilities of ions, molecules, or particles in an electric field can be exploited to perform useful separations. Primary emphasis is placed on electrophoresis and dielectrophoresis. Analogous separation processes involving magnetic and centrifugal force fields are widely applied in the process industry (see Secs. 18 and 19).

Theory of Electrical Separations

General References: Newman, *Adv. Electrochem. Electrochem. Eng.*, **5,** 87 (1967); *Ind. Eng. Chem.*, **60**(4), 12 (1968). Ptasinski and Kerkhof, *Sep. Sci. Technol.*, **27,** 995 (1992).

For electrolytic solutions, migration of charged species in an electric field constitutes an additional mechanism of mass transfer. Thus the flux of an ionic species N_i in (g·mol)/(cm²·s) in dilute solutions can be expressed as

$$N_i = -z_i u_i \mathcal{F} c_i \nabla E - D_i \nabla c_i + c_i v \tag{22-13}$$

The ionic mobility u_i is the average velocity imparted to the species under the action of a unit force (per mole). v is the stream velocity, cm/s. In the present case, the electrical force is given by the product of the electric field ∇E in V/cm and the charge $z_i\mathcal{F}$ per mole, where $\mathcal{F}$ is the Faraday constant in C/g equivalent and z_i is the valence of the ith species. Multiplication of this force by the mobility and the concentration c_i [(g·mol)/cm³] yields the contribution of migration to the flux of the ith species.

The diffusive and convective terms in Eq. (22-13) are the same as in nonelectrolytic mass transfer. The ionic mobility u_i, (g·mol·cm²)/(J·s), can be related to the ionic-diffusion coefficient D_i, cm²/s, and the ionic conductance of the ith species λ_i, cm²/(Ω·g equivalent):

$$u_i = D_i/RT = \lambda_i/|z_i|\mathcal{F}^2 \tag{22-14}$$

where T is the absolute temperature, K; and R is the gas constant, 8.3143 J/(K·mol). Ionic conductances are tabulated in the literature (Robinson and Stokes, *Electrolyte Solutions,* Academic, New York, 1959). For practical purposes, a bulk electrolytic solution is electrically neutral.

$$\sum_i z_i c_i = 0 \tag{22-15}$$

since the forces required to effect an appreciable separation of charge are prohibitively large.

The **current density** (A/cm²) produced by movement of charged species is described by summing the terms in Eq. (22-16) for all species:

$$i = \mathcal{F} \sum_i z_i \mathbf{N}_i = -\kappa \nabla E - \mathcal{F} \sum_i z_i D_i \nabla c_i \tag{22-16}$$

where the electrical conductivity κ in S/cm is given by

$$\kappa = \mathcal{F}^2 \sum_i z_i^2 u_i c_i \tag{22-17}$$

In solutions of uniform composition, the diffusional terms vanish and Eq. (22-16) reduces to Ohm's law.

Conservation of each species is expressed by the relation

$$\partial c_i/\partial t = -\nabla \cdot \mathbf{N}_i \tag{22-18}$$

provided that the species is not produced or consumed in homogeneous chemical reactions. In two important cases, this conservation law reduces to the equation of convective diffusion:

$$(\partial c_i/\partial t) + \mathbf{v}\nabla \cdot c_i = D \nabla^2 c_i \tag{22-19}$$

First, when a large excess of inert electrolyte is present, the electric field will be small and migration can be neglected for minor ionic components; Eq. (22-19) then applies to these minor components, where D is the ionic-diffusion coefficient. Second, Eq. (22-19) applies when the solution contains only one cationic and one anionic species. The electric field can be eliminated by means of the electroneutrality relation.

In the latter case the diffusion coefficient D of the electrolyte is given by

$$D = (z_+u_+D_- - z_-u_-D_+)/(z_+u_+ - z_-u_-) \tag{22-20}$$

which represents a compromise between the diffusion coefficients of the two ions. When Eq. (22-19) applies, many solutions can be obtained by analogy with heat transfer and nonelectrolytic mass transfer.

Because the solution is electrically neutral, conservation of charge is expressed by differentiating Eq. (22-16):

$$\nabla \cdot \mathbf{i} = 0 = -\kappa \nabla^2 E - \mathcal{F} \sum_i z_i D_i \nabla^2 c_i \tag{22-21}$$

For solutions of uniform composition, Eq. (22-21) reduces to Laplace's equation for the potential:

$$\nabla^2 E = 0 \tag{22-22}$$

This equation is the starting point for determination of the current-density distributions in many electrochemical cells.

Near an interface or at solution junctions, the solution departs from electroneutrality. Charges of one sign may be preferentially adsorbed at the interface, or the interface may be charged. In either case, the charge at the interface is counterbalanced by an equal and opposite charge composed of ions in the solution. Thermal motion prevents this countercharge from lying immediately adjacent to the interface, and the result is a "diffuse-charge layer" whose thickness is on the order of 10 to 100 Å.

A tangential electric field ∇E_t acting on these charges produces a relative motion between the interface and the solution just outside the diffuse layer. In view of the thinness of the diffuse layer, a balance of the tangential viscous and electrical forces can be written

$$\mu(\partial^2 v_t/\partial y^2) + \rho_e \nabla E_t = 0 \tag{22-23}$$

where μ is the viscosity and ρ_e is the electric-charge density, C/cm³. Furthermore, the variation of potential with the normal distance satisfies Poisson's equation:

$$\partial^2 E/\partial y^2 = -(\rho_e/\varepsilon) \tag{22-24}$$

with ε defined as the **permittivity** of the solution. [The relative dielectric constant is $\varepsilon/\varepsilon_0$, where ε_0 is the permittivity of free space; $\varepsilon_0 = 8.8542 \times 10^{-14}$ C/(V·cm).] Elimination of the electric-charge density between Eqs. (22-23) and (22-24) with two integrations, gives a relation between ∇E_t and the velocity v_0 of the bulk solution relative to the interface.

$$\mu[v_t(\infty) - v_t(0)] = \varepsilon \nabla E_t [E(\infty) - E(0)] \tag{22-25}$$

or

$$v_0 = -(\varepsilon \nabla E_t \zeta/\mu) \tag{22-26}$$

The potential difference across the mobile part of the diffuse-charge layer is frequently called the **zeta potential,** $\zeta = E(0) - E(\infty)$. Its value depends on the composition of the electrolytic solution as well as on the nature of the particle-liquid interface.

There are four related electrokinetic phenomena which are generally defined as follows: *electrophoresis*—the movement of a charged surface (i.e., suspended particle) relative to a stationary liquid induced by an applied electrical field, *sedimentation potential*—the electric field which is crested when charged particles move relative to a stationary liquid, *electroosmosis*—the movement of a liquid relative to a stationary charged surface (i.e., capillary wall), and *streaming potential*—the electric field which is created when liquid is made to flow relative to a stationary charged surface. The effects summarized by Eq. (22-26) form the basis of these electrokinetic phenomena.

For many particles, the diffuse-charge layer can be characterized adequately by the value of the zeta potential. For a spherical particle of radius r_0 which is large compared with the thickness of the diffuse-charge layer, an electric field uniform at a distance from the particle will produce a tangential electric field which varies with position on the particle. Laplace's equation [Eq. (22-22)] governs the distribution

of potential outside the diffuse-charge layer; also, the Navier-Stokes equation for a creeping-flow regime can be applied to the velocity distribution. On account of the thinness of the diffuse-charge layer, Eq. (22-26) can be used as a local boundary condition, accounting for the effect of this charge in leading to movement of the particle relative to the solution. The result of this computation gives the velocity of the particle as

$$v = \varepsilon\zeta \nabla E/\mu \tag{22-27}$$

and it may be convenient to tabulate the mobility of the particle

$$U = v/\nabla E = \varepsilon\zeta/\mu \tag{22-28}$$

rather than its zeta potential. Note that this mobility gives the velocity of the particle for unit electric field rather than for unit force on the particle. Related equations can be developed for the velocity of electroosmotic flow. The subsections presented below ("Electrophoresis," "Electrofiltration," and "Cross-Flow–Electrofiltration") represent both established and emerging commercial applications of electrokinetic phenomena.

Electrophoresis

General Reference: Wankat, *Rate-Controlled Separations,* Elsevier, London, 1990.

Electrophoretic Mobility Macromolecules move at speeds measured in tenths of micrometers per second in a field (gradient) of 1 V/cm. Larger particles such as bubbles or bacteria move up to 10 times as fast because U is usually higher. To achieve useful separations, therefore, voltage gradients of 10 to 100 V/cm are required. High voltage gradients are achieved only at the expense of power dissipation within the fluid, and the resulting heat tends to cause undesirable convection currents.

Several devices are available commercially to measure mobility. One of these (Zeta-Meter Inc., New York) allows direct microscopic measurement of individual particles. Another allows measurement in more concentrated suspensions (Numinco Instrument Corp., Monroeville, Pa.). The state of the charge can also be measured by a streaming-current detector (Waters Associates, Inc., Framingham, Mass.). For macromolecules, more elaborate devices such as the Tiselius moving-boundary apparatus are used.

Mobility is affected by the dielectric constant and viscosity of the suspending fluid, as indicated in Eq. (22-28). The ionic strength of the fluid has a strong effect on the thickness of the double layer and hence on ζ. As a rule, mobility varies inversely as the square root of ionic strength [Overbeek, *Adv. Colloid Sci.,* **3,** 97 (1950)].

Modes of Operation There is a close analogy between sedimentation of particles or macromolecules in a gravitational field and their electrophoretic movement in an electric field. Both types of separation have proved valuable not only for analysis of colloids but also for preparative work, at least in the laboratory. Electrophoresis is applicable also for separating mixtures of simple cations or anions in certain cases in which other separating methods are ineffectual.

Electrodecantation or electroconvection is one of several operations in which one mobile component (or several) is to be separated out from less mobile or immobile ones. The mixture is introduced between two vertical semipermeable membranes; for separating cations, anion membranes are used, and vice versa. When an electric field is applied, the charged component migrates to one or another of the membranes; but since it cannot penetrate the membrane, it accumulates at the surface to form a dense concentrated layer of particles which will sink toward the bottom of the apparatus. Near the top of the apparatus immobile components will be relatively pure. Murphy [*J. Electrochem. Soc.,* **97**(11), 405 (1950)] has used silver-silver chloride electrodes in place of membranes. Frilette [*J. Phys. Chem.,* **61,** 168 (1957)], using anion membranes, partially separated H^+ and Na^+, K^+ and Li^+, and K^+ and Na^+. Unfortunately no simple electrodecantation apparatus is available for bench-scale testing. A rather complex device described by Polson and Largier [in Alexander and Block (eds.), *Analytical Methods of Protein Chemistry,* vol. I, Pergamon, New York, 1960] is available commercially (Quickfit Reeve Angel, Inc., Clifton, NJ).

Countercurrent electrophoresis can be used to split a mixture of mobile species into two fractions by the electrical analog of elutriation. In such countercurrent electrophoresis, sometimes termed an ion still, a flow of the suspending fluid is maintained parallel to the direction of the voltage gradient. Species which do not migrate fast enough in the applied electric field will be physically swept out of the apparatus. An apparatus based mainly on this principle but using also natural convection currents has been developed (Bier, *Electrophoresis,* vol. II, Academic, New York, 1967).

Membrane electrophoresis which is based upon differences in ion mobility, has been studied by Glueckauf and Kitt [*J. Appl. Chem.,* **6,** 511 (1956)]. Partial exclusion of coions by membranes results in large differences in coion mobilities. Superposing a cation and an anion membrane gives high transference numbers (about 0.5) for both cations and anions while retaining the selectivity of mobilities. Large voltages are required, and flow rates are low.

In continuous-flow zone electrophoresis the "solute" mixture to be separated is injected continuously as a narrow source within a body of carrier fluid flowing between two electrodes. As the "solute" mixture passes through the transverse field, individual components migrate sideways to produce zones which can then be taken off separately downstream as purified fractions.

Resolution depends upon differences in mobilities of the species. Background electrolyte of low ionic strength is advantageous, not only to increase electrophoretic (solute) mobilities, but also to achieve low electrical conductivity and thereby to reduce the thermal-convection current for any given field [Finn, in Schoen (ed.), *New Chemical Engineering Separation Techniques,* Interscience, New York, 1962].

The need to limit the maximum temperature rise has resulted in two main types of apparatus, illustrated in Fig. 22-26. The first consists of multicomponent ribbon separation units—apparatus capable of separating small quantities of mixtures which may contain few or many species. In general, such units operate with high voltages, low currents, a large transverse dimension, and a narrow thickness between cooling faces. Numerous units developed for analytic chemistry, generally with filter-paper curtains but sometimes with granular "anticonvectant" packing, are of this type. The second type consists of block separation units—apparatus designed to separate larger quantities of a mixture into two (or at most three) species or fractions. Such units generally use low to moderate voltages and high currents, with cooling by circulation of cold electrolyte through the electrode compartments. Scale-up can readily be accomplished by extending the thickness dimension w.

Both types of units have generally been operated in trace mode; that is, "background" or "elutant" electrolyte is fed to the unit along with the mixture to be separated. A desirable and possible means of

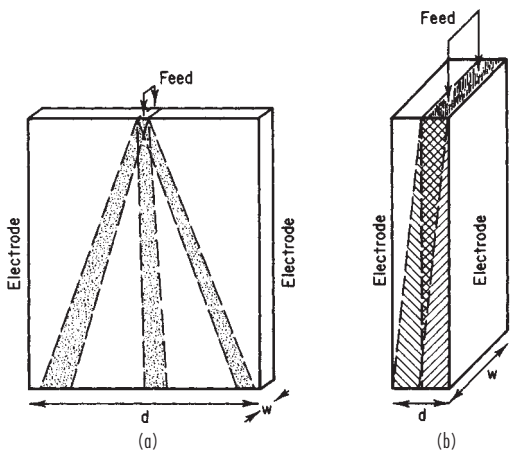


FIG. 22-26 Types of arrangement for zone electrophoresis or electrochromatography. (*a*) Ribbon unit, with $d > w$; cooling at side faces. (*b*) Block unit, with $w > d$; cooling at electrodes.

operation for preparative applications is in bulk mode, in which one separated component follows the other without background electrolyte being present, except that other ions may be required to bracket the separated zones. Overlap regions between components should be recycled, and pure components collected as products.

For block units, the need to stabilize flow has given rise to a number of distinct techniques.

Free flow. Dobry and Finn [*Chem. Eng. Prog.,* **54,** 59 (1958)] used upward flow, stabilized by adding methyl cellulose, polyvinyl alcohol, or dextran to the background solution. Upward flow was also used in the electrode compartments, with cooling efficiency sufficient to keep the main solution within 1°C of entering temperature.

Density gradients to stabilize flow have been employed by Philpot [*Trans. Faraday Soc.,* **36,** 38 (1940)] and Mel [*J. Phys. Chem.,* **31,** 559 (1959)]. Mel's Staflo apparatus [*J. Phys. Chem.,* **31,** 559 (1959)] has liquid flow in the horizontal direction, with layers of increasing density downward produced by sucrose concentrations increasing to 7.5 percent. The solute mixture to be separated is introduced in one such layer. Operation at low electrolyte concentrations, low voltage gradients, and low flow rates presents no cooling problem.

Packed beds. A packed cylindrical electrochromatograph 9 in (23 cm) in diameter and 48 in (1.2 m) high, with operating voltages in the 25- to 100-V range, has been developed by Hybarger, Vermeulen, and coworkers [*Ind. Eng. Chem. Process Des. Dev.,* **10,** 91 (1971)]. The annular bed is separated from inner and outer electrodes by porous ceramic diaphragms. The unit is cooled by rapid circulation of cooled electrolyte between the diaphragms and the electrodes.

An interesting modification of zone electrophoresis resolves mixtures of ampholytes on the basis of **differing isoelectric points** rather than differing mobilities. Such **isoelectric spectra** develop when a pH gradient is established parallel to the electric field. Each species then migrates until it arrives at the region of pH where it possesses no net surface charge. A strong focusing effect is thereby achieved [Kolin, in Glick (ed.), *Methods of Biochemical Analysis,* vol. VI, Interscience, New York, 1958].

Electrofiltration

General Reference: P. Krishnaswamy and P. Klinkowski, "Electrokinetics and Electrofiltration," in *Advances in Solid-Liquid Separation,* H. S. Muralidhara (ed.), Battelle Press, Columbus, OH, 1986.

Process Concept The application of a direct electric field of appropriate polarity when filtering should cause a net charged-particle migration relative to the filter medium (electrophoresis). The same direct electric field can also be used to cause a net fluid flow relative to the pores in a fixed filter cake or filter medium (electroosmosis). The exploitation of one or both of these phenomena form the basis of conventional electrofiltration.

In conventional filtration, often the object is to form a high-solids-content filter cake. At a single-filter surface, a uniform electric field can be exploited in one of two ways. The first method of exploitation occurs when the electric field is of a polarity such that the charged-particle migration occurs toward the filter medium. In this case, the application of the electric field increases the velocity of the solid particles toward the filter surface (electrosedimentation), thereby hastening the clarification of the feed suspension and, at the same time, increasing the compaction of the filter cake collected on the filter surface. In this first case, electroosmotic flow occurs in a direction away from the filter media. The magnitude of the pressure-driven fluid flow toward the filter surface far exceeds the magnitude of the electroosmotic flow away from the surface so that the electroosmotic flow results in only a minor reduction of the rate of production of filtrate. The primary benefits of the applied electric field in this case are increased compaction, and hence increased dewatering, of the filter cake and an increased rate of sedimentation or movement of the particles in bulk suspension toward the filter surface.

The second method of exploitation occurs when the electric field is of a polarity such that the charged-particle migration occurs away from the filter medium. The contribution to the net-particle velocity of the electrophoretically induced flow away from the filter medium is generally orders of magnitude less than the contribution to the net-particle velocity of the flow induced by drag due to the pressure-induced flow of the bulk liquid toward the filter media. (In conventional or cake filtration, the velocity of liquid in dead-end flow toward the filter is almost always sufficient to overcome any electrophoretic migration of particles away from the filter media so that the prevention of the formation of filter cake is not an option. This will not necessarily be the case for cross-flow electrofiltration.) The primary enhancement to filtration caused by the application of an electrical field in this manner is the increase in the filtrate flux due to electroosmotic flow through the filter cake. This electroosmotic flow is especially beneficial during the latter stages of filtration when the final filter-cake thickness has been achieved. At this stage, electroosmosis can be exploited to draw filtrate out from the pore structure of the filter cake. This type of drying of the filter cake is sometimes called **electroosmotic dewatering.**

Commercial Applications Krishnaswamy and Klinkowski, op. cit., describe the Dorr-Oliver EAVF®. The EAVF® combines vacuum filtration with electrophoresis and electroosmosis and has been described as a series of parallel platelike electrode assemblies suspended in a tank containing the slurry to be separated. When using the EAVF®, solids are collected at both electrodes, one collecting a compacted cake simply by electrophoretic attraction and the second collecting a compacted cake though vacuum filtration coupled with electroosmotic dewatering. Upon the completion of a collection cycle, the entire electrode assembly is withdrawn from the slurry bath and the cake is removed. The EAVF® is quoted as being best suited for the dewatering of ultrafine slurries (particle sizes typically less than 10 μm).

Cross-Flow–Electrofiltration

General References: Henry, Lawler, and Kuo, *Am. Inst. Chem. Eng. J.,* **23**(6), 851 (1977). Kuo, Ph.D. dissertation, West Virginia University, 1978.

Process Concept The application of a direct electric field of appropriate polarity when filtering should cause a net charged-particle migration away from the filter medium. This electrophoretic migration will prevent filter-cake formation and the subsequent reduction of filter performance. An additional benefit derived from the imposed electric field is an electroosmotic flux. The presence of this flux in the membrane and in any particulate accumulation may further enhance the filtration rate.

Cross-flow–electrofiltration (CF-EF) is the multifunctional separation process which combines the electrophoretic migration present in electrofiltration with the particle diffusion and radial-migration forces present in cross-flow filtration (CFF) (microfiltration includes cross-flow filtration as one mode of operation in "Membrane Separation Processes" which appears later in this section) in order to reduce further the formation of filter cake. Cross-flow–electrofiltration can even eliminate the formation of filter cake entirely. This process should find application in the filtration of suspensions when there are charged particles as well as a relatively low conductivity in the continuous phase. Low conductivity in the continuous phase is necessary in order to minimize the amount of electrical power necessary to sustain the electric field. Low-ionic-strength aqueous media and nonaqueous suspending media fulfill this requirement.

Cross-flow–electrofiltration has been investigated for both aqueous and nonaqueous suspending media by using both rectangular- and tubular-channel processing configurations (Fig. 22-27). Henry, Lawler, and Kuo (op. cit.), using a rectangular-channel system with a 0.6-μ-pore-size polycarbonate Nuclepore filtration membrane, investigated CF-EF for 2.5-μm kaolin-water and 0.5- to 2-μm oil-in-water emulsion systems. Kuo (op. cit.), using similar equipment, studied 5-μm kaolin-water, ~100-μm Cr_2O_3-water, and ~6-μm Al_2O_3-methanol and/or -butanol systems. For both studies electrical fields of 0 to 60 V/cm were used for aqueous systems, and to 5000 V/cm were used for nonaqueous systems. The studies covered a wide range of processing variables in order to gain a better understanding of CF-EF fundamentals. Lee, Gidaspow, and Wasan [*Ind. Eng. Chem. Fundam.,* **19**(2), 166 (1980)] studied CF-EF by using a porous stainless-steel tube (pore size = 5 μm) as the filtration medium. A platinum wire running down the center of the tube acted as one electrode, while the

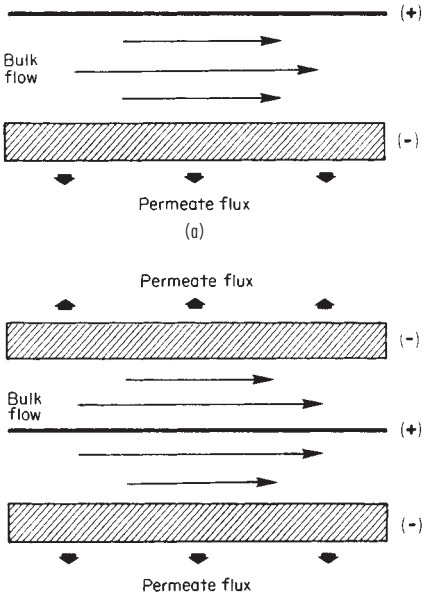


FIG. 22-27 Alternative electrode configurations for cross-flow–electrofiltration.

porous steel tube itself acted as the other electrode. Nonaqueous suspensions of 0.3- to 2-μm Al_2O_3-tetralin and a coal-derived liquid diluted with xylene and tetralin were studied. By operating with applied electric fields (1000 to 10,000 V/cm) above the critical voltage, clear particle-free filtrates were produced. It should be noted that the pore size of the stainless-steel filter medium (5 μm) was greater than the particle size of the suspended Al_2O_3 solids (0.3 to 2 μm). Cross-flow—electrofiltration has also been applied to biological systems. Brors, Kroner, and Deckwer [ECB6: Proc. 6th Eur. Cong. Biotech., 511 (1994)] separated malate dehydrogenase from the cellular debris of Baker's yeast using CF-EF. A two- to fivefold increase in the specific enzyme transport rate was reported when electric field strengths of 20 to 40 V/cm were used.

Theory Cross-flow–electrofiltration can theoretically be treated as if it were cross-flow filtration with superimposed electrical effects. These electrical effects include electroosmosis in the filter medium and cake and electrophoresis of the particles in the slurry. The addition of the applied electric field can, however, result in some qualitative differences in permeate-flux-parameter dependences.

The membrane resistance for CF-EF can be defined by specifying two permeate fluxes as

$$J_{om} = \Delta P / R_{om} \tag{22-29}$$

$$J_m = \Delta P / R_m \tag{22-30}$$

where J_{om} is the flux through the membrane in the absence of an electric field and any other resistance, m/s; J_m is the same flux in the presence of an electric field; and R_{om} is the membrane resistance in the absence of an electric field, (N·s)/m^3. When electroosmotic effects do occur,

$$J_m = J_{om} + K_m E \tag{22-31}$$

where K_m is the electroosmotic coefficient of the membrane, m^2/(V·s); and E is the applied-electric-field strength, V/m. Equations (22-29), (22-30), and (22-31) can be combined and rearranged to give Eq. (22-32), the membrane resistance in the presence of an electric field.

$$R_m = \frac{R_{om}}{1 + \left(\dfrac{K_m E}{J_{om}}\right)} \tag{22-32}$$

Similarly, cake resistance can be represented as

$$R_c = \frac{R_{oc}}{1 + \left(\dfrac{K_c E}{J_{oc}}\right)} \tag{22-33}$$

where J_{oc} is the flux through the cake in the absence of an electric field or any other resistance, R_{oc} is the cake resistance in the absence of an electric field, and K_c is the electroosmotic coefficient of the cake. The cake resistance is not a constant but is dependent upon the cake thickness, which is in turn a function of the transmembrane pressure drop and electrical-field strength.

Particulate systems require the addition of the term $\mu_e E$ in order to account for the electrophoretic migration of the particle. The constant μ_e is the electrophoretic mobility of the particle, m^2/(V·s). For the case of the CF-EF, the film resistance R_f can be represented as

$$R_f = \frac{\Delta P}{k \ln\left(\dfrac{C_s}{C_b}\right) + U_r + \mu_e E} \tag{22-34}$$

The resistances, when incorporated into equations descriptive of cross-flow filtration, yield the general expression for the permeate flux for particulate suspensions in cross-flow-electrofiltration systems.

There are three distinct regimes of operation in CF-EF. These regimes (Fig. 22-28) are defined by the magnitude of the applied electric field with respect to the critical voltage E_c. The critical voltage is defined as the voltage at which the net particle migration velocity toward the filtration medium is zero. At the critical voltage, there is a balance between the electrical-migration and radial-migration velocities away from the filter and the velocity at which the particles are swept toward the filter by bulk flow. There is no diffusive transport at $E = E_c$ (Fig. 22-28*b*) because there is no gradient in the particle concentration normal to the filter surface. At field strengths below the critical voltage (Fig. 22-28*a*), all migration velocities occur in the same direction as in the cross-flow-filtration systems discussed earlier. At values of applied voltage above the critical voltage (Fig. 22-28*c*) qualitative differences are observed. In this case, the electrophoretic-migration velocity away from the filter medium is greater than the velocity caused by bulk flow toward the filtration medium. Particles concentrate away from the filter medium. This implies that particle concentration is lowest next to the filter medium (in actuality, a clear boundary layer has been observed). The influence of fluid shear still improves the transfer of particles down the concentration gradient, but in this case it is toward the filtration medium. When the particles are small and diffusive transport dominates radial migration, increasing the circulation velocity will decrease the permeate flux rate in this regime. When the particles are large and radial migration dominates, the increase in circulation velocity will still improve the filtration rate. These effects are illustrated qualitatively in Fig. 22-29*a*. The solid lines represent systems in which the particle diffusive effect dominates the radial-migration effect, while the dashed lines represent the inverse. Figure 22-29*b* illustrates the increase in filtration rate with increasing electric field strength. For field strengths $E > E_c$, increases in permeate flux rate are due only to electroosmosis in the filtration medium.

One potential difficulty with CF-EF is the electrodeposition of the particles at the electrode away from the filtration medium. This phenomenon, if allowed to persist, will result in performance decay of CF-EF with respect to maintenance of the electric field. Several approaches such as momentary reverses in polarity, protection of the electrode with a porous membrane or filter medium, and/or utilization of a high fluid shear rate can minimize electrodeposition.

Dielectrophoresis

GENERAL REFERENCES: Pohl, in Moore (ed.), *Electrostatics and Its Applications,* Wiley, New York, 1973, chap. 14 and chap. 15 (with Crane). Pohl, in Catsimpoolas (ed.), *Methods of Cell Separation,* vol. I, Plenum Press, New York, 1977, chap. 3. Pohl, *Dielectrophoresis: The Behavior of Matter in Nonuniform Electric Fields,* Cambridge, New York, 1978.

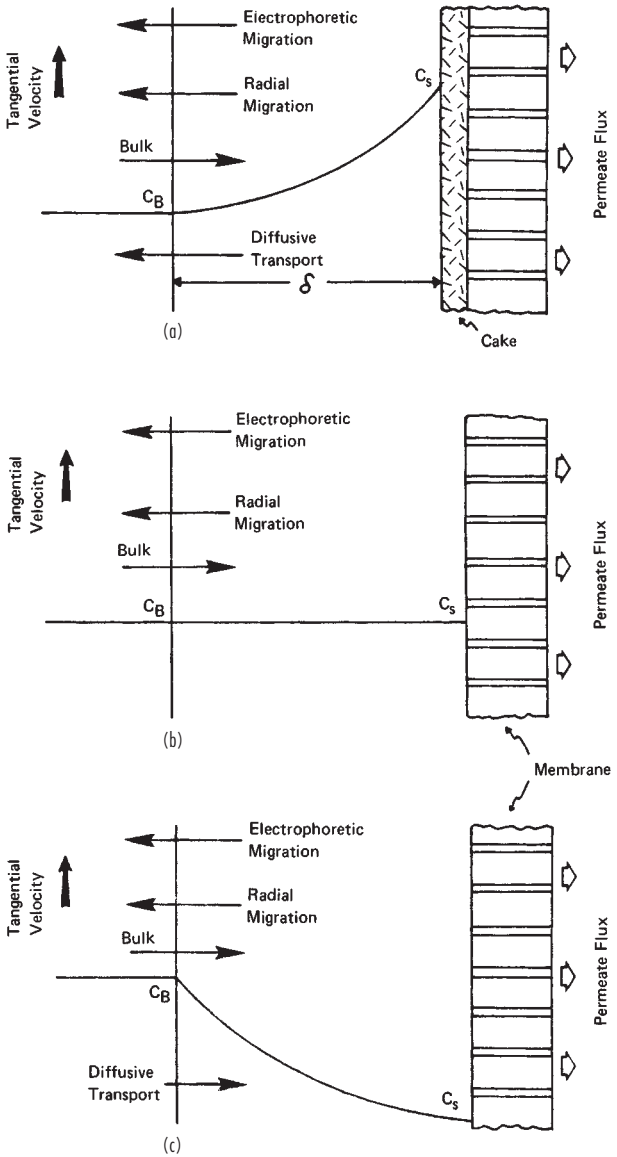


FIG. 22-28 Regimes of operation of cross-flow–electrofiltration: (*a*) voltage less than critical, (*b*) voltage equal to the critical voltage, (*c*) voltage greater than critical.

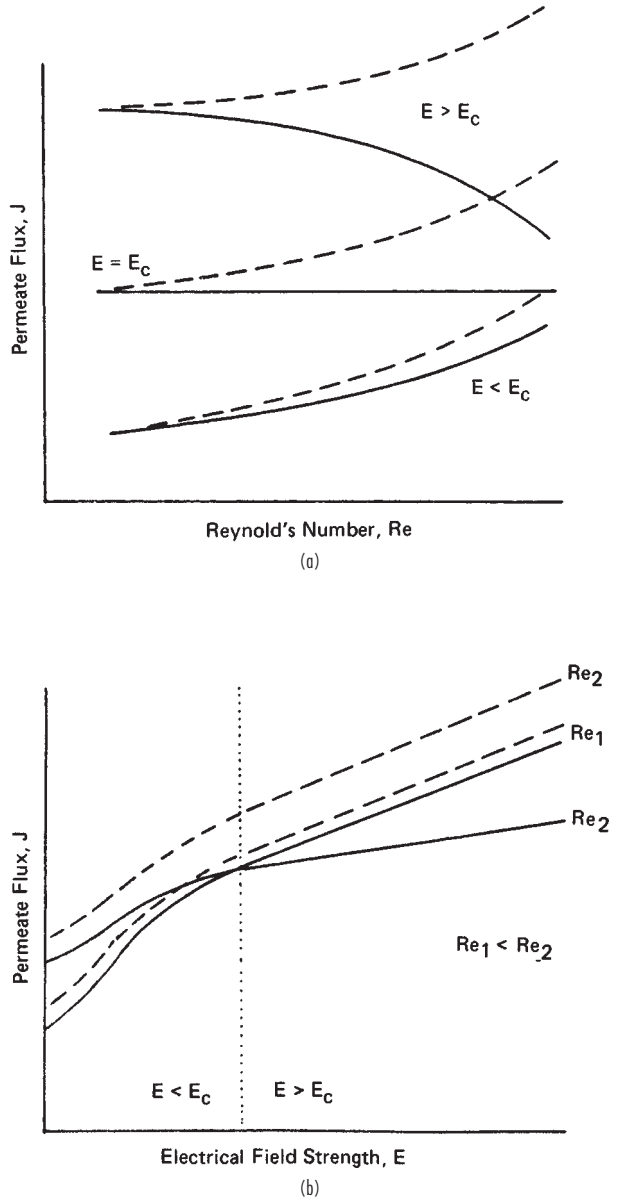


FIG. 22-29 Qualitative effects of Reynolds number and applied-electric-field strength on the filtration permeate flux *J*. Dashed lines indicate large particles (radial migration dominates); solid lines, small particles (particle diffusion dominates).

Introduction Dielectrophoresis (DEP) is defined as the motion of neutral, polarizable matter produced by a nonuniform electric (ac or dc) field. DEP should be distinguished from electrophoresis, which is the motion of charged particles in a uniform electric field (Fig. 22-30).

The DEP of numerous particle types has been studied, and many applications have been developed. Particles studied have included aerosols, glass, minerals, polymer molecules, living cells, and cell organelles. Applications developed include filtration, orientation, sorting or separation, characterization, and levitation and materials handling. Effects of DEP are easily exhibited, especially by large particles, and can be applied in many useful and desirable ways. DEP effects can, however, be observed on particles ranging in size even down to the molecular level in special cases. Since thermal effects tend to disrupt DEP with molecular-sized particles, they can be controlled only under special conditions such as in molecular beams.

Principle The principle of particle and cell separation, control, or characterization by the action of DEP lies in the fact that a net force can arise upon even neutral particles situated in a nonuniform electric field. The force can be thought of as rising from the imaginary two-step process of (1) induction or alignment of an electric dipole in a particle placed in an electric field followed by (2) unequal forces on the ends of that dipole. This arises from the fact that the force of an electric field upon a charge is equal to the amount of the charge and to the *local* field strength at that charge. Since the two (equal) charges of the (induced or oriented) dipole of the particle lie in unequal field strengths of the diverging field, a net force arises. If the particle is suspended in a fluid, then the polarizability of that medium enters, too. If, for example, the particle is more polarizable than the fluid, then the

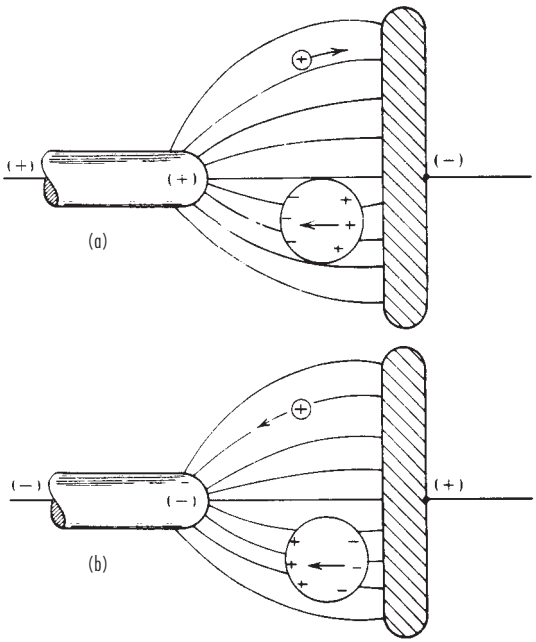


FIG. 22-30 Comparison of behaviors of neutral-charged bodies in an alternating nonuniform electric field. (*a*) Positively charged body moves toward negative electrode. Neutral body is polarized, then is attracted toward point where field is strongest. Since the two charge regions on the neutral body are equal in amount of charge but the force is proportional to the local field, a net force toward the region of more intense field results. (*b*) Positively charged body moves toward the negative electrode. Again, the neutral body is polarized, but it does not reverse direction although the field is reversed. It still moves toward the region of highest field intensity.

net force is such as to impel the particle to regions of greater field strength. Note that this statement implies that the effect is independent of the absolute sign of the field direction. This is found to be the case. Even rapidly alternating (ac) fields can be used to provide *unidirectional* motion of the suspended particles.

Formal Theory A small neutral particle at equilibrium in a static electric field experiences a net force due to DEP that can be written as $\mathbf{F} = (\mathbf{p} \cdot \nabla)\mathbf{E}$, where $\mathbf{p}$ is the dipole moment vector and $\mathbf{E}$ is the external electric field. If the particle is a simple dielectric and is isotropically, linearly, and homogeneously polarizable, then the dipole moment can be written as $\mathbf{p} = \alpha v\mathbf{E}$, where α is the (scalar) polarizability, v is the volume of the particle, and $\mathbf{E}$ is the external field. The force can then be written as:

$$\mathbf{F} = \alpha v(\mathbf{E} \cdot \nabla)\mathbf{E} = \tfrac{1}{2}\alpha v\nabla|\mathbf{E}|^2 \qquad (22\text{-}35)$$

This force equation can now be used to find the force in model systems such as that of an ideal dielectric sphere (relative dielectric constant K_2) in an ideal perfectly insulating dielectric fluid (relative dielectric constant K_1). The force can now be written as

$$\mathbf{F} = 2\pi a^3\varepsilon_0 K_1\left(\frac{K_2 - K_1}{K_2 + 2K_1}\right)\nabla|\mathbf{E}|^2 \qquad (22\text{-}36)$$

(ideal dielectric sphere in ideal fluid).

Heuristic Explanation As we can see from Fig. 22-31, the DEP response of *real* (as opposed to perfect insulator) particles with frequency can be rather complicated. We use a simple illustration to account for such a response. The force is proportional to the difference between the dielectric permittivities of the particle and the surrounding medium. Since a part of the polarization in real systems is thermally activated, there is a delayed response which shows as a phase lag between $\mathbf{D}$, the dielectric displacement, and $\mathbf{E}$, the electric-field intensity. To take this into account we may replace the simple (absolute) dielectric constant ε by the complex (absolute) dielectric

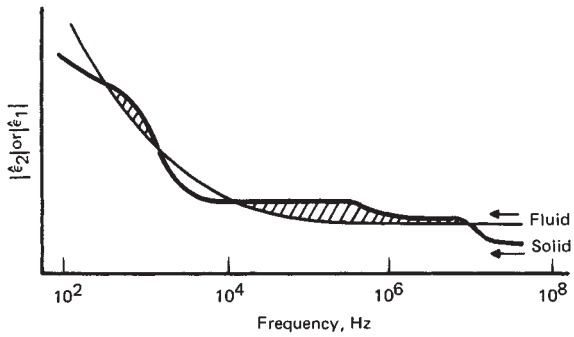


FIG. 22-31 A heuristic explanation of the dielectrophoretic-collection-rate (DCR)-frequency spectrum. The curves for the absolute values of the complex permittivities of the fluid medium and of the suspended particles are shown lying nearly, but not entirely, coincident over the frequency range of the applied electric field. When the permittivity (dielectric constant) of the particles exceeds that of the suspending medium, the collection, or "positive dielectrophoresis," occurs. In the frequency ranges in which the permittivity of the particles is less than that of the suspending medium no collection at the regions of higher field intensity occurs. Instead there is "negative dielectrophoresis," i.e., movement of the particles into regions of lower field intensity.

constant $\hat{\varepsilon} = \varepsilon' - i\varepsilon'' = \varepsilon' - i\sigma/w$, where ω is the angular frequency of the applied field. For treating spherical objects, for example, the replacement

$$F \propto \frac{\varepsilon_1(\varepsilon_2 - \varepsilon_1)}{\varepsilon_2 + 2\varepsilon_1} \rightarrow \mathrm{Re}\left\{\frac{\hat{\varepsilon}^\circ(\hat{\varepsilon}_2 - \hat{\varepsilon}_1)}{\hat{\varepsilon}_2 + 2\hat{\varepsilon}_1}\right\} \qquad (22\text{-}37)$$

can be made, where $\hat{\varepsilon}^\circ$ is the complex conjugate of $\hat{\varepsilon}$.

With this force expression for real dielectrics, we can now explain the complicated DEP response with the help of Fig. 22-31.

A particle, such as a living cell, can be imagined as having a number of different frequency-dependent polarization mechanisms contributing to the total effective polarization of the particle $|\hat{\varepsilon}_2|$. The heavy curve in Fig. 22-31 shows that the various mechanisms in the particle drop out stepwise as the frequency increases. The light curve in Fig. 22-31 shows the polarization for a simple homogeneous liquid that forms the surrounding medium. This curve is a smooth function which becomes constant at high frequency. As the curves cross each other (and hence $|\varepsilon_2| = |\varepsilon_1|$), various responses occur. The particle can thus be attracted to the strongest field region, be repelled from that region, or experience no force depending on the frequency.

Limitations It is desirable to have an estimate for the smallest particle size that can be effectively influenced by DEP. To do this, we consider the force on a particle due to DEP and also due to the osmotic pressure. This latter diffusional force will randomize the particles and tend to destroy the control by DEP. Figure 22-32 shows a plot of these two forces, calculated for practical and representative conditions, as a function of particle radius. As we can see, the smallest particles that can be effectively handled by DEP appear to be in range of 0.01 to 0.1 μm (100 to 1000 Å).

Another limitation to be considered is the volume that the DEP force can affect. This factor can be controlled by the design of electrodes. As an example, consider electrodes of cylindrical geometry. A practical example of this would be a cylinder with a wire running down the middle to provide the two electrodes. The field in such a system is proportional to $1/r$. The DEP force is then $\mathbf{F}_{\mathrm{DEP}} \propto \nabla|E^2| \propto 1/r^3$, so that any differences in particle polarization might well be masked merely by positional differences in the force. At the outer cylinder the DEP force may even be too small to affect the particles appreciably. The most desirable electrode shape is one in which the force is independent of position within the nonuniform field. This "isomotive" electrode system is shown in Fig. 22-33.

Applications of Dielectrophoresis Over the past 20 years the use of DEP has grown rapidly to a point at which it is in use for biological, colloidal, and mineral materials studies and handling. The effects of nonuniform electric fields are used for handling particulate matter far more often than is usually recognized. This includes the

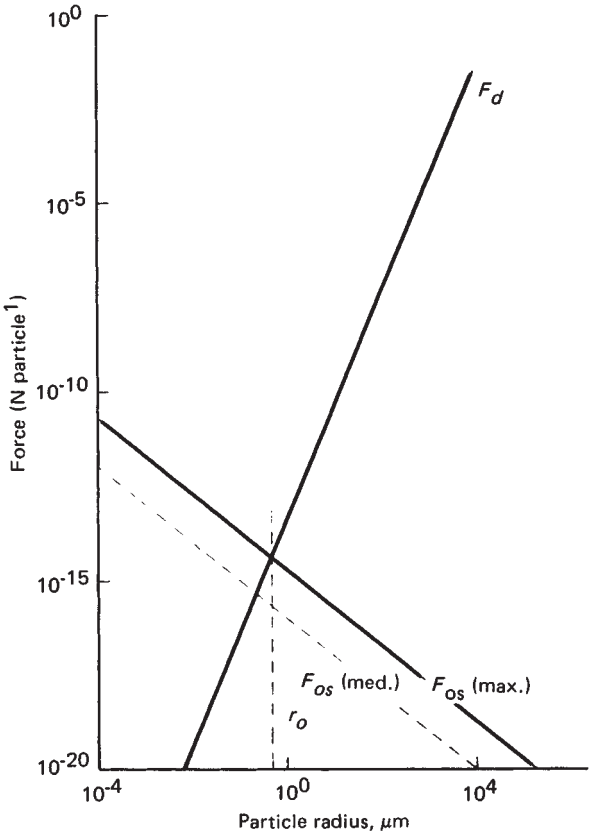


FIG. 22-32 Comparison of the dielectrophoretic (F_d) and osmotic (F_{os}) forces as functions of the particle size.

removal of particulate matter by "electrofiltration," the sorting of mixtures, or its converse, the act of mixing, as well as the coalescence of suspensions. In addition to these effects involving the translational motions of particles, some systems apply the orientational or torsional forces available in nonuniform fields. One well-known example of the latter is the placing of "tip-up" grit on emery papers commercially. Xerography and many other imaging processes are examples of multibillion-dollar industries which depend upon DEP for their success.

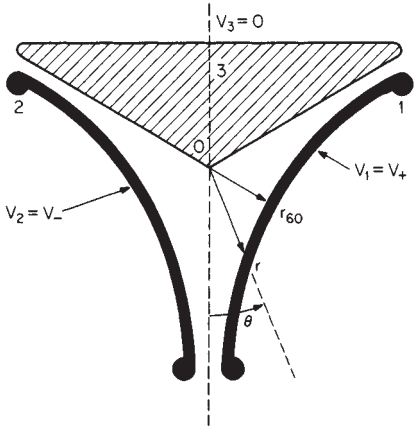


FIG. 22-33 A practical isomotive field geometry, showing r_{60}, the critical radius characterizing the isomotive electrodes. Electrode 3 is at ground potential, while electrodes 1 and 2 are at $V_1 = V_+$ and $V_2 = V_- = -V_+$ respectively. The inner faces of electrodes 1 and 2 follow $r = r_0\,[\sin(3\theta/2)]^{-2/3}$, while electrode 3 forms an angle of 120° about the midline.

A clear distinction between **electrophoresis** (field action on an object carrying excess free charges) and **dielectrophoresis** (field gradient action on neutral objects) must be borne in mind at all times.

A dielectrofilter [Lin and Benguigui, *Sep. Purif. Methods*, **10**(1), 53 (1981); Sisson et al., *Sep. Sci. Technol.*, **30**(7–9), 1421 (1995)] is a device which uses the action of an electric field to aid the filtration and removal of particulates from fluid media. A dielectrofilter can have a very obvious advantage over a mechanical filter in that it can remove particles which are much *smaller* than the flow channels in the filter. In contrast, the ideal mechanical filter must have all its passages smaller than the particles to be removed. The resultant flow resistance can be use-restrictive and energy-consuming unless a phenomenon such as dielectrofiltration is used.

Dielectrofiltration can (and often does) employ both electrophoresis and dielectrophoresis in its application. The precise physical process which dominates depends on a number of physical parameters of the system. Factors such as field intensity and frequency and the electrical conductivity and dielectric constants of the materials present determine this. Although these factors need constant attention for optimum operation of the dielectrofilter, this additional complication is often more than compensated for by the advantages of dielectrofiltration such as greater throughput and lesser sensitivity to viscosity problems, etc. To operate the dielectrofilter in the dominantly electrophoretic mode requires that excess free charges of one sign or the other reside on the particulate matter. The necessary charges can be those naturally present, as upon a charged sol; or they may need to be artificially implanted such as by passing the particles through a corona discharge. Dielectrofiltration by the corona-charging, electrophoresis-dominated Cottrell technique is now widely used.

To operate the dielectrofilter (dominantly dielectrophoretic mode), on the other hand, one must avoid the presence of free charge on the particles. If the particles can become charged during the operation, a cycle of alternate charging and discharging in which the particles dash to and from the electrodes can occur. This is most likely to occur if static or very low frequency fields are used. For this reason, corona and like effects may be troublesome and need often to be minimized. To be sure, the DEP force is proportional to the field applied [actually to $\nabla(E)^2$], but fields which are too intense can produce such troublesome charge injection. A compromise for optimal operation is necessary between having $\nabla(E)^2$ so low that DEP forces are insufficient for dependable operation, on the one hand, and having **E** so high that troublesome discharges (e.g., coronalike) interfere with dependable operation of the dielectrofilter. In insulative media such as air or hydrocarbon liquids, for example, one might prefer to operate with fields in the range of, say, 10 to 10,000 V/cm. In more conductive media such as water, acetone, or alcohol, for example, one would usually prefer rather lower fields in the range of 0.01 to 100 V/cm. The higher field ranges cited might become unsuitable if conductive sharp asperities are present.

Another factor of importance in dielectrofiltration is the need to have the DEP effect firmly operative upon *all* portions of the fluid passing through. Oversight of this factor is a most common cause of incomplete dielectrofiltration. Good dielectrofilter design will emphasize this crucial point. To put this numerically, let us consider the essential field factor for DEP force, namely $\nabla(\mathbf{E}_0)^2$. Near sharp points, e.g., **E,** the electric field varies with the radial distance r as $E \propto r^{-2}$; hence our DEP force factor will vary as $\nabla(E)^2 \propto r^{-5}$. In the neighborhood of sharp "line" sources such as at the edge of electrode plates, $E \propto r^{-1}$, hence, $\nabla(E)^2 \propto r^{-3}$. If, for instance, the distance is varied by a factor of 4 from the effective field source in these cases, the DEP force can be expected to weaken by a factor of 1024 or 64 respectively for the point source and the line source. The matter is even more keenly at issue when field-warping dielectrics (defined later) are used to effect maximal filtration. In this case the field-warping material is made to produce dipole fields as induced by the applied electric field. If we ask how the crucial factor, $\nabla(E)^2$, varies with distance away from such a dipole, we find that since the field E_d about a dipole varies

approximately as r^{-3}, then $\nabla(E)^2$ can be expected to vary as r^{-7}. It then becomes critically important that the particles to be removed from the passing fluid do, indeed, pass very close to the surface of the field-warping material, or it will not be effectively handled. Clearly, it would be difficult to maintain successfully uniform dielectrofiltration treatment of fluid passing through such wildly variant regions. The problems can be minimized by ensuring that all the elements of the passing fluid go closely by such field sources in the dielectrofilter. In practice this is done by constructing the dielectrofilter from an assembly of highly comminuted electrodes or else by a set of relatively simple and widely spaced metallic electrodes between which is set an assembly of more or less finely divided solid dielectric material having a complex permittivity different from that of the fluid to be treated. The solid dielectric (fibers, spheres, chunks) serves to produce field nonuniformities or **field warpings** to which the particles to be filtered are to be attracted. In treating fluids of low dielectric constant such as air or hydrocarbon fluids, one sees field-warping materials such as sintered ceramic balls, glass-wool matting, open-mesh polyurethane foam, alumina, chunks, or $BaTiO_3$ particles.

An example of a practical dielectrofilter which uses both of the features described, namely, sharp electrodes *and* dielectric field-warping filler materials, is that described in Fig. 22-34 [H. J. Hall and R. F. Brown, *Lubric. Eng.*, **22,** 488 (1966)]. It is intended for use with hydraulic fluids, fuel oils, lubricating oils, transformer oils, lubricants, and various refinery streams. Performance data are cited in Fig. 22-35. It must be remarked that in the opinion of Hall and Brown the action of the dielectrofilter was "electrostatic" and due to free charge on the particles dispersed in the liquids. It is the present authors' opinion, however, that both electrophoresis and dielectrophoresis are operative here but that the dominant mechanism is that of DEP, in which neutral particles are polarized and attracted to the regions of highest field intensity.

A second commercial example of dielectric filtration is the Gulftronic® separator [G. R. Fritsche, *Oil & Gas J.*, **75,** 73 (1977)] which was commercialized in the late 1970s by Gulf Science and Technology Company. Instead of using needle-point electrodes as shown in Fig. 22-34, the Gulftronic® separator relied on the use of a bed of glass beads to produce the field nonuniformities required for dielectric filtration. Either ac or dc electric fields could be used in this separator. The Gulftronic® separator has been used primarily to remove catalyst fines from FCC decant oils and has been reported to exhibit removal efficiencies in excess of 80 percent for this fine-particle separation problem.

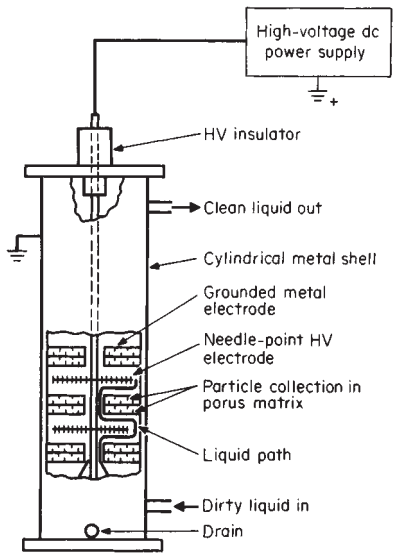


FIG. 22-34 Diagram illustrating the function of an electrostatic liquid cleaner.

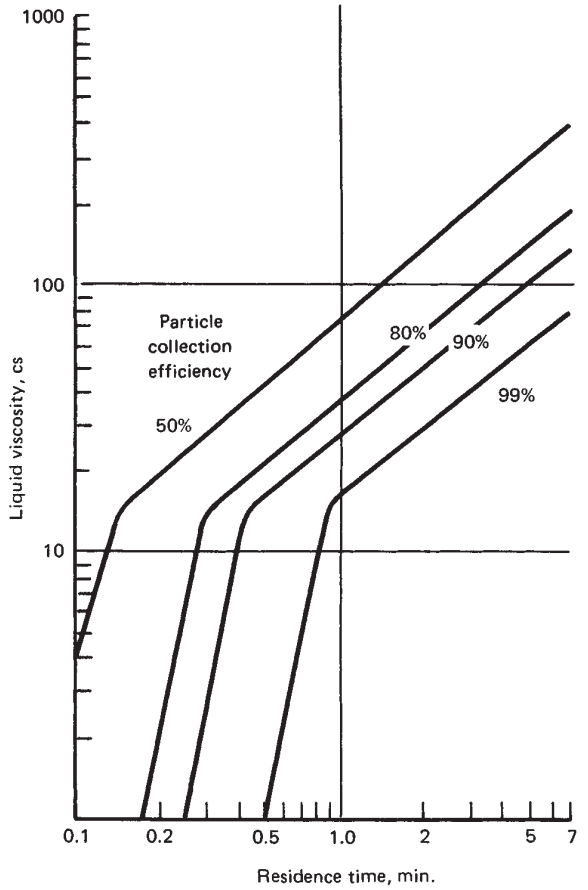


FIG. 22-35 Performance data for a typical high-efficiency electrostatic liquid cleaner.

Another example of the commercial use of DEP is in polymer clarification [A. N. Wennerberg, U.S. Patent 2,914,453, 1959; assignor to Standard Oil Co. (Indiana)]. Here, either ac or dc potentials were used while passing suspensions to be clarified through regions with an area-to-electrode-area ratio of 10:1 or 100:1 and with fields in the order of 10 kV/cm. Field warping by the presence of various solid dielectrics was observed to enhance filtration considerably, as expected for DEP. The filtration of molten or dissolved polymers to free them of objectionable quantities of catalyst residues, for example, was more effective if a solid dielectric material such as Attapulgus clay, silica gel, fuller's earth, alumina, or bauxite was present in the region between the electrodes. The effectiveness of percolation through such absorptive solids for removing color bodies is remarkably enhanced by the presence of an applied field. A given amount of clay is reported to remove from 4 to 10 times as much color as would be removed in the absence of DEP. Similar results are reported by Lin et al. [Lin, Yaniv, and Zimmels, *Proc. XIIIth Int. Miner. Process. Congr.*, Wrocław, Poland, 83–105 (1979)].

The instances cited were examples of the use of DEP to filter liquids. We now turn to the use of DEP to aid in dielectrofiltration of gases. Fielding et al. observe that the effectiveness of high-quality fiberglass air filters is dramatically improved by a factor of 10 or more by incorporating DEP in the operation. Extremely little current or power is required, and no detectable amounts of ozone or corona need result. The DEP force, once it has gathered the particles, continues to act on the particles already sitting on the filter medium, thereby improving adhesion and minimizing blowoff.

The degree by which the DEP increases the effectiveness of gas fil-

tration, or the dielectrophoretic augmentation factor (DAF), is definable. It is the ratio of the volumes of aerosol-laden gas which can be cleaned effectively by the filter with and without the voltage applied. For example, the application of 11 kV/cm gave a DAF of 30 for 1.0-μm-diameter dioctyl phthalate particles in air, implying that the penetration of the glass filter is reduced thirtyfold by the application of a field of 1100 kV/m. Similar results were obtained by using "standard" fly ash supplied by the Air Pollution Control Office of the U.S. Environmental Protection Agency. The data obtained for several aerosols tested are shown in Table 22-13 and in Fig. 22-36. The relation $DAF = kV^2/v$ is observed to hold approximately for each aerosol. Here, the DEP augmentation factor DAF is observed to depend upon a constant K, a characteristic of the material, upon the square of the applied voltage, and upon the inverse of the volume flow rate v through the filter.

It is worth noting that in the case of the air filter described DEP serves as an augmenting rather than as an exclusive mechanism for the removal of particulate material. It is a unique feature of the dielectrophoretic gas filter that the DEP force is maximal when the particulates are at or on the fiber surface. This causes the deposits to be strongly retained by this particular filtration mechanism. It thus contrasts importantly with other types of gas filter in which the filtration mechanism no longer acts after the capture of the particle. In particular, in the case of the older electrostatic mechanisms involving only coulombic attraction, a simple charge alternation on the particle, such as caused by normal conduction, often evokes disruption of the filter operation because of particle repulsion from the contacting electrode. On the other hand, ordinary mechanical filtration depends upon the action of adventitious particle trapping or upon van der Waals forces, etc., to hold the particles. The high efficiency possible with electrofilters suggests their wider use.

TABLE 22-13 Dielectrophoretic Augmentation of Filtration of a Liquid Aerosol*

Air speed, cm/s	DAF at 2 kV	3.5 kV	5 kV	7 kV
0.3-μm-diameter dioctyl phthalate aerosol				
3	8	19	95	330
6	3	13	39	120
9	3	11	28	100
15	2	6	13	42
20	2	5	9	27
28	2	4	6	14
39	2	3	4	9
50	1	2	3	6
1.0-μm-diameter dioctyl phthalate aerosol				
3	30	110	300	1100
6	6	3	95	360
9	4	18	50	170
15	3	10	20	50
20	2	6	13	35
28	2	4	8	18
39	2	3	5	11
50	1	2	3	7
Fly-ash aerosol				
6	10	30	80	
10	8	30	80	
14	5	20	40	
20	4	10	30	70
35	3	7	10	20
45	1	2	6	
53	1	2	7	10

*Experimentally measured dielectrophoretic augmentation factor DAF as a function of air speed and applied voltage for a glass-fiber filter (HP-100, Farr Co.). Cf. Fielding, Thompson, Bogardus, and Clark, *Dielectrophoretic Filtration of Solid and Liquid Aerosol Particulates,* Prepr. 75-32.2, 68th ann. meet., Air Pollut. Control Assoc., Boston, June 1975.

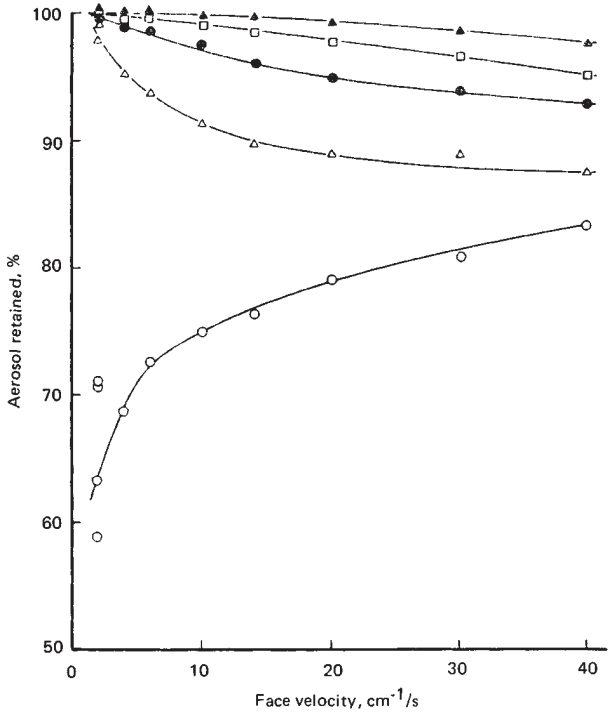


FIG. 22-36 Efficiency of an electrofilter as a function of gas flow rate at 5 different voltages. Experimental materials: 1-μm aerosol of dioctyl phthalate; glass-fiber filter. Symbols: ○, no voltage applied; Δ, 2 kV; ●, 3.5 kV; □, 5 kV; ▲, 7 kV. (*After Fielting et al.,* Dielectrophoretic Filtration of Solid and Liquid Aerosol Particulates, *Prepr. 75-32.2, 68th ann. meet., Air Pollut. Control Assoc., Boston, June 1975.*)

SURFACE-BASED SOLID-LIQUID SEPARATIONS INVOLVING A SECOND LIQUID PHASE

General References: Fuerstenau, "Fine Particle Flotation," in Somasundaran (ed.), *Fine Particles Processing,* vol. 1, American Institute of Mining, Metallurgical, and Petroleum Engineers, New York, 1980. Henry, Prudich, and Lau, *Colloids Surf.,* **1,** 335 (1980). Henry, Prudich, and Vaidyanathan, *Sep. Purif. Methods,* **8**(2), 31 (1979). Jacques, Hovarongkura, and Henry, *Am. Inst. Chem. Eng. J.,* **25**(1), 160 (1979). Stratton-Crawley, "Oil Flotation: Two Liquid Flotation Techniques," in Somasundaran and Arbiter (eds.), *Beneficiation of Mineral Fines,* American Institute of Mining, Metallurgical, and Petroleum Engineers, New York, 1979.

Process Concept Three potential surface-based regimes of separation exist when a second, immiscible liquid phase is added to another, solids-containing liquid in order to effect the removal of solids. These regimes (Fig. 22-37) are:

1. Distribution of the solids into the bulk second liquid phase
2. Collection of the solids at the liquid-liquid interface
3. Bridging or clumping of the solids by the added fluid in order to form an agglomerate followed by settling or filtration

These separation techniques should find particular application in systems containing fine particles. The surface chemical differences involved among these separation regimes are only a matter of degree; i.e., all three regimes require the wetting of the solid by the second liquid phase. The addition of a surface-active agent is sometimes needed in order to achieve the required solids wettability. In spite of this similarity, applied processing (equipment configuration, operating conditions, etc.) can vary widely. Collection at the interface would normally be treated as a flotation process (see also Sec. 22: "Adsorptive-Bubble Separation Methods"; and Sec. 19: "Flotation"), distribu-

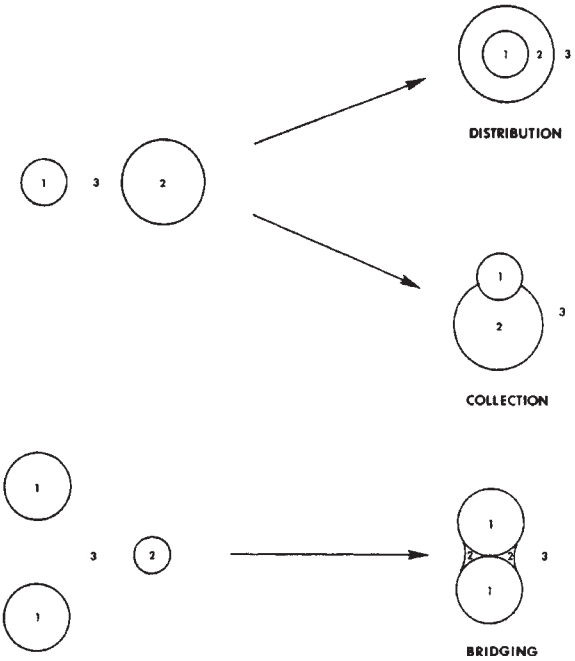


FIG. 22-37 Regimes of separation in a liquid-solid-liquid system. Phase 1 = particle; phase 2 = liquid (dispersed); phase 3 = liquid (continuous).

tion to the bulk liquid as a liquid-liquid extraction analog, and particle bridging as a settling (sedimentation) or filtration process.

Even though surface-property-based liquid-solid-liquid separation techniques have yet to be widely used in significant industrial applications, several studies which demonstrate their effectiveness have appeared in literature.

Albertsson (*Partition of Cell Particles and Macromolecules,* 3d ed., Wiley, New York, 1986) has extensively used particle distribution to fractionate mixtures of biological products. In order to demonstrate the versatility of particle distribution, he has cited the example shown in Table 22-14. The feed mixture consisted of polystyrene particles, red blood cells, starch, and cellulose. Liquid-liquid particle distribution has also been studied by using mineral-matter particles (average diameter = 5.5 μm) extracted from a coal liquid as the solid in a xylene-water system [Prudich and Henry, *Am. Inst. Chem. Eng. J.*, **24**(5), 788 (1978)]. By using surface-active agents in order to enhance the water wettability of the solid particles, recoveries of better than 95 percent of the particles to the water phase were observed. All particles remained in the xylene when no surfactant was added.

Particle collection at a liquid-liquid interface is a particularly favorable separation process when applied to fine-particle systems. Advantages of this type of processing include:

- Decreased liquid-liquid interfacial tension (when compared with a gas-liquid system) results in higher liquid-liquid interfacial areas, which favor solid-particle droplet collisions.
- Liquid-solid interactions due to long-range intermolecular forces are much larger than are gas-solid interactions. This means that it is easier to collect fine particles at a liquid-liquid interface than at a gas-liquid interface.
- The increased momentum of liquid droplets (when compared with gas) should favor solid-particle collection.

Fuerstenau [Lai and Fuerstenau, *Trans. Am. Inst. Min. Metall. Pet. Eng.*, **241,** 549 (1968); Raghavan and Fuerstenau, *Am. Inst. Chem. Eng.* Symp. Ser., **71**(150), 59 (1975)] has studied this process with respect to the removal of alumina particles (0.1 μm) and hematite particles (0.2 μm) from an aqueous solution by using isooctane. The use of isooctane as the collecting phase for the hematite particles resulted in an increase in particle recovery of about 50 percent over that measured when air was used as the collecting phase under the same conditions. The effect of the wettability of the solid particles (as measured by the three-phase contact angle) on the recovery of hematite in the water-isooctane system is shown in Fig. 22-38. This behavior is typical of particle collection. Particle collection at an oil-water interface has also been studied with respect to particle removal from a coal liquid. Particle removals averaging about 80 percent have been observed when water is used as the collecting phase (Lau, master's thesis, West Virginia University, 1979). Surfactant addition was necessary in order to control the wettability of the solids.

Particle bridging has been chiefly investigated with respect to spherical agglomeration. Spherical agglomeration involves the collecting or transferring of the fine particles from suspension in a liquid phase into spherical aggregates held together by a second liquid phase. The aggregates are then removed from the slurry by filtration or settling. Like the other liquid-solid-liquid separation techniques, the solid must be wet by the second liquid phase. The spherical agglomeration process has resulted in the development of a pilot unit called the Shell Pelletizing Separator [Zuiderweg and Van Lookeren Campagne, *Chem. Eng.* (*London*), **220,** CE223 (1968)]. A detailed discussion of spherical agglomeration can be found in Sec. 20: "Size Enlargement."

The ability to determine in advance which of the separation regimes is most advantageous for a given liquid-solid-liquid system would be desirable. No set of criteria with which to make this determination presently exists. Work has been done with respect to the identification of system parameters which make these processes technically feasible. The results of these studies can be used to guide the selection of the second liquid phase as well as to suggest approximate operating conditions (dispersed-liquid droplet size, degree and type of mixing, surface-active-chemical addition, etc.).

TABLE 22-14 Separations of Particles between Two Phases

System	Top phase	Bottom phase
Polyethylene glycol / salt	Polystyrene	All others
PEG / Dextran; 20,000 MW	Algae	All others
PEG / Dextran; 200,000 MW	Red cells	All others
Methyl cellulose / Dextran	Cellulose particles	Starch

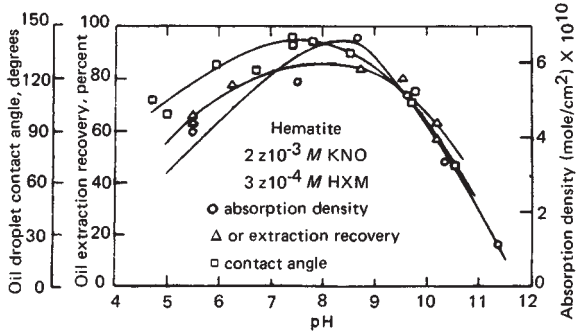


FIG. 22-38 The variation of adsorption density, oil-droplet contact angle, and oil-extraction recovery of hematite as a function of pH. To convert gram-moles per square centimeter to pound-moles per square foot, multiply by 2.048. [*From Raghavan and Fuerstenau,* Am. Inst. Chem. Eng. Symp. Ser., ***71****(150), 59 (1975).*]

Theory Theoretical analyses of spherical particles suspended in a planar liquid-liquid interface have appeared in literature for some time, the most commonly presented forms being those of a free energy and/or force balance made in the absence of all external body forces. These analyses are generally used to define the boundary criteria for the shift between the collection and distribution regimes, the bridging regime not being considered. This type of analysis shows that for a spherical particle possessing a three-phase contact angle between 0 and 180°, as measured through the receiving or collecting phase, collection at the interface is favored over residence in either bulk phase. These equations are summarized, using a derivation of Young's equation, as

$$\frac{\gamma_{s2} - \gamma_{s1}}{\gamma_{12}} > 1 \text{ particles wet to phase 1} \qquad (22\text{-}38)$$

$$\frac{\gamma_{s2} - \gamma_{s1}}{\gamma_{12}} < -1 \text{ particles wet to phase 2} \qquad (22\text{-}39)$$

$$\left|\frac{\gamma_{s2} - \gamma_{s1}}{\gamma_{12}}\right| \le 1 \text{ particle at interface} \qquad (22\text{-}40)$$

where γ_{ij} is the surface tension between phases i and j, N/m (dyn/cm); s indicates the solid phase; and subscripts 1 and 2 indicate the two liquid phases.

Several additional studies [Winitzer, *Sep. Sci.,* **8**(1), 45 (1973); ibid., **8**(6), 647 (1973); Maru, Wasan, and Kintner, *Chem. Eng. Sci.,* **26,** 1615 (1971); and Rapacchietta and Neumann, *J. Colloid Interface Sci.,* **59**(3), 555 (1977)] which include body forces such as gravitational acceleration and buoyancy have been made. A typical example of a force balance describing such a system (Fig. 22-39) is summarized in Eq. (22-41).

$$[(\gamma_{s1} - \gamma_{s2}) \cos \delta + \gamma_{12} \cos B]L = g[V_{\text{total}}\rho_s - V_1\rho_1 - V_2\rho_2] \qquad (22\text{-}41)$$

where V_1 is the volume of the particle in fluid phase 1, V_2 is the volume in fluid phase 2, L is the particle circumference at the interface between the two liquid phases, ρ_i is the density of phase i, and g is the gravitational constant. The left-hand side of the equation represents the surface forces acting on the solid particle, while the right-hand side includes the gravitational and buoyancy forces. This example illustrates the fact that body forces can have a significant effect on system behavior. The solid-particle size as well as the densities of the solid and both liquid phases are introduced as important system parameters.

A study has also been performed for particle distribution for cases in which the radii of curvature of the solid and the liquid-liquid interface are of the same order of magnitude [Jacques, Hovarongkura, and Henry, *Am. Inst. Chem. Eng. J.,* **25**(1), 160 (1979)]. Differences between the final and initial surface free energies are used to analyze this system. Body forces are neglected. Results (Fig. 22-40) demonstrate that n, the ratio of the particle radius to the liquid-liquid-interface radius, is an important system parameter. Distribution of the particle from one phase to the other is favored over continued residence in the original phase when the free-energy difference is negative. For a solid particle of a given size, these results show that as the second-phase droplet size decreases, the contact angle required in order to effect distribution decreases (the required wettability of the solid by the second phase increases). The case of particle collection at a curved liquid-liquid interface has also been studied in a similar manner [Smith and Van de Ven, *Colloids Surf.,* **2,** 387 (1981)]. This study shows that collection is preferred over distribution for any n in systems without external body forces when the contact angle lies between 0 and 180°.

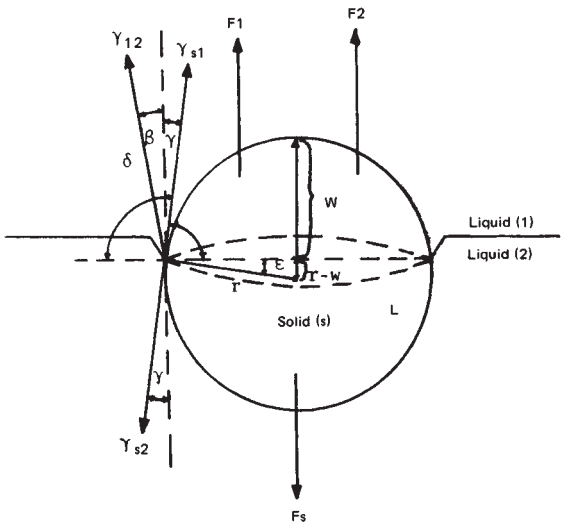


FIG. 22-39 Solid sphere suspended at the liquid-liquid interface. F_1 and F_2 are buoyancy forces; F_s is gravity. [*From Winitzer,* Sep. Sci., *8(1), 45 (1973).*]

While thermodynamic-stability studies can be valuable in evaluating the technical feasibility of a process, they are presently inadequate in determining which separation regime will dominate a particular liquid-solid-liquid system. These analyses ignore important processing phenomena such as the mechanism of encounter of the dispersed-phase liquid with the solid particles, the strength of particle attachment, and the mixing-energy input necessary to effect the separation. No models of good predictive value which take all these variables into account have yet been offered. Until the effects of these and other system variables can be adequately understood, quantified, and combined into such a predictive model, no a priori method of performance prediction will be possible.

ADSORPTIVE-BUBBLE SEPARATION METHODS

General References: Lemlich (ed.), *Adsorptive Bubble Separation Techniques,* Academic, New York, 1972. Carleson, "Adsorptive Bubble Separation Processes" in Scamehorn and Harwell (eds.), *Surfactant-Based Separation Processes,* Marcel Dekker, New York, 1989.

Principle The adsorptive-bubble separation methods, or adsubble methods for short [Lemlich, *Chem. Eng.* **73**(21), 7 (1966)], are based on the selective adsorption or attachment of material on the surfaces of gas bubbles passing through a solution or suspension. In most of the methods, the bubbles rise to form a foam or froth which carries the material off overhead. Thus the material (desirable or undesirable) is removed from the liquid, and not vice versa as in, say, filtration. Accordingly, the foaming methods appear to be particularly (although not exclusively) suited to the removal of small amounts of material from large volumes of liquid.

For any adsubble method, if the material to be removed (termed the **colligend**) is not itself surface-active, a suitable surfactant (termed the **collector**) may be added to unite with it and attach or adsorb it to the bubble surface so that it may be removed (Sebba, *Ion Flotation,* Elsevier, New York, 1962). The union between colligend and collector may be by chelation or other complex formation. Alternatively, a charged colligend may be removed through its attraction toward a collector of opposite charge.

Definitions and Classification Figure 22-41 outlines the most widely accepted classification of the various adsubble methods [Karger, Grieves, Lemlich, Rubin, and Sebba, *Sep. Sci.,* **2,** 401 (1967)]. It is based largely on actual usage of the terms by various workers, and so the definitions include some unavoidable inconsistencies and overlap.

Among the methods of foam separation, **foam fractionation** usually implies the removal of dissolved (or sometimes colloidal) material. The overflowing foam, after collapse, is called the *foamate.* The solid lines of Fig. 22-42 illustrate simple continuous foam fractionation. (Batch operation would be represented by omitting the feed and bottoms streams.)

On the other hand, **flotation** usually implies the removal of solid particulate material. Most important under the latter category is **ore flotation,** which is covered separately in Sec. 19.

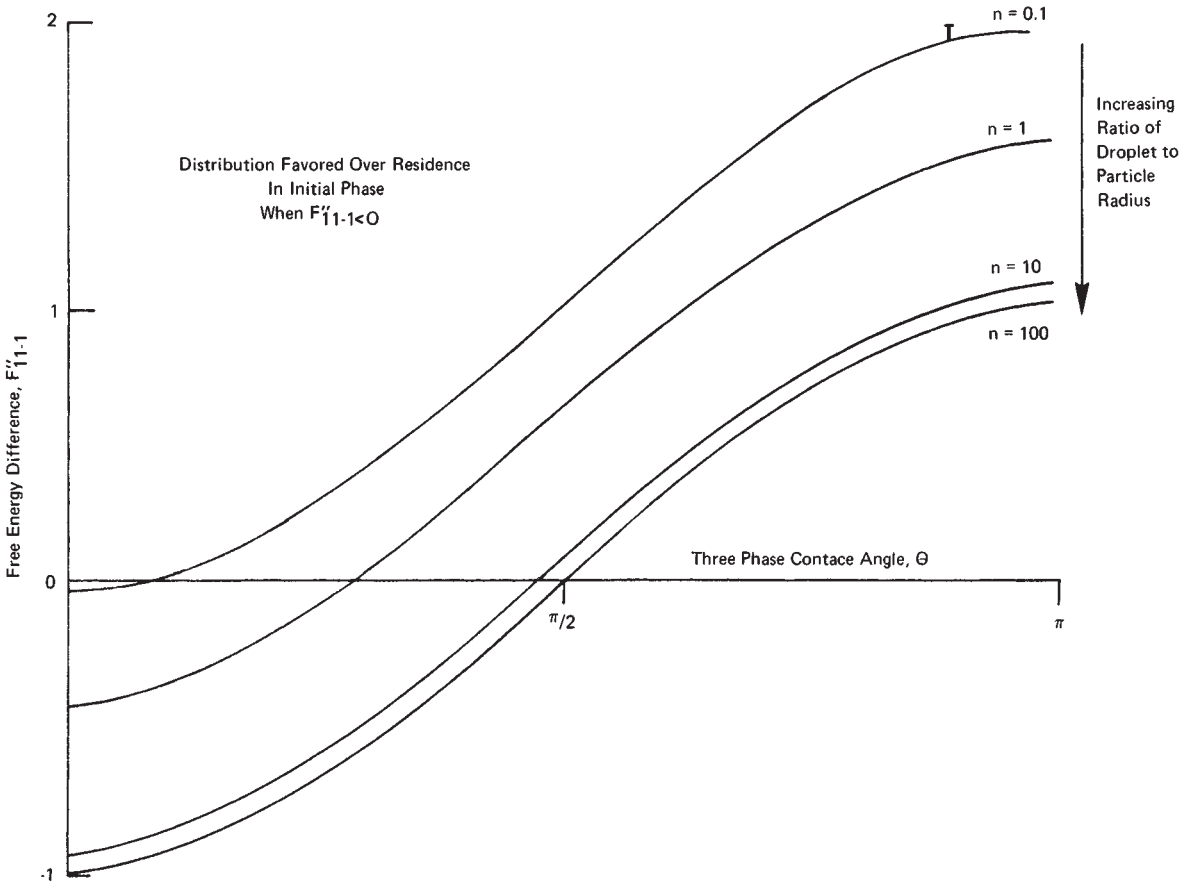


FIG. 22-40 Normalized free-energy difference between distributed (II) and nondistributed (I) states of the solid particles versus three-phase contact angle (collection at the interface is not considered). A negative free-energy difference implies that the distributed state is preferred over the nondistributed state. Note especially the significant effect of *n*, the ratio of the liquid droplet to solid-particle radius. [*From Jacques, Hovarongkura, and Henry,* Am. Inst. Chem. Eng. J., **25**(*1*), *160* (*1979*).]

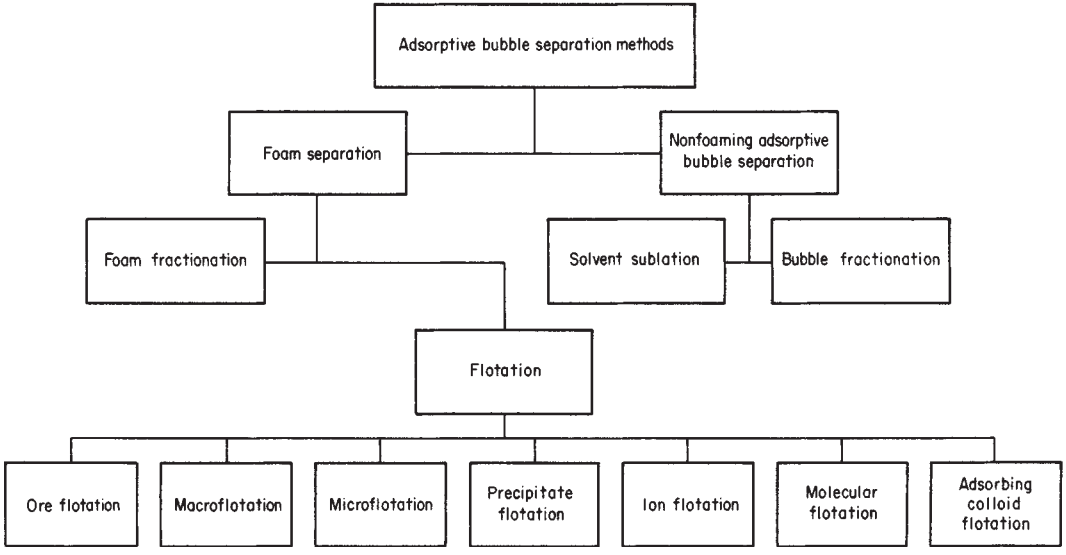


FIG. 22-41 Classification for the adsorptive-bubble separation methods.

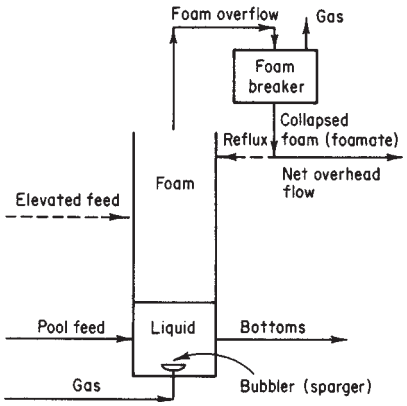


FIG. 22-42 Four alternative modes of continuous-flow operation with a foam-fractionation column: (1) The simple mode is illustrated by the solid lines. (2) Enriching operation employs the dashed reflux line. (3) In stripping operation, the elevated dashed feed line to the foam replaces the solid feed line to the pool. (4) For combined operation, reflux and elevated feed to the foam are both employed.

Also under the category of flotation are to be found **macroflotation,** which is the removal of macroscopic particles; **microflotation** (also called **colloid flotation**), which is the removal of microscopic particles, particularly colloids or microorganisms [Dognon and Dumontet, *Comptes Rendus,* **135,** 884 (1941)]; **molecular flotation,** which is the removal of surface-inactive molecules through the use of a collector (surfactant) which yields an insoluble product; **ion flotation,** which is the removal of surface-inactive ions via a collector which yields an insoluble product, especially a removable scum [Sebba, *Nature,* **184,** 1062 (1959)]; **adsorbing colloid flotation,** which is the removal of dissolved material in piggyback fashion by adsorption on colloidal particles; and **precipitate flotation,** in which a precipitate is removed by a collector which is not the precipitating agent [Baarson and Ray, "Precipitate Flotation," in Wadsworth and Davis (eds.), *Unit Processes in Hydrometallurgy,* Gordon and Breach, New York, 1964, p. 656]. The last definition has been narrowed to precipitate flotation of the first kind, the second kind requiring no separate collector at all [Mahne and Pinfold, *J. Appl. Chem.,* **18,** 52 (1968)].

A separation can sometimes be obtained even in the absence of any foam (or any floated floc or other surrogate). In **bubble fractionation** this is achieved simply by lengthening the bubbled pool to form a vertical column [Dorman and Lemlich, *Nature,* **207,** 145 (1965)]. The ascending bubbles then deposit their adsorbed or attached material at the top of the pool as they exit. This results in a concentration gradient which can serve as a basis for separation. Bubble fractionation can operate either alone or as a booster section below a foam fractionator, perhaps to raise the concentration up to the foaming threshold.

In **solvent sublation** an immiscible liquid is placed atop the main liquid to trap the material deposited by the bubbles as they exit (Sebba, *Ion Flotation,* Elsevier, New York, 1962). The upper liquid should dissolve or at least wet the material. With appropriate selectivity, the separation so achieved can sometimes be much greater than that with bubble fractionation alone.

The droplet analogs to the adsubble methods have been termed the **adsoplet methods** (from adsorptive droplet separation methods) [Lemlich, "Adsorptive Bubble Separation Methods," *Ind. Eng. Chem.,* **60**(10), 16 (1968)]. They are omitted from Fig. 22-41, since they involve adsorption or attachment at *liquid-liquid* interfaces. Among them are **emulsion fractionation** [Eldib, "Foam and Emulsion Fractionation," in Kobe and McKetta (eds.), *Advances in Petroleum Chemistry and Refining,* vol. 7, Interscience, New York, 1963, p. 66], which is the analog of foam fractionation; and **droplet fractionation** [Lemlich, loc. cit.; and Strain, *J. Phys. Chem.,* **57,** 638 (1953)], which is the analog of bubble fractionation. Similarly, the old beneficiation operation called bulk oil flotation (Gaudin, *Flotation,* 2d ed., McGraw-Hill, New York, 1957) is the analog of modern ore flotation. By and large, the adsoplet methods have not attracted the attention accorded to the adsubble methods.

Of all the adsubble methods, foam fractionation is the one for which chemical engineering theory is the most advanced. Fortunately, some of this theory also applies to other adsubble methods.

Adsorption The separation achieved depends in part on the selectivity of adsorption at the bubble surface. At equilibrium, the adsorption of dissolved material follows the Gibbs equation (Gibbs, *Collected Works,* Longmans Green, New York, 1928).

$$d\gamma = -\mathbf{R}T\Sigma\Gamma_i d\ln a_i \tag{22-42}$$

Γ_i is the surface excess (Davies and Rideal, *Interfacial Phenomena,* 2d ed., Academic, New York, 1963). For most purposes, it is sufficient to view Γ_i as the concentration of adsorbed component i at the surface in units of, say (g·mol)/cm^2. **R** is the gas constant, T is the absolute temperature, γ is the surface tension, and a_i is the activity of component i. The minus sign shows that material which concentrates at the surface generally lowers the surface tension, and vice versa. This can sometimes be a guide in determining preliminarily what materials can be separated.

When applied to a nonionic surfactant in pure water at concentrations below the critical micelle concentration, Eq. (22-42) simplifies into Eq. (22-43)

$$\Gamma_s = -\frac{1}{\mathbf{R}T}\frac{d\gamma}{d\ln C_s} \tag{22-43}$$

C is the concentration in the bulk, and subscript s refers to the surfactant. Under some conditions, Eq. (22-43) may apply to an ionic surfactant as well (Lemlich, loc. cit.).

The major surfactant in the foam may usually be considered to be present at the bubble surfaces in the form of an adsorbed monolayer with a substantially constant Γ_s, often of the order of 3×10^{-10} (g·mol)/cm^2, for a molecular weight of several hundred. On the other hand, trace materials follow the linear-adsorption isotherm $\Gamma_i = K_i C_i$ if their concentration is low enough. For a wider range of concentration a Langmuir or other type of isotherm may be applicable (Davies and Rideal, loc. cit.).

Factors Affecting Adsorption K_i for a colligend can be adversely affected (reduced) through an insufficiency of collector. It can also be reduced through an excess of collector, which competes for the available surface against the collector-colligend complex [Schnepf, Gaden, Mirocznik, and Schonfeld, *Chem. Eng. Prog.,* **55**(5), 42 (1959)].

Excess collector can also reduce the separation by forming micelles in the bulk which adsorb some of the colligend, thus keeping it from the surface. This effect of the micelles on K_i for the colligend is given theoretically [Lemlich, "Principles of Foam Fractionation," in Perry (ed.), *Progress in Separation and Purification,* vol. 1, Interscience, New York, 1968, chap. 1] by Eq. (22-44) [Lemlich (ed.), *Adsorptive Bubble Separation Techniques,* Academic, New York, 1972] if Γ_s is constant when $C_s > C_{sc}$:

$$\frac{1}{K_2} = \frac{1}{K_1} + \frac{C_s - C_{sc}}{\Gamma_s E} \tag{22-44}$$

K_1 is K_i just below the collector's critical micelle concentration, C_{sc}. K_2 is K_i at some higher collector concentration, C_s. E is the relative effectiveness, in adsorbing colligend, of surface collector versus micellar collector. Generally, $E > 1$. Γ_s is the surface excess of collector. More about each K is available [Lemlich, "Adsubble Methods," in Li (ed.), *Recent Developments in Separation Science,* vol. 1, CRC Press, Cleveland, 1972, pp. 113–127; Jashnani and Lemlich, *Ind. Eng. Chem. Process Des. Dev.,* **12,** 312 (1973)].

The controlling effect of various ions can be expressed in terms of thermodynamic equilibria [Karger and DeVivo, *Sep. Sci.,* **3,** 393 1968)]. Similarities with ion exchange have been noted. The selectivity of counterionic adsorption increases with ionic charge and decreases with hydration number [Jorne and Rubin, *Sep. Sci.,* **4,** 313 (1969); and Kato and Nakamori, *J. Chem. Eng. Japan,* **9,** 378 (1976)].

By analogy with other separation processes, the relative distribution in multicomponent systems can be analyzed in terms of a selectivity coefficient $\alpha_{mn} = \Gamma_m C_n / \Gamma_n C_m$ [Rubin and Jorne, *Ind. Eng. Chem. Fundam.*, **8,** 474 (1969); *J. Colloid Interface Sci.*, **33,** 208 (1970)].

Operation in the Simple Mode If there is no concentration gradient within the liquid pool and if there is no coalescence within the rising foam, then the operation shown by the solid lines of Fig. 22-42 is truly in the simple mode, i.e., a single theoretical stage of separation. Equations (22-45) and (22-46) will then apply to the steady-flow operation.

$$C_Q = C_W + (GS\Gamma_W/Q) \tag{22-45}$$

$$C_W = C_F - (GS\Gamma_W/F) \tag{22-46}$$

C_F, C_W, and C_Q are the concentrations of the substance in question (which may be a colligend or a surfactant) in the feed stream, bottoms stream, and foamate (collapsed foam) respectively. G, F, and Q are the volumetric flow rates of gas, feed, and foamate respectively. Γ_W is the surface excess in equilibrium with C_W. S is the surface-to-volume ratio for a bubble. For a spherical bubble, $S = 6/d$, where d is the bubble diameter. For variation in bubble sizes, d should be taken as $\Sigma n_i d_i^3 / \Sigma n_i d_i^2$, where n_i is the number of bubbles with diameter d_i in a representative region of foam.

Finding Γ Either Eq. (22-45) or Eq. (22-46) can be used to find the surface excess indirectly from experimental measurements. To assure a close approach to operation as a single theoretical stage, coalescence in the rising foam should be minimized by maintaining a proper gas rate and a low foam height [Brunner and Lemlich, *Ind. Eng. Chem. Fundam.* **2,** 297 (1963)]. These precautions apply particularly with Eq. (22-45).

For laboratory purposes it is sometimes convenient to recycle the foamate directly to the pool in a manner analogous to an equilibrium still. This eliminates the feed and bottoms streams and makes for a more reliable approach to steady-state operation. However, this recycling may not be advisable for colligend measurements in the presence of slowly dissociating collector micelles.

To avoid spurious effects in the laboratory, it is advisable to employ a prehumidified chemically inert gas.

Bubble Sizes Subject to certain errors (de Vries, *Foam Stability,* Rubber-Stichting, Delft, 1957), foam bubble diameters can be measured photographically. Some of these errors can be minimized by taking pains to generate bubbles of fairly uniform size, say, by using a bubbler with identical orifices or by just using a bubbler with a single orifice (gas rate permitting). Otherwise, a correction for planar statistical sampling bias in the foam should be incorporated with actual diameters [de Vries, op. cit.] or truncated diameters [Lemlich, *Chem. Eng. Commun.* **16,** 153 (1982)]. Also, size segregation can reduce mean mural bubble diameter by roughly half the standard deviation [Cheng and Lemlich, *Ind. Eng. Chem. Fundam.* **22,** 105 (1983)]. Bubble diameters can also be measured in the liquid pool, either photographically or indirectly via measurement of the gas flow rate and stroboscopic determination of bubble frequency [Leonard and Lemlich, *Am. Inst. Chem. Eng. J.*, **11,** 25 (1965)].

Bubble sizes at formation generally increase with surface tension and orifice diameter. Prediction of sizes in swarms from multiple orifices is difficult. In aqueous solutions of low surface tension, bubble diameters of the order of 1 mm are common. Bubbles produced by the more complicated techniques of pressure flotation or vacuum flotation are usually smaller, with diameters of the order of 0.1 mm or less.

Enriching and Stripping Unlike truly simple foam fractionation without significant changes in bubble diameter, coalescence in a foam column destroys some bubble surface and so releases adsorbed material to trickle down through the rising foam. This downflow constitutes internal reflux, which enriches the rising foam by countercurrent action. The result is a richer foamate, i.e., higher C_Q than that obtainable from the single theoretical stage of the corresponding simple mode. Significant coalescence is often present in rising foam, but the effect on bubble diameter and enrichment is frequently overlooked.

External reflux can be furnished by returning some of the externally broken foam to the top of the column. The concentrating effect of reflux, even for a substance which saturates the surface, has been verified [Lemlich and Lavi, *Science,* **134,** 191 (1961)].

Introducing the feed into the foam some distance above the pool makes for stripping operation. The resulting countercurrent flow in the foam further purifies the bottoms, i.e., lowers C_W.

Enriching, stripping, and combined operations are shown in Fig. 22-42.

Foam-Column Theory The counterflowing streams within the foam are viewed as consisting *effectively* of a descending stream of interstitial liquid (equal to zero for the simple mode) and an ascending stream of interstitial liquid plus bubble surface. (By considering this ascending surface as analogous to a vapor, the overall operation becomes analogous in a way to distillation *with entrainment.*)

An effective concentration $\overline{C}$ in the ascending stream at any level in the column is defined by Eq. (22-47):

$$\overline{C} = C + (GS\Gamma/U) \tag{22-47}$$

where U is the volumetric rate of interstitial liquid upflow, C is the concentration in this ascending liquid at that level, and Γ is the surface excess in equilibrium with C. Any effect of micelles should be included.

For simplicity, U can usually be equated to Q. An effective equilibrium curve can now be plotted from Eq. (22-47) in terms of $\overline{C}$ (or rather $\overline{C}°$) versus C.

Operating lines can be found in the usual way from material balances. The slope of each such line is $\Delta\overline{C}/\Delta C = L/U$, where L is the downflow rate in the particular column section and C is now the concentration in the descending stream.

The number of theoretical stages can then be found in one of the usual ways. Figure 22-43 illustrates a graphical calculation for a stripper.

Alternatively, the number of transfer units (NTU) in the foam based on, say, the ascending stream can be found from Eq. (22-48):

$$\text{NTU} = \int_{\overline{C}_W}^{C_Q} \frac{d\overline{C}}{\overline{C}° - \overline{C}} \tag{22-48}$$

$\overline{C}°$ is related to C by the effective equilibrium curve, and $\overline{C}°_W$ is similarly related to C_W. $\overline{C}$ is related to C by the operating line.

To illustrate this integration analytically, Eq. (22-48) becomes Eq. (22-49) for the case of a stripping column removing a colligend which is subject to the linear-equilibrium isotherm $\Gamma = KC$.

$$\text{NTU} = \frac{F}{GSK - W} \ln \frac{FW + F(GSK - W)C_F/C_W}{GSK(GSK + F - W)} \tag{22-49}$$

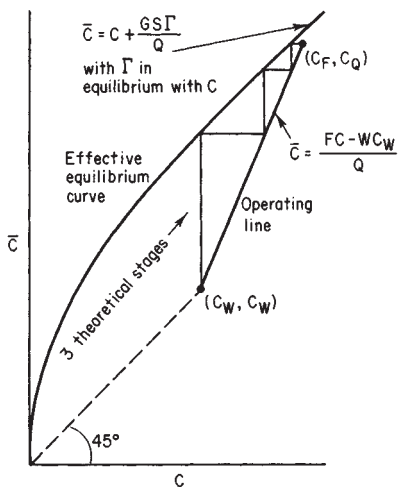


FIG. 22-43 Graphical determination of theoretical stages for a foam-fractionation stripping column.

As another illustration, Eq. (22-48) becomes Eq. (22-50) for an enriching column which is concentrating a surfactant with a constant Γ:

$$\text{NTU} = R \ln \frac{RGS\Gamma(F - D)}{(R + 1)GS\Gamma(F - D) - (R + 1)FD(C_D - C_F)} \qquad (22\text{-}50)$$

Unless the liquid pool is purposely lengthened vertically in order to give additional separation via bubble fractionation, it is usually taken to represent one theoretical stage. A bubbler submergence of 30 cm or so is usually ample for a solute with a molecular weight that does not exceed several hundred.

In a colligend stripper, it may be necessary to add some collector to the pool as well as the feed because the collector is also stripped off.

Limiting Equations If the height of a foam-fractionation column is increased sufficiently, a concentration pinch will develop between the counterflowing interstitial streams (Brunner and Lemlich, loc. cit.). For an enricher, the separation attained will then approach the predictions of Eq. (22-51) and, interestingly enough, Eq. (22-46).

$$C_D = C_W + (GS\Gamma_W/D) \qquad (22\text{-}51)$$

D is the volumetric rate at which net foamate (net overhead liquid product) is withdrawn. $D = Q/(R + 1)$. The concentration in the net foamate is C_D. In the usual case of total foam breakage (no dephlegmation), $C_D = C_Q$.

If the tall column is a stripper, the separation will approach that of Eqs. (22-52) and (22-53):

$$C_Q = C_F + (\text{GS}\Gamma_F/Q) \qquad (22\text{-}52)$$

$$C_W = C_F - (\text{GS}\Gamma_F/W) \qquad (22\text{-}53)$$

For a sufficiently tall combined column, the separation will approach that of Eqs. (22-54) and (22-53):

$$C_D = C_F + (\text{GS}\Gamma_F/D) \qquad (22\text{-}54)$$

The formation of micelles in the foam breaker does not affect the limiting equations because of the theoretically unlimited opportunity in a sufficiently tall column for their transfer from the reflux to the ascending stream [Lemlich, "Principles of Foam Fractionation," in Perry (ed.), *Progress in Separation and Purification,* vol. 1, Interscience, New York, 1968, chap. 1].

In practice, the performance of a well-operated foam column several feet tall may actually approximate the limiting equations, provided there is little channeling in the foam and provided that reflux is either absent or is present at a low ratio.

Column Operation To assure intimate contact between the counterflowing interstitial streams, the volume fraction of liquid in the foam should be kept below about 10 percent—and the lower the better. Also, rather uniform bubble sizes are desirable. The foam bubbles will thus pack together as blunted polyhedra rather than as spheres, and the suction in the capillaries (Plateau borders) so formed will promote good liquid distribution and contact. To allow for this desirable deviation from sphericity, $S = 6.3/d$ in the equations for enriching, stripping, and combined column operation [Lemlich, *Chem. Eng.,* **75**(27), 95 (1968); **76**(6), 5 (1969)]. Diameter d still refers to the sphere.

Visible channeling or significant deviations from plug flow of the foam should be avoided, if necessary by widening the column or lowering the gas and/or liquid rates. The superficial gas velocity should probably not exceed 1 or 2 cm/s. Under proper conditions, HTU values of several cm have been reported [Hastings, Ph.D. dissertation, Michigan State University, East Lansing, 1967; and Jashnani and Lemlich, *Ind. Eng. Chem. Process Des. Dev.,* **12,** 312 (1973)]. The foam column height equals NTU × HTU.

For columns that are wider than several centimeters, reflux and feed distributors should be used, particularly for wet foam [Haas and Johnson, *Am. Inst. Chem. Eng. J.,* **11,** 319 (1965)]. Liquid content within the foam can be monitored conductometrically [Chang and Lemlich, *J. Colloid Interface Sci.,* **73,** 224 (1980)]. See Fig. 22-44. Theoretically, as the limit $\mathscr{D} = K = 0$ is very closely approached, $\mathscr{D} = 3K$ [Lemlich, *J. Colloid Interface Sci.,* **64,** 107 (1978)].

Wet foam can be handled in a bubble-cap column (Wace and Banfield, *Chem. Process Eng.,* **47**(10), 70 (1966)] or in a sieve plate column [Aguayo and Lemlich, *Ind. Eng. Chem. Process Des. Dev.,* **13,** 153 (1974)]. Alternatively, individual short columns can be connected in countercurrent array [Banfield, Newson, and Alder, *Am. Inst. Chem. Eng. Symp. Ser.,* **1,** 3 (1965); Leonard and Blacyki, *Ind. Eng. Chem. Process Des. Dev.,* **17,** 358 (1978)].

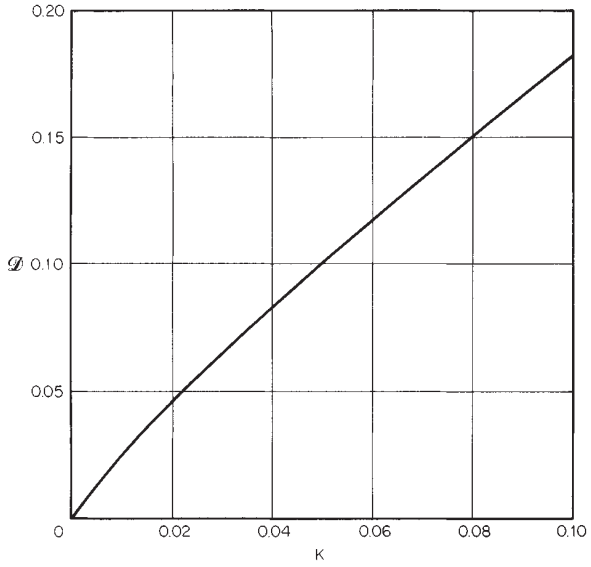


FIG. 22-44 Empirical relationship between $\mathscr{D}$, the volumetric fraction of liquid in common polydisperse foam, and K, the electrical conductivity of the foam divided by the electrical conductivity of the liquid. [*Chang and Lemlich,* J. Colloid Interface Sci., **73,** *224 (1980).*]

A high gas rate can be used to achieve maximum throughput in the simple mode (Wace, Alder, and Banfield, AERE-R5920, U.K. Atomic Energy Authority, 1968) because channeling is not a factor in that mode. A horizontal drainage section can be used overhead [Haas and Johnson, *Ind. Eng. Chem. Fundam.,* **6,** 225 (1967)]. The highly mobile dispersion produced by a very high gas rate is not a true foam but is rather a so-called **gas emulsion** [Bikerman, *Ind. Eng. Chem.,* **57**(1), 56 (1965)].

A very low gas rate in a column several feet tall with internal reflux can sometimes be used to effect difficult multicomponent separations in batch operation [Lemlich, "Principles of Foam Fractionation," in Perry (ed.), *Progress in Separation and Purification,* vol. 1, Interscience, New York, 1968, chap. 1].

The same end may be achieved by continuous operation at total external reflux with a small U bend in the reflux line for foamate holdup [Rubin and Melech, *Can. J. Chem. Eng.,* **50,** 748 (1972)].

The slowly rising foam in a tall column can be employed as the sorbent for continuous chromatographic separations [Talman and Rubin, *Sep. Sci.,* **11,** 509 (1976)]. Low gas rates are also employed in short columns to produce the scumlike froth of batch-operated ion flotation, microflotation, and precipitate flotation.

Foam Drainage and Overflow The rate of foam overflow on a gas-free basis (i.e., the total volumetric foamate rate Q) can be estimated from a detailed theory for foam drainage [Leonard and Lemlich, *Am. Inst. Chem. Eng. J.,* **11,** 18 (1965)]. From the resulting relationship for overflow [Fanlo and Lemlich, *Am. Inst. Chem. Eng. Symp. Ser.,* **9,** 75, 85 (1965)], Eq. (22-55) can be employed as a convenient approximation to the theory so as to avoid trial and error over the usual range of interest for foam of low liquid content ascending in plug flow:

$$\frac{Q}{G} = 22\left(\frac{v_G^3 \mu\mu_s^2}{g^3\rho^3 d^8}\right)^{1/4} \qquad (22\text{-}55)$$

The superficial gas velocity v_g is G/A, where A is the horizontal

cross-sectional area of the empty vertical foam column. Also, g is the acceleration of gravity, ρ is the liquid density, μ is the ordinary liquid viscosity, and μ_s is the effective surface viscosity.

To account for inhomogeneity in bubble sizes, d in Eq. (22-55) should be taken as $\sqrt{\Sigma n_i d_i^3/\Sigma n_i d_i}$ and evaluated at the top of the vertical column if coalescence is significant in the rising foam. Note that this average d for overflow differs from that employed earlier for S. Also, see "Bubble Sizes" regarding the correction for planar statistical sampling bias and the presence of size segregation at a wall.

For theoretical reasons, Q determined from Eq. (22-55) should be multiplied by the factor $(1 + 3Q/G)$ to give a final Q. However, for foam of sufficiently low liquid content this multiplication can be omitted with little error.

The effective surface viscosity is best found by experiment with the system in question, followed by back calculation through Eq. (22-55). From the precursors to Eq. (22-55), such experiments have yielded values of μ_s on the order of 10^{-4} (dyn·s)/cm for common surfactants in water at room temperature, which agrees with independent measurements [Lemlich, *Chem. Eng. Sci.*, **23,** 932 (1968); and Shih and Lemlich, *Am. Inst. Chem. Eng. J.*, **13,** 751 (1967)]. However, the expected high μ_s for aqueous solutions of such skin-forming substances as saponin and albumin was not attained, perhaps because of their nonnewtonian surface behavior [Shih and Lemlich, *Ind. Eng. Chem. Fundam.*, **10,** 254 (1971); and Jashnani and Lemlich, *J. Colloid Interface Sci.*, **46,** 13 (1974)].

The drainage theory breaks down for columns with tortuous cross section, large slugs of gas, or heavy coalescence in the rising foam.

Foam Coalescence Coalescence is of two types. The first is the growth of the larger foam bubbles at the expense of the smaller bubbles due to interbubble gas diffusion, which results from the smaller bubbles having somewhat higher internal pressures (Adamson, *The Physical Chemistry of Surfaces,* 4th ed., Wiley, New York, 1982). Small bubbles can even disappear entirely. In principle, the rate at which this type of coalescence proceeds can be estimated [Ranadive and Lemlich, *J. Colloid Interface Sci.*, **70,** 392 (1979)].

The second type of coalescence arises from the rupture of films between adjacent bubbles [Vrij and Overbeek, *J. Am. Chem. Soc.*, **90,** 3074 (1968)]. Its rate appears to follow first-order reaction kinetics with respect to the number of bubbles [New, *Proc. 4th Int. Congr. Surf. Active Substances,* Brussels, 1964, **2,** 1167 (1967)] and to decrease with film thickness [Steiner, Hunkeler, and Hartland, *Trans. Inst. Chem. Eng.*, **55,** 153 (1977)]. Many factors are involved [Bikerman, *Foams,* Springer-Verlag, New York, 1973; and Akers (ed.), *Foams,* Academic, New York, 1976].

Both types of coalescence can be important in the foam separations characterized by low gas flow rate, such as batchwise ion flotation producing a scum-bearing froth of comparatively long residence time. On the other hand, with the relatively higher gas flow rate of foam fractionation, the residence time may be too short for the first type to be important, and *if* the foam is sufficiently stable, even the second type of coalescence may be unimportant.

Unlike the case for Eq. (22-55), when coalescence is significant, it is better to find S from d evaluated at the feed level for Eqs. (22-52) to (22-54) and at the pool surface for Eqs. (22-46) and (22-51).

Foam Breaking It is usually desirable to collapse the overflowing foam. This can be accomplished by chemical means (Bikerman, op. cit.) if external reflux is not employed or by thermal means [Kishimoto, *Kolloid Z.*, **192,** 66 (1963)] if degradation of the overhead product is not a factor.

Foam can also be broken with a rotating perforated basket [Lemlich, "Principles of Foam Fractionation," in Perry (ed.), *Progress in Separation and Purification,* vol. 1, Interscience, New York, 1968, chap. 1]. If the foamate is aqueous (as it usually is), the operation can be improved by discharging onto Teflon instead of glass [Haas and Johnson, *Am. Inst. Chem. Eng. J.*, **11,** 319 (1965)]. A turbine can be used to break foam [Ng, Mueller, and Walden, *Can. J. Chem. Eng.*, **55,** 439 (1977)]. Foam which is not overly stable has been broken by running foamate onto it [Brunner and Stephan, *Ind. Eng. Chem.*, **57**(5), 40 (1965)]. Foam can also be broken by sound or ultrasound, a rotating disk, and other means [Ohkawa, Sakagama, Sakai, Futai, and Takahara, *J. Ferment. Technol.*, **56,** 428, 532 (1978)].

If desired, dephlegmation (partial collapse of the foam to give reflux) can be accomplished by simply widening the top of the column, provided the foam is not too stable. Otherwise, one of the more positive methods of foam breaking can be employed to achieve dephlegmation.

Bubble Fractionation Figure 22-45 shows continuous bubble fractionation. This operation can be analyzed in a simplified way in terms of the adsorbed carry-up, which furthers the concentration gradient, and the dispersion in the liquid, which reduces the gradient [Lemlich, *Am. Inst. Chem. Eng. J.*, **12,** 802 (1966); **13,** 1017 (1967)].

To illustrate, consider the limiting case in which the feed stream and the two liquid takeoff streams of Fig. 22-45 are each zero, thus resulting in batch operation. At steady state the rate of adsorbed carry-up will equal the rate of downward dispersion, or $af\Gamma = \overline{D}AdC/dh$. Here a is the surface area of a bubble, f is the frequency of bubble formation. $\overline{D}$ is the dispersion (effective diffusion) coefficient based on the column cross-sectional area A, and C is the concentration at height h within the column.

There are several possible alternative relationships for Γ (Lemlich, op. cit.). For simplicity, consider $\Gamma = K'C$, where K' is not necessarily the same as the equilibrium constant K. Substituting and integrating from the boundary condition of $C = C_B$ at $h = 0$ yield

$$C/C_B = \exp(Jh) \tag{22-56}$$

C_B is the concentration at the bottom of the column, and parameter $J = K'af/\overline{D}A$. Combining Eq. (22-56) with a material balance against the solute in the initial charge of liquid gives

$$\frac{C}{C_i} = \frac{JH \exp(Jh)}{\exp(JH) - 1} \tag{22-57}$$

C_i is the concentration in the initial charge, and H is the total height of the column.

The foregoing approach has been extended to steady continuous flow as illustrated in Fig. 22-45 [Cannon and Lemlich, *Chem. Eng. Prog. Symp. Ser.*, **68**(124), 180 (1972); Bruin, Hudson, and Morgan, *Ind. Eng. Chem. Fundam.*, **11,** 175 (1972); and Wang, Granstrom, and Kown, *Environ. Lett.*, **3,** 251 (1972), **4,** 233 (1973), **5,** 71 (1973)]. The extension includes a rough method for estimating the optimum feed location as well as a very detailed analysis of column performance which takes into account the various local phenomena around each rising bubble (Cannon and Lemlich, op. cit.).

Uraizee and Narsimhan [*Sep. Sci. Technol.*, **30**(6), 847 (1995)] have provided a model for the continuous separation of proteins from dilute solutions. Although their work is focused on protein separation, the model should find general application to other separations.

In agreement with experiment [Shah and Lemlich, *Ind. Eng. Chem. Fundam.*, **9,** 350 (1970); and Garmendia, Perez, and Katz,

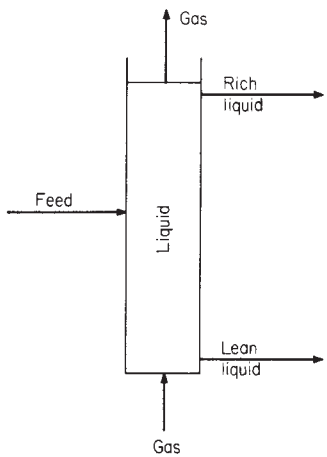


FIG. 22-45 Continuous bubble fractionation.

J. Chem. Educ., **50,** 864 (1973)], theory shows that the degree of separation that is obtained increases as the liquid column is made taller. But unfortunately it decreases as the column is made wider. In simple terms, the latter effect can be attributed to the increase in the dispersion coefficient as the column is widened.

In this last connection it is important that the column be aligned precisely vertically (Valdes-Krieg, King, and Sephton, *Am. Inst. Chem. Eng. J.,* **21,** 400 (1975)]. Otherwise, the bubbles with their dragged liquid will tend to rise up one side of the column, thus causing liquid to flow down the other side, and in this way largely destroy the concentration gradient. A vertical foam-fractionation column should also be carefully aligned to be plumb.

The escaping bubbles from the top of a bubble-fractionation column can carry off an appreciable quantity of adsorbed material in an aerosol of very fine film drops [various papers, *J. Geophys. Res., Oceans Atmos.,* **77**(27), (1972)]. If the residual solute is thus appreciably depleted, C_i in Eq. (22-57) should be replaced with the average residual concentration.

This carry-off of film drops, which may also occur with breaking foam, in certain cases can partially convert water pollution into air pollution. If such is the case, it may be desirable to recirculate the gas. Such recirculation is also indicated if hydrocarbon vapors or other volatiles are incorporated in the gas stream to improve adsorptive selectivity [Maas, *Sep. Sci.,* **4,** 457 (1969)].

A small amount of collector (surfactant) or other appropriate additive in the liquid may greatly increase adsorption (Shah and Lemlich, op. cit.). Column performance can also be improved by skimming the surface of the liquid pool or, when possible, by removing adsorbed solute in even a tenuous foam overflow. Alternatively, an immiscible liquid can be floated on top. Then the concentration gradient in the tall pool of main liquid, plus the trapping action of the immiscible layer above it, will yield a combination of bubble fractionation and solvent sublation.

Systems Separated Some of the various separations reported in the literature are listed in Rubin and Gaden, "Foam Separation," in Schoen (ed.), *New Chemical Engineering Separation Techniques,* Interscience, New York, 1962, chap. 5; Lemlich, *Ind. Eng. Chem.,* **60**(10), 16 (1968); Pushkarev, Egorov, and Khrustalev, *Clarification and Deactivation of Waste Waters by Frothing Flotation,* in Russian, Atomizdat, Moscow, 1969; Kuskin and Golman, *Flotation of Ions and Molecules,* in Russian, Nedra, Moscow, 1971; Lemlich (ed.), *Adsorptive Bubble Separation Techniques,* Academic, New York, 1972; Lemlich, "Adsubble Methods," in Li (ed.), *Recent Developments in Separation Science,* vol. 1, CRC Press, Cleveland, 1972, chap. 5; Grieves, *Chem. Eng. J.,* **9,** 93 (1975); Valdes-Krieg King, and Sephton, *Sep. Purif. Methods,* **6,** 221 (1977); Clarke and Wilson, *Foam Flotation,* Marcel Dekker, New York, 1983; and Wilson and Clarke, "Bubble and Foam Separations in Waste Treatment," in Rousseau (ed.), *Handbook of Separation Processes,* Wiley, New York, 1987.

Of the numerous separations reported, only a few can be listed here. Except for minerals beneficiation [ore flotation] which is covered in Sec. 21, the most important industrial applications are usually in the area of pollution control.

A pilot-sized foaming unit reduced the alkyl benzene sulfonate concentration of 500,000 gal of sewage per day to nearly 1 mg/L, using a *G/F* of 5 and producing a *Q/F* of no more than 0.03 [Brunner and Stephan, *Ind. Eng. Chem.,* **57**(5), 40 (1965); and Stephan, *Civ. Eng.,* **35**(9), 46 (1965)]. A full-scale unit handling over 45,420 m^3/day (12 million gal/day) performed nearly as well. The foam also carried off some other pollutants. However, with the widespread advent of biodegradable detergents, large-scale foam fractionation of municipal sewage has been discontinued.

Other plant-scale applications to pollution control include the flotation of suspended sewage particles by depressurizing so as to release dissolved air [Jenkins, Scherfig, and Eckhoff, "Applications of Adsorptive Bubble Separation Techniques to Wastewater Treatment," in Lemlich (ed.), *Adsorptive Bubble Separation Techniques,* Academic, New York, 1972, chap. 14; and Richter, *Internat. Chem. Eng.,* **16,** 614 (1976)]. Dissolved-air flotation is also employed in treating wastewater from pulp and paper mills [Coertze, *Prog. Water Technol.,* **10,** 449 (1978); and Severeid, *TAPPI* **62**(2), 61, 1979]. In addition, there is the flotation, with electrolytically released bubbles [Chambers and Cottrell, *Chem. Eng.,* **83**(16), 95 (1976)], of oily iron dust [Ellwood, *Chem. Eng.,* **75**(16), 82 (1968)] and of a variety of wastes from surface-treatment processes at the maintenance and overhaul base of an airline [Roth and Ferguson, *Desalination,* **23,** 49 (1977)].

Fats and, through the use of lignosulfonic acid, proteins can be flotated from the wastewaters of slaughterhouses and other food-processing installations [Hopwood, *Inst. Chem. Eng. Symp. Ser.,* **41,** M1 (1975)]. After further treatment, the floated sludge has been fed to swine.

A report of the recovery of protein from potato-juice wastewater by foaming [Weijenberg, Mulder, Drinkenberg, and Stemerding, *Ind. Eng. Chem. Process Des. Dev.,* **17,** 209 (1978)] is reminiscent of the classical recovery of protein from potato and sugar-beet juices [Ostwald and Siehr, *Kolloid Z.,* **79,** 11 (1937)]. The isoelectric pH is often a good choice for the foam fractionation of protein (Rubin and Gaden, loc. cit.). Adding a salt to lower solubility may also help. Additional applications of foam fractionation to the separation of protein have been reported by Uraizee and Narsimhan [*Enzyme Microb. Technol.* **12,** 232 (1990)].

With the addition of appropriate additives as needed, the flotation of refinery wastewaters reduced their oil content to less than 10 mg/L in pilot-plant operation [Steiner, Bennett, Mohler, and Clere, *Chem. Eng. Prog.,* **74**(12), 39 (1978)] and full-scale operation (Simonsen, *Hydrocarb. Process. Pet. Refiner,* **41**(5), 145, 1962]. Experiments with a cationic collector to remove oils reportedly confirmed theory [Angelidon, Keskavarz, Richardson, and Jameson, *Ind. Eng. Chem. Process Des. Dev.,* **16,** 436 (1977)].

Pilot-plant [Hyde, Miller, Packham, and Richards, *J. Am. Water Works Assoc.,* **69,** 369 (1977)] and full-scale [Ward, *Water Serv.,* **81,** 499 (1977)] flotation in the preparation of potable water is described.

Overflow at the rate of 2700 m^3 (713,000 gal) per day from a zinc-concentrate thickener is treated by ion flotation, precipitate flotation, and untrafine-particle flotation [Nagahama, *Can. Min. Metall. Bull.,* **67,** 79 (1974)]. In precipitate flotation only the surface of the particles need be coated with collector. Therefore, in principle less collector is required than for the equivalent removal of ions by foam fractionation or ion flotation.

By using an anionic collector and external reflux in a combined (enriching and stripping) column of 3.8-cm (1.5-in) diameter with a feed rate of 1.63 m/h [40 gal/(h·ft^2)] based on column cross section, *D/F* was reduced to 0.00027 with C_w/C_F for Sr^{2+} below 0.001 [Shonfeld and Kibbey, *Nucl. Appl.,* **3,** 353 (1967)]. Reports of the adsubble separation of 29 heavy metals, radioactive and otherwise, have been tabulated [Lemlich, "The Adsorptive Bubble Separation Techniques," in Sabadell (ed.), *Proc. Conf. Traces Heavy Met. Water,* 211–223, Princeton University, 1973, EPA 902/9-74-001, U.S. EPA, Reg. II, 1974). Some separation of ^{15}N from ^{14}N by foam fractionation has been reported [Hitchcock, Ph.D. dissertation, University of Missouri, Rolla, 1982].

The numerous separations reported in the literature include surfactants, inorganic ions, enzymes, other proteins, other organics, biological cells, and various other particles and substances. The scale of the systems ranges from the simple Crits test for the presence of surfactants in water, which has been shown to operate by virtue of transient foam fractionation [Lemlich, *J. Colloid Interface Sci.,* **37,** 497 (1971)], to the natural adsubble processes that occur on a grand scale in the ocean [Wallace and Duce, *Deep Sea Res.,* **25,** 827 (1978)]. For further information see the reviews cited earlier.

MEMBRANE SEPARATION PROCESSES

General References: Noble and Stern (eds.), *Membrane Separations Technology,* Elsevier, 1995. Howell, Sanchez, and Field, *Membranes in Bioprocessing,* Chapman & Hall, 1993. Ho and Sirkar (eds.), *Membrane Handbook,* Van Nostrand Reinhold, 1992. Mulder, *Basic Principles of Membrane Technology,* Kluwer Academic Publishers, 1992. Bhave, *Inorganic Membranes: Synthesis, Characteristics, and Applications,* Chapman & Hall, 1991. Baker, Cussler, Eykamp, Koros, Riley, and Strathmann, *Membrane Separation Systems,* U.S. Department of Energy, DOE/ER/30133-H1, 1990. Porter (ed.), *Handbook of Industrial Membrane Technology,* Noyes, 1990. Wankat, *Rate-Controlled Separations,* chapters 12 and 13, Elsevier, 1990. Rautenbach and Albrecht, *Membrane Processes,* Wiley, 1989. Mohr, Leeper, Engelgau, and Charboneau, *Membrane Applications and Research in Food Processing,* Noyes, 1989. Li and Strathmann, *Separation Technology,* United Engineering Trustees, 1988. Cheryan, *Ultrafiltration Handbook,* Technomic Publishing, Lancaster, PA, 1986. Speigler and Laird, *Principles of Desalination, 2d ed.,* Academic Press, 1980. Many membrane research papers are published in *J. Membrane Sci.,* Elsevier.

Topics Omitted from This Section In order to concentrate on the membrane processes of widest industrial interest, several are left out.

Dialysis and Hemodialysis Historically, dialysis has found some industrial use. Today, much of that is supplanted by ultrafiltration. Donan dialysis is treated briefly under electrodialysis. Hemodialysis is a huge application for membranes, and it dominates the membrane field in area produced and in monetary value. This medical application is omitted here.

An excellent description of the engineering side of both topics is provided by Kessler and Klein [in Ho and Sirkar (eds.), op. cit., pp. 163–216]. A comprehensive treatment of diffusion appears in: Von Halle and Shachter, "Diffusional Separation Methods," in *Encyclopedia of Chemical Technology,* pp. 149–203, Wiley, 1993.

Facilitated Transport Transport by a reactive phase through a membrane is promising but problematic. Way and Noble [in Ho and Sirkar (eds.), op. cit., pp. 833–866] have a description and a complete bibliography.

Liquid Membranes Several types of liquid membranes exist: molten salt, emulsion, immobilized/supported, and hollow-fiber-contained liquid membranes. Araki and Tsukube (*Liquid Membranes: Chemical Applications,* CRC Press, 1990) and Sec. IX and Chap. 42 in Ho and Sirkar (eds.) (op. cit., pp. 724, 764–808) contain detailed information and extensive bibliographies.

Catalytic Membranes Falconer, Noble, and Sperry (Chap. 14—"Catalytic Membrane Reactors" in Noble and Stern, op. cit., p. 669–712) give a detailed review and an extensive bibliography. Additional information can be found in a work by Tsotsis et al. ["Catalytic Membrane Reactors," pp. 471–551, in Becker and Pereira (eds.), *Computer-Aided Design of Catalysts,* Dekker, 1993].

BACKGROUND AND DEFINITIONS

This section describes the use of separation processes which utilize membranes. Placement in this chapter is in recognition of the recent ascendency of industrial-scale membrane-based separations, but it also reflects the view that within a decade, many of these separation processes will be mainstream unit operations. Some approach that status already. Figure 22-46 shows the relative size of things important in membrane separations.

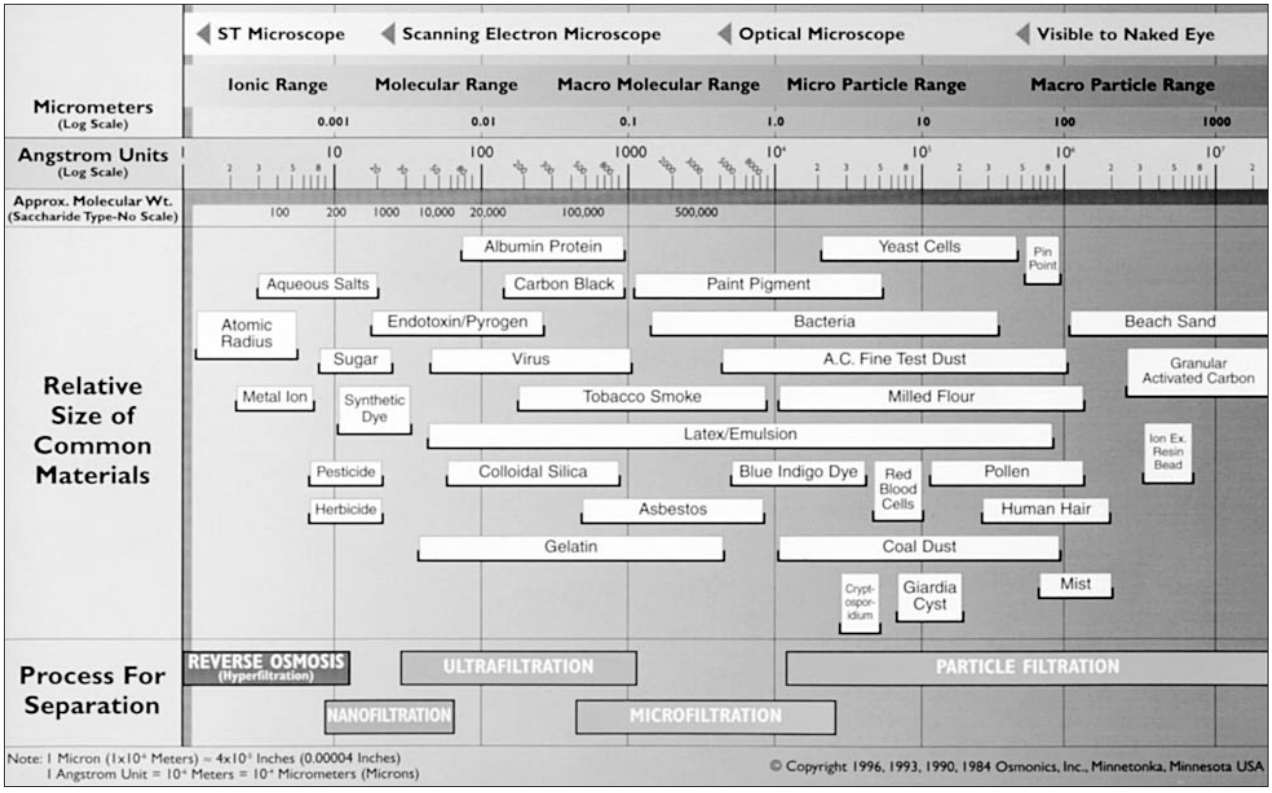


FIG. 22-46 The filtration spectrum. (*Copyright © 1996. Reprinted by permission of Osmonics, Minnetonka, MN.*)

Advantages to Membrane Separation This subsection covers the commercially important membrane applications. All except electrodialysis are pressure driven. All except pervaporation involve no phase change. All tend to be inherently low-energy consumers in theory if not in practice. They operate by a different mechanism than do other separation methods, so they have a unique profile of strengths and weaknesses. In some cases they provide unusual sharpness of separation, but in most cases they perform a separation at lower cost, provide more valuable products, and do so with fewer undesirable side effects than older separations methods. The membrane interposes a new phase between feed and product. It controls the transfer of mass between feed and product. It is a kinetic, not an equilibrium process. In a separation, a membrane will be selective because it passes some components much more rapidly than others. Many membranes are very selective. Membrane separations are often simpler than the alternatives.

General Examples No artificial membrane yet compares to the ones surrounding every cell in nature, but many are very sophisticated in what they do. Thousands of tons of drinking water are produced every day in the Middle East, on islands, and in certain coastal areas by passing pressurized seawater across a very thin membrane that permeates water with practically none of the dissolved salts. Huge quantities of nitrogen are purified from air by membranes operating from the output of a simple, single stage air compressor. Tons of water are purified to an exquisite degree for use in making microchips, most of the purification having been accomplished by passing the water through membranes. Municipalities depend on electrodialysis to remove salt from brackish aquifers to provide high-quality potable water.

Basic Equations All of the processes described in this section depend to some extent on the following background theory. Substances move through membranes by several mechanisms. For porous membranes, such as are used in microfiltration, viscous flow dominates the process. For electrodialytic membranes, the mass transfer is caused by an electrical potential resulting in ionic conduction. For all membranes, Fickian diffusion is of some importance, and it is of dominant importance in gas permeation and reverse osmosis. In the following, almost every step is accompanied by a new assumption. Generally, they are reasonable assumptions, but when using the result, it is important to remember the many assumptions used to reach the convenient form of the equation. The driving force for Fickian transport of a substance is a gradient in chemical potential:

$$N_i = -D_i C \frac{d(\mu_i/RT)}{dx} \tag{22-58}$$

where N_i is the mass of component i transported, kmol/m^2·s, D_i is diffusivity of component i, m^2/s, C is concentration, kmol/m^3, μ_i is chemical potential of the substance diffusing, J/kmol·K, and x is distance, m.

In most cases, activity coefficients are close to one, and Fick's first law is written as:

$$N_i = -D_i \frac{dC_i}{dx} \tag{22-59}$$

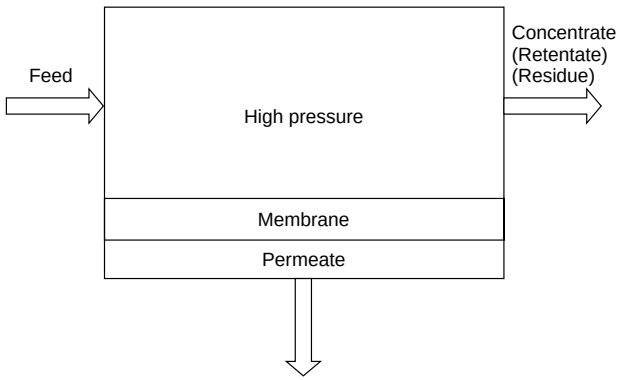
Assuming D_i is constant, and in particular that it is independent of C_i, and that the concentrations in the fluid phases are in equilibrium with the membrane. Fick's law may be written:

$$N_i = D_i \frac{(C_f - C_p)}{z} = D_i \frac{\Delta C}{z} \tag{22-60}$$

where z is the thickness of the membrane active layer, and C_f and C_p are concentrations in the feed and the permeate, respectively. D_i is the diffusivity in the membrane. The concentration of a component in the membrane phase will be quite different than its concentration in the fluid phase even though they are in equilibrium. The diffusivity in the membrane phase will always be much different than it is in the fluid phases, which must be remembered when applying Eq. (22-60). More complete nomenclature is shown in Fig. 22-47.

If Henry's law applies, the concentrations in fluid phases and the membrane are related by:

$$C_i = S \cdot p_i \tag{22-61}$$



Quantity	Feed or high-pressure side	Permeate or low-pressure side	Concentrate, etc.
Flow	$Q_f N$	(J)(A),N	Q_r
Concentration	C_f	C_p	C_c
Partial pressure	p_{feed}	$p_{permeate}$	$p_{residue}$
Gas feed	L	V	R

FIG. 22-47 Schematic of pressure-driven processes showing nomenclature.

where S is a proportionality factor, kmol/m^3·Pa, specific for a membrane and a penetrant and p_i is the partial pressure of component i, Pa.

If the membrane and its immediate surroundings are isothermal (generally except for pervaporation) and if S is a function only of temperature, then:

$$N_i = \left(\frac{S \cdot \overline{D}_i}{z}\right)(p_f - p_p) \tag{22-62}$$

In membrane separations, the product $S \cdot \overline{D}_i$ is referred to as the permeability, ρ_i (kmol/m·s·Pa). The rate of passage of material through a membrane is referred to as flux, with symbol J_i. J_i is equal to N_i in the equations given above. Generally J_i has the dimensions of velocity, m/s (more conveniently, μm/s), or conventionally as ℓ/m^2·hr, gal/ft^2·day, or ft^3/ft^2·day. For most applications, throughput is expressed in volumes instead of moles or mass.

An important consideration is that the "goodness" of the separation is almost independent of the membrane thickness, z, and the *rate* of the process is *inversely* proportional to z, giving rise to a major emphasis on making the separating layer of a membrane very thin. It is rare that z is known for a commercial membrane, and J_i is stated without regard to z.

Basic Concepts

Membrane Porosity Separation membranes run a gamut of porosity (see Fig. 22-48). Polymeric and metallic gas separation membranes, electrodialysis membranes, pervaporation membranes, and reverse osmosis membranes are nonporous, although there is lingering controversy over the nonporosity of the latter. Porous membranes are used for microfiltration and ultrafiltration. Nanofiltration membranes are probably charged porous structures.

Solution-Diffusion Mass passes through nonporous membranes either by ionic conduction (electrodialysis) or by dissolving in the membrane [Eq. (22-61)] then diffusing through the membrane in response to a chemical potential gradient, which may be a change in concentration vapor pressure or an electric potential. Materials have differing Henry's law constants, which was an early emphasis in membrane material selection. Currently, especially in gas membranes, the structural differences leading to enhanced diffusivity selection is an important research area.

Pores Even porous membranes can give very high selectivity. Molecular sieve membranes exist that give excellent separation factors for gases. Their commercial scale preparation is a formidable obstacle. At the other extreme, UF_6 separations use Knudsen flow barriers, with a very low separation factor. Microfiltration (MF) and ultrafiltration (UF) membranes are clearly porous, their pores ranging in size from 3 nm to 3 μm. Nanofiltration (NF) membranes have smaller pores.

TABLE 22-15 Liquid Flux Conversion Factors

To convert	Into	Multiply by	Inverse
U.S. gallons/ft^2·day (gfd)	Liters/m^2·hr (ℓmh)	1.6976	0.5891
gfd	μm/s	0.4715	2.121
ℓmh	μm/s	0.2778	3.600

Separation Factor The separation factor, α, is defined consistent with other separation methods. It is important to recall that in membranes, α is the result of differing rates, and that it has no equilibrium implications. The convention in membrane separations is to define the separation so that α > 1.

$$\alpha = \frac{(C_i/C_j)_p}{(C_i/C_j)_f} \tag{22-63}$$

α is widely used in gas separations, and is used occasionally in other separations.

Retention, Rejection, and Reflection **Retention** and **rejection** are used almost interchangeably. A third term, **reflection,** includes a measure of solute-solvent coupling, and is the term used in irreversible thermodynamic descriptions of membrane separations. It is important in only a few practical cases. Rejection is the term of trade in reverse osmosis (RO) and NF, and retention is usually used in UF and MF.

$$R = 1 - \left(\frac{C_p}{C_f}\right) \tag{22-64}$$

where C is the concentration of the material being retained/rejected.

By convention, C_f is measured in the bulk feed, not at the membrane. Clearly, the concentration at the membrane is the important one, but the convention is well established and it simplifies calculations on yield and material balance. Concentration at the membrane, C_{wall} may be calculated by the method shown in Eq. (22-91).

Cross Flow Most membrane processes are operated in cross flow, and only a few have the option to operate in the more conventional dead-end flow. In cross flow, the retentate passes parallel to the separating membrane, often at a velocity an order of magnitude higher than the velocity of the stream passing through the membrane. Microfiltration is the major membrane process in which a significant number if applications may be run with dead-end flow.

Staging Membranes are rarely staged. Except for gas separations, it is unusual for the product to pass through more than one membrane. If the membrane does not make the required separation in one pass, other means of separation will normally be employed. Exceptions are noted for specific applications.

Flux is the term used to describe how fast a product passes through a membrane. A velocity, almost always reported as volume/area-time, it does not take membrane thickness into account. For most users,

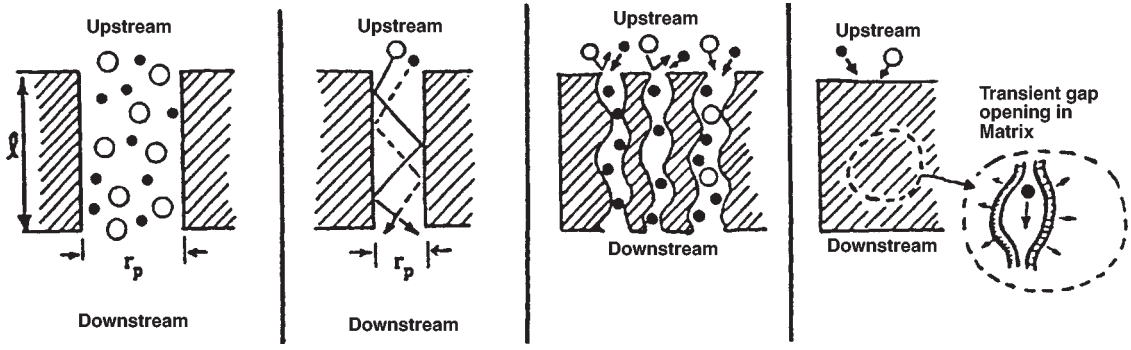


FIG. 22-48 Transport mechanisms for separation membranes: (*a*) Viscous flow, used in UF and MF. No separation achieved in RO, NF, ED, GAS, or PV. (*b*) Knudsen flow used in some gas membranes. Pore diameter < mean free path. (*c*) Ultramicroporous membrane—precise pore diameter used in gas separation. (*d*) Solution-diffusion used in gas, RO, PV. Molecule dissolves in the membrane and diffuses through. Not shown: Electrodialysis membranes and metallic membranes for hydrogen.

membrane thickness is unknown. Flux is specific for the membrane, for the application, for the operating conditions, and usually for time. Some generalization is possible. The rate-limiting step is very different among the operations, and membrane operations have quite different equations for flux.

Fouling Flux declines with time in most membrane operations. A decline to 80 percent of initial output can take minutes or months. The principal cause is fouling, defined as an irreversible decline in output resulting from interaction with components in the feed. "Irreversible" is not synonymous with permanent, and describes a decline that can't be recovered by merely restoring a previous set of process conditions. Cleaning is a common way of restoring much or all of a fouled membrane's former output. Some forms of fouling are permanent, such as those that change membrane structure. Compaction, resulting from polymer creep, is permanent but is not fouling.

Membrane Types A detailed taxonomy of membranes is beyond the scope of this handbook. Membranes may be made from physical solids (metal, ceramic, etc.), homogeneous films (polymer, metal, etc.), heterogeneous solids (polymer mixes, mixed glasses, etc.), solutions (usually polymer), asymmetric structures, and liquids.

Ceramic membranes are quite important since microporous ceramics are the principal barrier in UF_6 separation. Similar devices are used for microfiltration membranes and to a lesser extent for ultrafiltration. Homogeneous films are transformed into microporous devices by irradiation followed by selective leaching of the radiation damaged tracks, by stretching (Gortex® is one well-known example), or by electrochemical attack on aluminum. A few membranes are made by selective leaching of one component from a solid, as in membranes derived from glass or by selective extraction of polymer blends.

Liquid membranes are a specialty, either adsorbed in capillaries or emulsified. They are much studied, but little commercial application is found.

Polymeric membranes dominate the membrane separation field because they are well developed and quite competitive in separation performance and economics. Their usual final form is as **hollow fibers** or **capillaries** or as **flat sheet,** either of which is incorporated into a large module. Fiber-type membranes are solution or melt spun, and undergo some sort of transformation into a membrane shortly after the spinning head. **Thermal inversion** involves quenching a solution to a temperature regime where the polymer precipitates. **Solvent spinning** involves quenching in a nonsolvent, such as water, to produce a highly heterogeneous structure. Flat sheet membrane is made by preparing a casting dope of polymer in solvent, then casting it into a uniform film, then removing the solvent or introducing a nonsolvent (usually both) in such a way as to produce a membrane with a thin, active, separating layer backed by a porous, but mechanically robust sublayer.

An important variant is the composite membrane in which a relatively porous membrane (which often has its own skin) is coated by an even more selective layer, applied by a technique resulting in a very thin separating layer.

Module Types The term "module" is universally used, but the definitions vary. Here, a **module** is the simplest membrane element that can be used in practice. (Figs. 22-48 to 22-53). Module design must deal with five major issues, plus a host of minor ones. First is economy of manufacture. Second, a module must provide support and seals to maintain membrane integrity against damage and leaks. Third, it must deploy the feed stream so as to make intimate contact with the membrane, provide sufficient mass transfer to keep polarization in control, and do so with a minimum waste of energy. Fourth, the module must permit easy egress of permeate. Fifth, the module must permit the membrane to be cleaned when necessary. Many module types have been invented, quite a few were used commercially, but the winning designs as of 1996 are variations on a few simple themes.

Hollow Fiber-Capillary Hollow fiber refers to very small diameter membranes. The most successful one has an outer diameter of only 93 μm and is used for reverse osmosis. Capillary membranes are larger-diameter membranes used for liquid separations. The distinction between them has blurred to the point where there is a virtual continuum of membrane diameters for gases and liquids from the smallest all the way up to 25-mm tubes.

Gas separation membranes have diameters as small as 135 μm outer diameter by 95 μm inner diameter. For low-pressure applications such as air, they may run with tube-side feed. Gas membranes operating at high pressure (above 1.5 MPa) are almost always run with shell-side feed. The outer diameter for gas membranes may be as high as 500 μm.

Self-supported cylindrical membranes for liquid separations are made from 250 μm up to 6 mm, but there is no obvious limit to future offerings. Membrane devices for liquids are almost always tube-side feed, with two major exceptions at the extremes of porosity. High-pressure RO is almost always shell-side feed, and one supplier of very low-pressure MF also runs with shell-side feed.

All types of membrane in this configuration are fashioned into modules by potting the ends with a curable liquid (Figs. 22-49 and 22-50).

Tubular Tubular membranes (Fig. 22-51) are supported by a pressure vessel, usually perforated or porous. It can be as simple as a wrapped nonwoven fabric, or as robust as a stainless-steel tube. All run with tube-side feed. They are mainly used for UF, with some RO applications, particularly for food and dairy. The primary diameters available are 12 and 25 mm. Tubes are often connected in series; parallel bundles, gasketed or potted, are also common.

Monolith Ceramic membranes are usually monoliths of tubular capillaries (Fig. 22-52), although one supplier has square passages. Channel sizes are in the millimeter range. By strict definition, a monolith becomes a module by attaching end fittings and a means of permeate collection. In practice, many monoliths are usually incorporated into one modular housing.

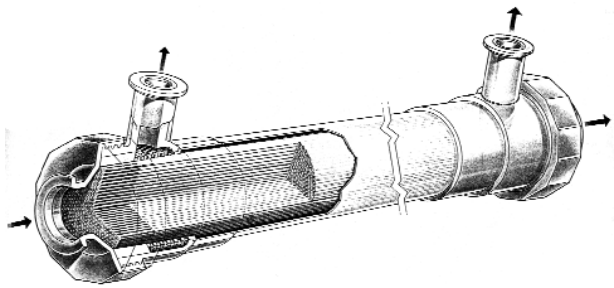


FIG. 22-49 Cutaway view of low-pressure capillary-membrane module. (*Courtesy Pall Corporation.*)

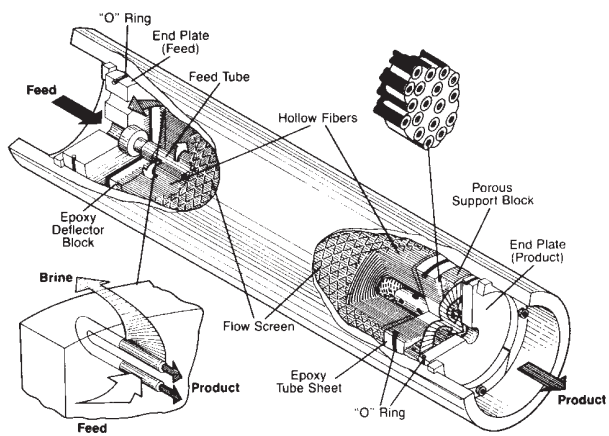


FIG. 22-50 Cutaway view of high-pressure hollow-fine-fiber reverse-osmosis module. (*Courtesy DuPont.*)

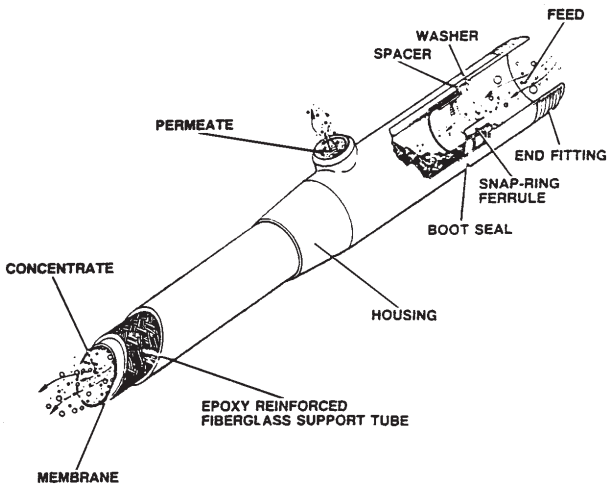


FIG. 22-51 25-mm diameter tubular-membrane assembly. (*Courtesy Koch Membrane Systems.*)

Spiral Flat-sheet membrane may be fashioned into an inexpensive and compact module by spiral winding (Fig. 22-53). Membrane is laminated with a feed spacer separating two sheets of membrane. The permeate side of the membrane contacts a fluid-conductive fabric, in turn connected to a perforated central pipe. The edges are glued to make a complete seal between the feed and permeate sides of the device, and the finished round module is fitted into a pressure vessel where feed enters through one face of the cylinder and leaves through the other. Permeate is collected from the central tube. Multiple leaves are used because the pressure drop in the permeate-conducting fabric becomes limiting at leaf lengths much over 1 m. The spiral-wound

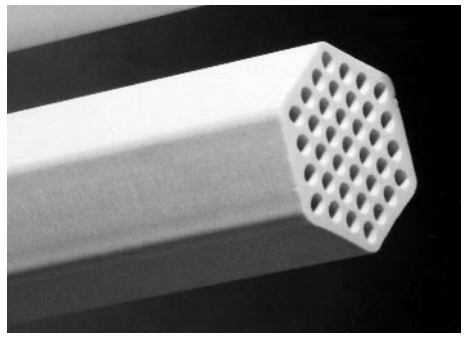


FIG. 22-52 Ceramic element cutaway. Membrane is inside 3 mm circular channels. (*Courtesy SCT/U.S. Filter.*)

membrane module is now a highly evolved device, made as large as 16 inches (400 mm) in diameter, using many leaves. It has slowly increased its market share and is now the dominant design (meaning the "base case" against which other module types are measured) in RO and UF. Spiral-wound modules are occasionally used in gas separation and pervaporation.

Plate-and-Frame Conceptually the simplest, it is very much like a filter press. Once found in RO, UF, and MF, it is still the only module commonly used in electrodialysis (ED). A few applications in pressure-driven membrane separation remain (see Sec. 18 for a description of a plate-and-frame filter press).

Other The cassette (Fig. 22-54), a modification of a plate-and-frame device that is favored because of the ease of scale-up from laboratory to small plants is widely used in pharmaceutical microfiltration and ultrafiltration. An entirely different module also called a **cassette** is used in the MF of water. There are a host of other clever module designs in use, and new ones appear frequently.

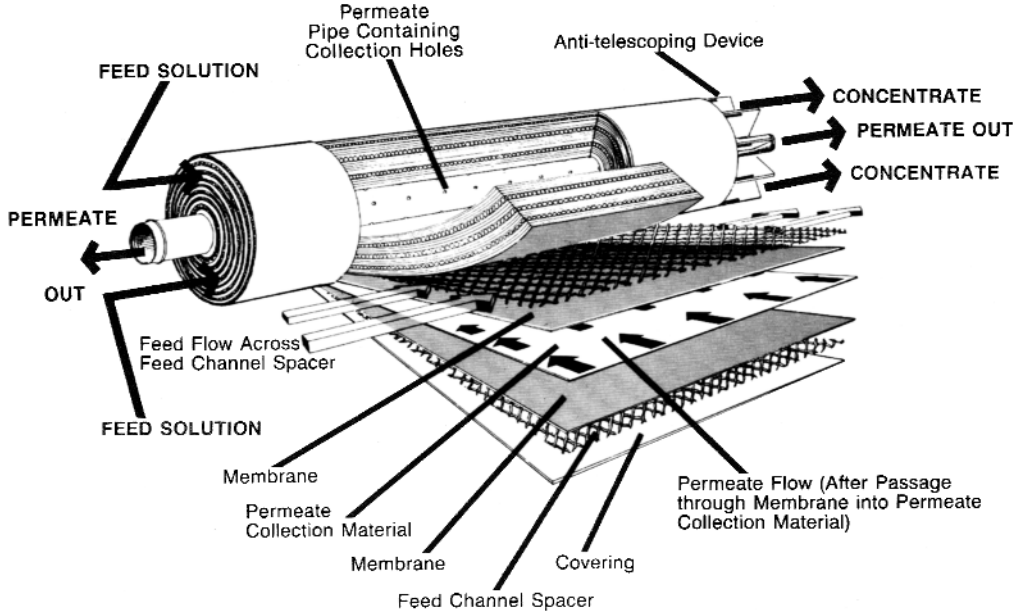


FIG. 22-53 Spiral-wound module used in many membrane processes. Permeate collection material is wound on a perforated permeate pipe. A membrane "sandwich" is constructed over the permeate carrier using glue seams as seals. Membrane "sandwiches" are separated by feed-channel spacers, through which the feed stream is passed. (*Courtesy Koch Membrane Systems.*)

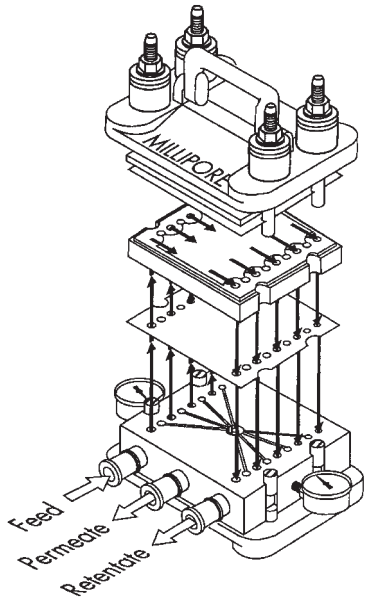


FIG. 22-54 Exploded view of cassette membrane assembly. (*Courtesy Millipore Corporation.*)

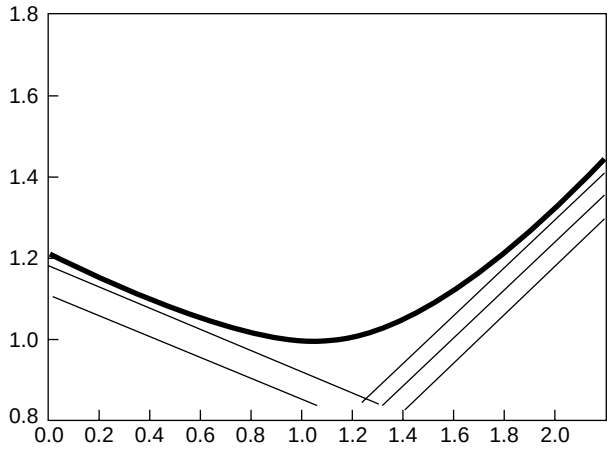


FIG. 22-55 Typical capital-cost schematic for membrane equipment showing trade-off for membrane area and mechanical equipment. Lines shown are from families for parallel lines showing limiting costs for membrane and for ancillary equipment. Abscissa: Relative membrane area installed in a typical membrane process. Minimum capital cost is at 1.0. Ordinate: Relative cost. Line with positive slope is total membrane cost. Line with negative slope is total ancillary equipment cost. Curve is total capital cost. Minimum cost is at 1.0.

Economics The economics of each membrane process are distinct, but there is an underlying concept that is almost universal. What all membrane processes have in common is a membrane device per se, having a characteristic economy of scale cost = $r(\text{area})^a$, and equipment surrounding and supporting the membrane having an economy of scale cost = $s(\text{size})^b$. r and s are empirical constants. For all membrane equipment, $a > b$. For almost any membrane separation, there is a trade-off between the amount of membrane area required and the supporting equipment. Where polarization is the rate-limiting step, the designer can put in more pumps, supplying more depolarizing energy, thereby achieving higher fluxes and using less membrane. The result is lower investment for membranes, higher investment for pumps and pipes, higher energy operating costs, and lower membrane replacement costs. Similar arguments apply to operations that are not polarization limited, since they are then limited by some other physical factor such as pressure. In every installation, there is a trade-off between adding more membrane area and more ancillary equipment to make the membrane installed more productive. The values r and s vary with the *kind* of membranes and ancillary equipment used. Systems based on different *kinds* of membranes, ceramic versus organic, for example, will have different multipliers r although the exponent a should be about the same.

Figure 22-55 is a characteristic schematic of the balance between membrane area and ancillary equipment for a particular plant. For actual cases studied, the cost of membrane and its immediately related costs (manifolds, housings, etc.) varied with the 0.9 power of area. The cost of ancillary equipment (pumps, pipes, etc.) varied with the 0.4 power of size. Total capital cost represents the sum of the membrane related and the ancillary equipment, shown in Fig. 22-55 as a curve with a minimum at the point 1, 1. As the curve moves away from the minimum, costs rise approaching a line with slope 0.9 as membrane area increases, representing in the limit the cost of membrane. Moving to the left, the costs approach a line with slope –0.4, representing in the limit the costs of ancillary equipment. It is obvious that every plant needs some of both. For both membrane and ancillary equipment, there will be a series of parallel lines depending on the values of r and s for the different *kinds* of equipment chosen for the separation. For example, substituting a ceramic membrane for an organic membrane does not imply that the *kind* of pumping equipment employed will change. Assuming the ceramic membrane is costlier, using a membrane cost cure shifted upward will change the optimum-cost point, shifting it to the left.

An important caveat: The lines are shown as continuous functions, a considerable oversimplification. Pumps, pipes, valves, and even membrane assemblies come in discrete sizes and capacities, sometimes giving a project cost with a sharper minimum and one displaced from the ideal minimum. Every process has different characteristics, but the general shape of a broad economic minimum is characteristic.

Another similar curve can be drawn for total operating costs. The three biggest elements in operating costs are usually capital charges, membrane replacement, and energy. For most industrial installations, capital charges dominate everything. For municipal and a few other installations, power cost and membrane replacement are often of greater magnitude. Depending on the local economics and the process, the total operating cost minimum may be shifted a bit to the right or the left of the capital cost minimum, but usually not by a great amount. If membrane life is short, the optimum will move left, while if energy is costly, it will move right.

ELECTRODIALYSIS

General References: This section is based on three publications by Heiner Strathmann, to which the interested reader is referred for greater detail [chap. 6, pp. 213–281, in Noble and Stern (eds.), op. cit.; sec. V, pp. 217–262, in Ho and Sirkar, op. cit.; chap. 8, pp. 8-1–8-53, Baker et al., op. cit.].

Process Description *Electrodialysis* (ED) is a membrane separation process in which ionic species are separated from water, macrosolutes, and all uncharged solutes. Ions are induced to move by an electrical potential, and separation is facilitated by ion-exchange membranes. Membranes are highly selective, passing either anions or cations and very little else. The principle of ED is shown in Fig. 22-56.

The feed solution containing ions enters a compartment whose walls are a cation-exchange and an anion-exchange membrane. If the anion-exchange membrane is in the direction of the anode, as shown for the middle feed compartment, anions may pass through that membrane in response to an electrical potential. The cations can likewise

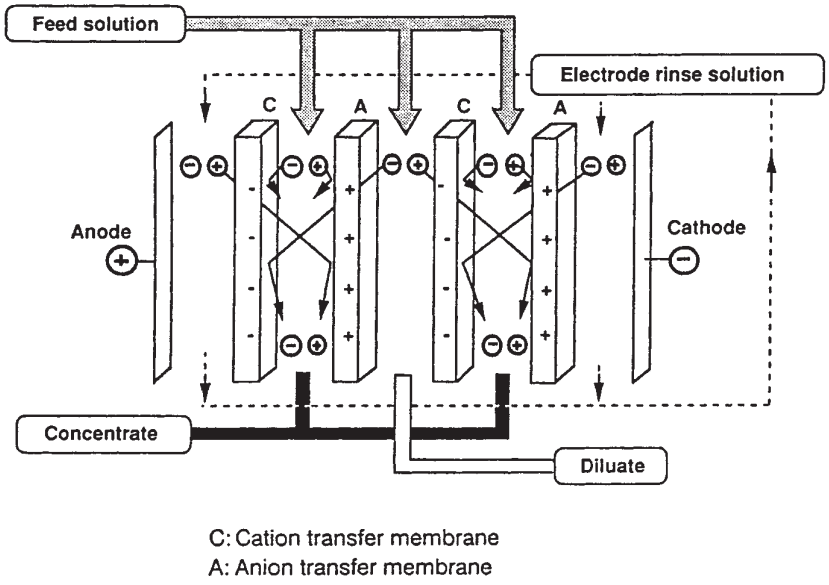


FIG. 22-56 Schematic diagram of electrodialysis. Solution containing electrolyte is alternately depleted or concentrated in response to the electrical field. Feed rates to the concentrate and diluate cells need not be equal. In practice, there would be many cells between electrodes.

move toward the cathode. When the ions arrive in the adjacent compartments, however, their further progress toward the electrodes is prevented by a membrane having the same electrical charge as the ion. The two feed compartments to the left and right of the central compartment are concentrate compartments. Ions entering these two compartments, either in the feed or by passing through a membrane, are retained, either by a same-charged membrane, or by the EMF driving the operation. The figure shows two cells (four membranes) between anode and cathode. In an industrial application, a membrane stack can be composed of hundreds of cells, where mobile ions are alternately being depleted and concentrated.

Many related processes use charged membranes and/or EMF. Electrodialytic water dissociation (water splitting), diffusion dialysis, Donnan dialysis, and electrolysis are related processes. **Electrolysis** (chlorine-caustic) is a process of enormous importance much of which is processed through very special membranes.

Leading Examples Electrodialysis has its greatest use in removing salts from brackish water, where feed salinity is around 0.05–0.5 percent. For producing high-purity water, ED can economically reduce solute levels to extremely low levels as a hybrid process in combination with an ion-exchange bed. ED is not economical for the production of potable water from seawater. Paradoxically, it is also used for the concentration of seawater from 3.5 to 20 percent salt. The concentration of monovalent ions and selective removal of divalent ions from seawater uses special membranes. This process is unique to Japan, where by law it is used to produce essentially all of its domestic table salt. ED is very widely used for deashing whey, where the desalted product is a useful food additive, especially for baby food.

Many ED-related processes are practiced on a small scale, or in unique applications. Electrodialysis may be said to do these things well: separate electrolytes from nonelectrolytes and concentrate electrolytes to high levels. It can do this even when the pH is very low. ED does not do well at: removing the last traces of salt (although the hybrid process, electrodeionization, is an exception), running at high pH, tolerating surfactants, or running under conditions where solubility limits may be exceeded. Hydroxyl ion and especially hydrogen ion easily permeate both types of ED membrane. Thus, processes that generate a pH gradient across a membrane are limited in their scope.

Water splitting, a closely related process, is useful for reconstituting an acid and a base out of a salt. It is used to reclaim salts produced during neutralization.

Membranes Ion-exchange membranes are highly swollen gels containing polymers with a fixed ionic charge. In the interstices of the polymer are mobile counterions. A schematic diagram of a cation-exchange membrane is depicted in Fig. 22-57.

Figure 22-57 is a schematic diagram of a cation-exchange membrane. The parallel, curved lines represent the polymer matrix composed of an ionic, crosslinked polymer. Shown in the polymer matrix are the fixed negative charges on the polymer, usually from sulfonate groups. The spaces between the polymer matrix are the water-swollen interstices. Positive ions are mobile in this phase, but negative ions are repelled by the negative charge from the fixed charges on the polymer.

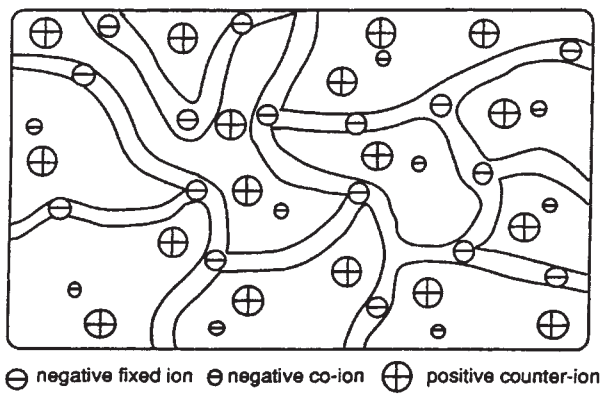


FIG. 22-57 Schematic diagram of a cation-exchange membrane showing the polymer matrix with fixed negative charges and mobile positive counterions. The density of fixed negative charges is sufficient to prevent the passage (exchange) of anions.

In addition to high permselectivity, the membrane must have low-electrical resistance. That means it is conductive to counterions and does not unduly restrict their passage. Physical and chemical stability are also required. Membranes must be mechanically strong and robust, they must not swell or shrink appreciably as ionic strength changes, and they must not wrinkle or deform under thermal stress. In the course of normal use, membranes may be expected to encounter the gamut of pH, so they should be stable from $0 < pH < 14$ and in the presence of oxidants.

Optimization of an ion-exchange membrane involves major trade-offs. Mechanical properties improve with cross-link density, but so does high electrical resistance. High concentration of fixed charges favors low electrical resistance and high selectivity, but it leads to high swelling, thus poor mechanical stability. Membrane developers try to combine stable polymeric backbones with stable ionic functional groups. The polymers are usually hydrophobic and insoluble. Polystyrene is the major polymer used, with polyethylene and polysulfone finding limited application.

Most commercial ion-exchange membranes are homogeneous, produced either by polymerization of functional monomers and cross-linking agents, or by chemical modification of polymers. Many heterogeneous membranes have been prepared both by melting and pressing a mixture of ion-exchange resin and nonfunctional polymer, or by dissolving or dispersing both functional and support resins in a solvent and casting into a membrane. Microheterogeneous membranes have been made by block and graft polymerization.

No membrane and no set of membrane properties has universal applicability. Manufacturers who service multiple applications have a variety of commercial membranes. One firm lists twenty different membranes having a broad spectrum of properties.

Cation-Exchange Membranes Polystyrene copolymerized with divinylbenzene, then sulfonated, is the major building block for cation-exchange membranes. These membranes have reasonable stability and versatility and are highly ionized over most of the pH range. Other chemistries mentioned in the literature include carboxylic acid membranes based on acrylic acid, PO_3^{2-}, HPO_2^-, AsO_3^{2-}, and SeO_3^-. Many specialty membranes have been produced for electrodialysis applications. A notable example is a membrane selective to monovalent cations made by placing a thin coating of positive charge on the cation-exchange membrane. Charge repulsion for polyvalent ions is much higher than that for monovalent ions, but the resistance of the membrane is also higher.

Anion-Exchange Membranes Quaternary amines are the major charged groups in anion-exchange membranes. Polystyrene-divinylbenzene polymers are common carriers for the quaternary amines. The literature mentions other positive groups based on N, P, and S. Anion-exchange membranes are problematic, for the best cations are less robust chemically than their cation exchange counterparts. Since most natural foulants are colloidal polyanions, they adhere preferentially to the anion-exchange membrane, and since the anion-exchange membrane is exposed to higher local pH there is a greater likelihood that precipitates will form there.

Membrane Efficiency The permselectivity of an ion-exchange membrane is the ratio of the transport of electric charge through the membrane by specific ions to the total transport of electrons. Membranes are not strictly semipermeable, for coions are not completely excluded, particularly at higher feed concentrations. For example, the Donnan equilibrium for a univalent salt in dilute solution is:

$$C_{Co}^{M} = \left(\frac{(C_{Co}^{F})^2}{C_R^M} \right) \left(\frac{\gamma_{\pm}^{F}}{\gamma_{\pm}^{M}} \right)^2 \tag{22-65}$$

where C_{Co}^{M} is the concentration of coions (the ions having the same electrical charge as the fixed charges on the membrane); C_{Co}^{F} is the concentration of such coions in the ambient solution; C_R^M is the concentration of fixed charges in the gel water of the membrane; and $\gamma_{\pm}^{F}$ and $\gamma_{\pm}^{M}$ are respectively the geometric mean of the activity coefficients of the salt ions in the ambient solution and in the membrane. Equation (22-65) is applicable only when $C_{Co}^{F} << C_R^M$. Since the membrane properties are constant, coion transport rises roughly with the square of concentration.

Process Description Figure 22-58 gives a schematic view of an ED cell pair, showing the salt-concentration profile. In the solution compartment on the left, labeled "Diluate," anions are being attracted to the right by the anode. The high density of fixed cations in membrane "A" is balanced by a high mobile anion concentration within it. Cations move toward the cathode at the left, and there is a similar high mobile cation concentration in the fixed anion membrane "C" separating the depleting compartment from the concentrating compartment further left (not shown). For the anion permeable membrane "A," two boundary layers are shown. They represent depletion in the boundary layer on the left, and an excess in the boundary layer on the right, both due to the concentration polarization effects common to all membrane processes—ions must diffuse through a boundary layer whether they are entering or leaving a membrane. That step must proceed down a concentration gradient.

With every change in ion concentration, there is an electrical effect generated by an electrochemical cell. The anion membrane shown in the middle has three cells associated with it, two caused by the concentration differences in the boundary layers, and one resulting from the concentration difference across the membrane. In addition, there are ohmic resistances for each step, resulting from the E/I resistance through the solution, boundary layers, and the membrane. In solution, current is carried by ions, and their movement produces a friction effect manifested as a resistance. In practical applications, I^2R losses are more important than the power required to move ions to a compartment with a higher concentration.

Transfer of Ions Mass transfer of ions in ED is described by many electrochemical equations. The equations used in practice are empirical. If temperature, the flux of individual components, elec-

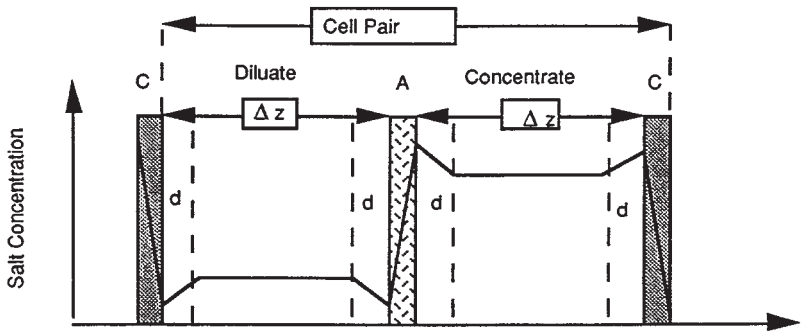


FIG. 22-58 Concentration profile of electrolyte across an operating ED cell. Ion passage through the membrane is much faster than in solution, so ions are enriched or depleted at the cell-solution interface. "d" is the concentration boundary layer. The cell gap, Δz should be small. The ion concentration in the membrane proper will be much higher than shown. (*Courtesy Elsevier.*)

troosmotic effects, streaming potential and other indirect effects are minor, an equation good to a reasonable level of approximation is:

$$J_n = C_{mn} U_{mn} \Delta\varphi/\Delta x \qquad (22\text{-}66)$$

where J is the component flux through the membrane kmol/m^2·s, C_{mn} is the concentration in phase m of component n, kmol/m^3, U_{mn} is the ion mobility of n in m, m^2/v·s, φ is the electrical potential, volts, and x is distance, m.

Equation (22-66) assumes that all mass transport is caused by an electrical potential difference acting only on cations and anions. Assuming the transfer of electrical charges is due to the transfer of ions.

$$i = F \sum_n |z_n J_n| \qquad (22\text{-}67)$$

where i is the current density, amperes/m^2, F is the Faraday constant and z is the valence. The transport number, T, is the ratio of the current carried by an ion to the current carried by all ions.

$$T_n = \frac{J_n z_n}{\sum_n J_n z_n} \qquad (22\text{-}68)$$

The transport number is a measure of the permselectivity of a membrane. If, for example, a membrane is devoid of coions, then all current through the membrane is carried by the counterion, and the transport number = 1. The transport numbers for the membrane and the solution are different in practical ED applications.

Concentration Polarization As is shown in the flow schematic, ions are depleted on one side of the membrane and enriched on the other. The ions leaving a membrane diffuse through a boundary layer into the concentrate, so the concentration of ions will be higher at the membrane surface, while the ions entering a membrane diffuse through a boundary layer from the diluate, so the bulk concentration in the diluate must be higher than it is at the membrane. These effects occur because the transport number of counterions in the membrane is always very much higher than their transport number in the solution. Were the transport numbers the same, the boundary layer effects would vanish. This concentration polarization is similar to that experienced in reverse osmosis, except that it has both depletion and enrichment components. The equations governing concentration polarization and depolarization of a membrane are given in the section describing ultrafiltration. The depolarizing strategies used for ED are similar to those employed in other membrane processes, as they involve induced flow past the membrane.

Two basic flow schemes are used: tortuous path flow and sheet flow (Fig. 22-59). Tortuous path spacers are cut to provide a long path between inlet and outlet, providing a relatively long residence time and high velocity past the membrane. The flow channel is open. Sheet flow units have a net spacer separating the membranes. Mass transfer is enhanced either by the spacer or by higher velocity.

Enhanced depolarization requires capital equipment and energy, but it achieves savings in overall capital costs (permits the use of a smaller stack) and energy (permits lower voltage.) The designer's task is to achieve an optimum balance in these requirements. Sheet-flow units have lower capital and operating costs in general, yet both sheet-flow and tortuous-flow units remain competitive. The fact that most ED reversal units (see below) are tortuous flow, and that ED reversal is the dominant technology for water and many waste treatment applications may explain the paradox.

Limiting Current Density As the concentration in the diluate becomes ever smaller, or as the current driving the process is increased, eventually a situation arises in which the concentration of ions at the membranes surrounding the diluate compartment approaches zero. When that occurs, there are insufficient ions to carry additional current, and the cell has reached the limiting current. Forcing the voltage higher results in the dissociation of water at the membrane, giving rise to a dramatic increase in pH due to OH^- ions emerging from the anion-exchange membrane. The high pH promotes precipitation of metal hydroxides and $CaCO_3$ on the membrane surface leading to flow restrictions, poor mass transfer, and subsequent membrane damage. Once a precipitate forms, its presence initiates a vicious cycle fostering the formation of more precipitates. The general expression for the limiting current density is $i_{lim} \sim (C_{bulk\ diluate})$ (diluate velocity)^m, where m is an experimental constant (often 0.6). Thus, the concentration at the membrane is limiting, and at constant current that is proportional to the bulk concentration and the mass-transfer coefficient. Flow in the compartment is laminar but mass transfer is enhanced by the spacer. A normal operating practice is to operate a stack at around 75 percent of the limiting current.

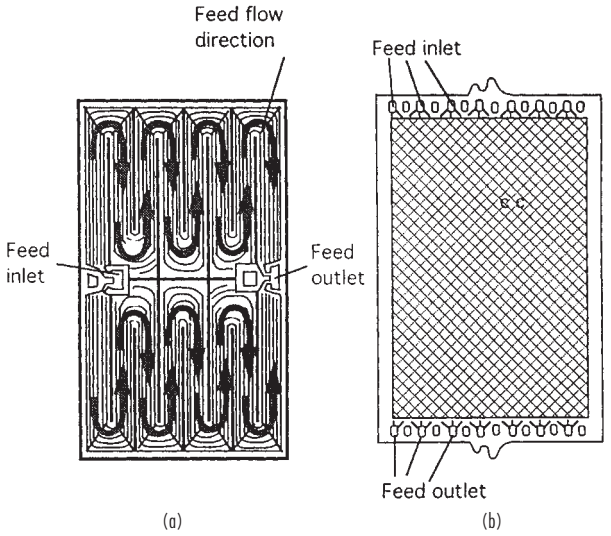


FIG. 22-59 Schematic of two ways to pass solution across an ED membrane. Tortuous flow (left) uses a special spacer to force the solution through a narrow, winding path, raising its velocity, mass transfer, and pressure drop. Sheet feed (right) passes the solution across the plate uniformly, with lower pressure drop and mass transfer. (*Courtesy Elsevier.*)

Process Configuration Figure 22-56 shows a basic cell pair. A stack is an assembly of many cell pairs, electrodes, gaskets, and manifolds needed to supply them. An exploded schematic of a portion of a sheet-flow stack is shown in Fig. 22-60.

Gaskets are very important, since they not only keep the streams separated and prevent leaks from the cell, they have the manifolds to conduct feeds, both concentrate and diluate, built into them. No other practical means of feeding the stack is used in the very cramped space required by the need to keep cells thin because the diluate has very low conductivity. The manifolds are formed by aligning holes in membrane and gasket.

The membranes are supported and kept apart by feed spacers. A typical cell gap is 0.5–2 mm. The spacer also helps control solution distribution and enhances mass transfer to the membrane. Given that an industrial stack may have up to 500 cell pairs, assuring uniform flow distribution is a major design requirement.

Since electrodialysis membranes are subject to fouling, it is sometimes necessary to disassemble a stack for cleaning. Ease of reassembly is a feature of ED.

Process Flow The schematic in Fig. 22-56 may imply that the feed rates to the concentrate and diluate compartments are equal. If they are, and the diluate is essentially desalted, the concentrate would leave the process with twice the salt concentration of the feed. A higher ratio is usually desired, so the flow rates of feed for concentrate and feed for diluate can be independently controlled. Since sharply differing flow rates lead to pressure imbalances within the stack, the usual procedure is to recirculate the brine stream using a feed-and-bleed technique This is usually true for ED reversal plants. Some nonreversal plants use slow flow on the brine side avoiding the recirculating pumps.. Diluate production rates are often 10× brine-production rates.

Electrodes No matter how many cells are put in series, there will be electrodes. The more cells, the less the relative importance of the

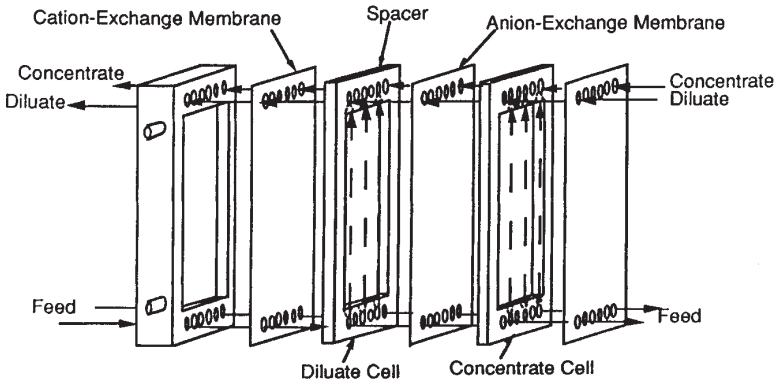


FIG. 22-60 Exploded view of a sheet-feed ED stack. Manifolds are built into the membranes and spacers as the practical way to maintain a narrow cell gap. (*Courtesy Elsevier.*)

electrodes. The cathode reactions are relatively mild, and depending on the pH:

$$2H^+ + 2e^- \rightarrow H_2$$

$$2H_2O + 2e^- \rightarrow 2OH^- + H_2$$

Anode reactions can be problematic. The anode may dissolve or be oxidized. Or, depending on the pH and the chloride concentration:

$$2H_2O \rightarrow O_2 + 4H^+ + 4e^-$$

$$4OH^- \rightarrow O_2 + 2H_2O + 4e^-$$

$$2Cl^- \rightarrow Cl_2 + 2e^-$$

Dissolution of metal is avoided by selecting a resistant material such as Pt, Pt coated on Ti, or Pt on Nb. Base metals are sometimes used, as are graphite electrodes.

Electrode isolation is practiced to minimize chlorine production and to reduce fouling. A flush solution free of chlorides or with reduced pH is used to bathe the electrodes in some plants. Further information on electrodes may be found in a work by David ["Electrodialysis," pp. 496–499, in Porter (ed.), op. cit.].

Peripheral Components In addition to the stack, a power supply, pumps for diluate and concentrate, instrumentation, tanks for cleaning, and other peripherals are required. Safety devices are mandatory given the dangers posed by electricity, hydrogen, and chlorine.

Pretreatment Feed water is pretreated to remove gross objects that could plug the stack. Additives that inhibit the formation of scale, frequently acid, may be introduced into the feed.

Electrodialysis Reversal Two basic operating modes for ED are used in large-scale installations. **Unidirectional operation** is the mode described above in the general explanation of the process. The electrodes maintain their polarity and the ions always move in a constant direction. **ED reversal** is an intermittent process in which the polarity in the stack is reversed periodically. The interval may be from several minutes to several hours. When the polarity is reversed, the identity of compartments is also reversed, and diluate compartments become concentrate compartments and vice versa. The scheme requires instruments and valves to redirect flows appropriately after a reversal. The advantages that often justify the cost are a major reduction in membrane scaling and fouling, a reduction in feed additives required to prevent scaling, and less frequent stack-cleaning requirements.

Water Splitting A modified electrodialysis arrangement is used as a means of regenerating an acid and a base from a corresponding salt. For instance, NaCl may be used to produce NaOH and HCl. Water splitting is a viable alternative to disposal where a salt is produced by neutralization of an acid or base. Other potential applications include the recovery of organic acids from their salts and the treating of effluents from stack gas scrubbers. The new component required is a bipolar membrane, a membrane that splits water into H^+ and OH^-. At its simplest, a bipolar membrane may be prepared by laminating a cation and an anion membrane. In the absence of mobile ions, water sorbed in the membrane splits into its components when a sufficient electrical gradient is applied. The intimate contact of the two membranes minimizes the problem of the low ionic conductivity of ion-depleted water. As the water is split, replacement water readily diffuses from the surrounding solution. Properly configured, the process is energy efficient.

A schematic of the production of acid and base by electrodialytic water dissociation is shown in Fig. 22-61. The bipolar membrane is inserted in the ED stack as shown. Salt is fed into the center compartment, and base and acid are produced in the adjacent compartments. The bipolar membrane is placed so that the cations are paired with OH^- ions and the anions are paired with H^+. Neither salt ion penetrates the bipolar membrane. As is true with conventional electrodialysis, many cells may be stacked between the anode and the cathode.

If recovery of both acid and base is unnecessary, one membrane is left out. For example, in the recovery of a weak acid from its salt, the anion-exchange membrane may be omitted. The process limitations relate to the efficiency of the membranes, and to the propensity for H^+ and OH^- to migrate through membranes of like fixed charge, limiting the attainable concentrations of acid and base to 3–5 N. The problem is at its worst for HCl and least troublesome for organic acids. Ion leakage limits the quality of the products, and the regenerated acids and bases are not of high enough quality to use in regenerating a mixed-bed ion-exchange resin.

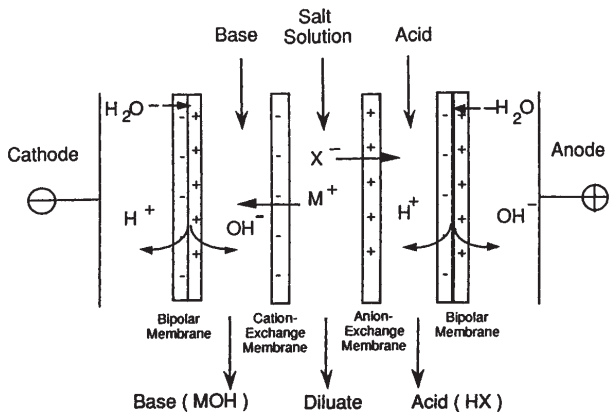


FIG. 22-61 Electrodialysis water dissociation (water splitting) membrane inserted into an ED stack. Starting with a salt, the device generates the corresponding acid and base by supplying H^+ and OH^- from the dissociation of water in a bipolar membrane. (*Courtesy Elsevier.*)

Diffusion Dialysis The propensity of H^+ and OH^- to penetrate membranes is useful in diffusion dialysis. An anion-exchange membrane will block the passage of metal cations while passing hydrogen ions. This process uses special ion-exchange membranes, but does not employ an applied electric current.

As an example, in the aircraft industry heavy-aluminum sections are shaped as airfoils, then masked. The areas where the metal is not required to be strong are then unmasked and exposed to NaOH to etch away unneeded metal for weight reduction. Sodium aluminate is generated, a potential waste problem. Cation-exchange membranes leak OH^- by a poorly understood mechanism that is not simply the transport of OH^- with its waters of hydration. The aluminate anion is retained in the feed stream while the caustic values pass through. NaOH recovery is high, because all the Na^+ participates in the driving force. There is considerable passage of water due to the osmotic pressure difference as well. This scheme operates efficiently only because aluminum hydroxide forms highly supersaturated solutions. Hydroxide precipitation within the apparatus is reported to be a minor problem. $Al(OH)_3$ is precipitated in a downstream crystallizer, and is reported to be of high quality.

Donnan Dialysis Another nonelectrical process using ED membranes is used to exchange ions between two solutions. The common application is to use H^+ to drive a cation from a dilute compartment to a concentrated one. A schematic is shown in Fig. 22-62. In the right compartment, the pH is 0, thus the H^+ concentration is 10^7 higher than in the pH 7 compartment on the left. H^+ diffuses leftward, creating an electrical imbalance that can only be satisfied by a cation diffusing rightward through the cation-selective membrane. By this scheme, Cu^{++} can be "pumped" from left to right against a significant concentration difference.

Electrodialysis-Moderated Ion Exchange The production of ultrapure water is facilitated by incorporating a mixed-bed ion-exchange resin between the membranes of an ion-exchange stack. Already pure water is passed through the bed, while an electric current is passed through the stack. Provided the ion-exchange beads are in contact with each other and with the membranes, an electrical current can pass through the bed even though the conductivity of the very pure water is quite low. In passing, the current conducts any ions present into adjacent compartments, simultaneously and continuously regenerating the resin in situ.

Energy Requirements The thermodynamic limit on energy is the ideal energy needed to move water from a saline solution to a pure phase. The theoretical minimum energy is given by:

$$\Delta G = RT \ln (a/a_s) \tag{22-69}$$

where ΔG is the Gibbs free energy required to move one mole of water from a solution, a is the activity of pure water ($\equiv 1$), and a_s is the activity of water in the salt solution. In a solution, the activity of water is approximately equal to the molar fraction of water in the solution. So that approximate activity is:

$$a_s = \frac{n_s}{n_s + \nu \cdot s_s} \qquad \frac{1}{a_s} = 1 + \frac{\nu \cdot s_s}{n_s} \tag{22-70}$$

where n_s is the number of moles of water in the salt solution, ν is the number of atoms in the salt molecule (2 for NaCl, 3 for $CaCl_2$) and s_s is the number of moles of salt in the salt solution. The ratio of moles of salt in the salt solution to the number of moles of water in the salt solution is a very small number for a dilute solution. This permits using the approximation $\ln(1+x) = x$, when x is of the magnitude 0.01, making this an applicable approximation for saline water. That permits rewriting Eq. (22-69) as:

$$\Delta G = \nu RT(s_s/n_s) \tag{22-71}$$

where ΔG is still the free energy required to move one mole of water from the saline solution to the pure water compartment.

The conditions utilized in the above development of minimum energy are not sufficient to describe electrodialysis. In addition to the desalination of water, salt is moved from a saline feed to a more concentrated compartment. That free-energy change must be added to the free energy given in Eq. (22-71), which describes the movement of water from salt solution, the reverse of the actions in the diluate compartment (but having equal free energy). *Schaffer & Mintz* develop that change, and after solving the appropriate material balances, they arrive at a practical simplified equation for a monovalent ion salt, where activities may be approximated by concentrations:

$$\Delta G = RT(C_f - C_d)\left(\frac{\ln C_{fc}}{C_{fc} - 1} - \frac{\ln C_{fd}}{C_{fd} - 1}\right); C_{fc} = \frac{C_f}{C_c}; C_{fd} = \frac{C_f}{C_d} \tag{22-72}$$

where C_f is the concentration of ions in the feed, C_d is the concentration in the diluate, and C_c is the concentration in the concentrate, all in kmol/m^3. When $C_{fc} \to 1$ and $C_{fd} \to$ infinity, the operation is one approximating the movement of salt from an initial concentration into an unlimited reservoir of concentrate, while the diluate becomes pure. This implies that the concentrate remains at a constant salt concentration. In that case, Eq. (22-72) reduces to $RT(C_f - C_d)$. As a numerical example of Eq. (22-72) consider the desalting of a feed with initial concentration 0.05 M to 0.005 M, roughly approximating the production of drinking water from a saline feed. If 10 ℓ of product are produced for every 3 ℓ of concentrate, the concentrate leaves the process at 0.2 M. The energy calculated from Eq. (22-72) is 0.067 kWh/m^3 at 25°C. If the concentrate flow is infinite, $C_c = 0.05$ M, and the energy decreases to 0.031 kWh/m^3.

This minimum energy is that required to move ions only, and that energy will be proportional to the ionic concentration in the feed. It assumes that all resistances are zero, and that there is no polarization. In a real stack, there are several other important energy dissipaters. One is overcoming the electrical resistances in the many components. Another is the energy needed to pump solution through the stack to reduce polarization and to remove products. Either pumping or desalting energy may be dominant in a working stack.

Energy Not Transporting Ions Not all current flowing in an electrodialysis stack is the result of the transport of the intended ions. Current paths that may be insignificant, minor, or significant include electrical leakage through the brine manifolds and gaskets, and transport of co-ions through a membrane. A related indirect loss of current is water transport through a membrane either by osmosis or with solvated ions, representing a loss of product, thus requiring increased current.

Pump Energy Requirements If there is no forced convection within the cells, the polarization limits the current density to a very uneconomic level. Conversely, if the circulation rate is too high, the energy inputs to the pumps will dominate the energy consumption of the process. Furthermore, supplying mechanical energy to the cells raises the pressure in the cells, and raises the pressure imbalance between portions of the stack, thus the requirements of the confining gear and the gaskets. Also, cell plumbing is a design problem made more difficult by high circulation rates.

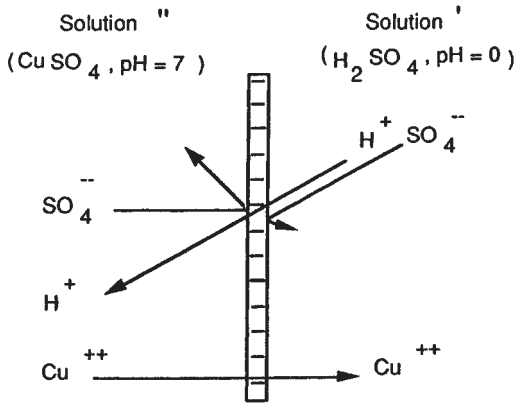


FIG. 22-62 Schematic of Donnan dialysis using a cation-exchange membrane. Cu^{2+} is "pumped" from the lower concentration on the left to a higher concentration on the right maintaining electrical neutrality accompanying the diffusion of H^+ from a low pH on the right to a higher pH on the left. The membrane's fixed negative charges prevent mobile anions from participating in the process. (*Courtesy Elsevier.*)

A rule of thumb for a modern ED stack is that the pumping energy is roughly 0.5 kWh/m^3, about the same as is required to remove 1700 mg/ℓ dissolved salts.

Equipment and Economics A very large electrodialysis plant would produce 500 ℓ/s of desalted water. A rather typical plant was built in 1993 to process 4700 m^3/day (54.4 ℓ/s). Capital costs for this plant, running on low-salinity brackish feed were $1,210,000 for all the process equipment, including pumps, membranes, instrumentation, and so on. Building and site preparation cost an additional $600,000. The building footprint is 300 m^2. For plants above a threshold level of about 40 m^3/day, process-equipment costs usually scale at around the 0.7 power, not too different from other process equipment. On this basis, process equipment (excluding the building) for a 2000 m^3/day plant would have a 1993 predicted cost of $665,000.

The greatest operating-cost component, and the most highly variable, is the charge to amortize the capital. Many industrial firms use capital charges in excess of 30 percent. Some municipalities assign long amortization periods and low-interest rates, reflecting their cost of capital. Including buildings and site preparation, the range of capital charges assignable to 1000 m^3 of product is $90 to $350.

On the basis of 1000 m^3 of product water, the operating cost elements (as shown in Table 22-16) are anticipated to be:

TABLE 22-16 Electrodialysis Operating Costs

$ 66	Membrane-replacement cost (assuming seven-year life)
32	Plant power
16	Filters and pretreatment chemicals
11	Labor
8	Maintenance
$133	Total

These items are highly site specific. Power cost is low because the salinity removed by the selected plant is low. The quality of the feed water, its salinity, turbidity, and concentration of problematic ionic and fouling solutes, is a major variable in pretreatment and in conversion.

REVERSE OSMOSIS AND NANOFILTRATION

Process Description *Reverse osmosis* (RO) and *nanofiltration* (NF) processes utilize a membrane that selectively restricts flow of solutes while permitting flow of the solvent. The processes are closely related, and NF is sometimes called "loose RO." They are kinetic processes, not equilibrium processes. The solvent is almost always water.

Leading Examples

Potable Water RO and NF both play a major role in providing potable water, defined either by the WHO criterion of <1000 ppm *total dissolved solids* (TDS) or the U.S. EPA limit of 500 ppm TDS. RO is most prominent in the Middle East and on islands where potable-water demand has outstripped natural supply. A plant awaiting startup at Al Jubail, Saudi Arabia produces over 1 m^3/s of fresh water (see Table 22-17). Small units are found on ships and boats. Seawater RO competes with *multistage flash distillation* (MSF) and *multieffect distillation* (MED) (see Sec. 13: "Distillation"). It is too expensive to compete with conventional civil supply (canals, pipelines, wells) in most locations. Low-pressure RO and NF compete with electrodialysis for the desalination of brackish water. The processes overlap economically, but they are sufficiently different so that the requirements of the application often favor one over the others.

TABLE 22-17 Water Volume Conversion Factors

To convert	Into	Multiply by	Inverse
1000 U.S. gallons	Cubic meters	3.785	0.2642
Acre-feet	Cubic meters	1233	8.11×10^{-4}
100 cubic feet	Cubic meters	2.831	0.3532
k-gal/day	m^3/s	4.381×10^{-5}	22,827
MGD	m^3/s	4.381×10^{-2}	22.827

Ocean water has an osmotic pressure of about 2.6 MPa, with some locations as high as 3.5 MPa. Recovery (r) is normally around 45 percent, occasionally higher. Osmotic pressure in the concentrate rises as $1/(1 - r)$ and significant overpressure (at least 1 MPa) is required to maintain good-quality permeate. Normal operating pressures are 6–8 MPa.

Brackish water has lower TDS than seawater. It ranges from diluted seawater to natural sources containing various salts. Some of the sources are quite large, and they may provide an attractive supplemental source of potable water. Disposal of the concentrate (brine) can be a problem for inland aquifers.

Where the TDS in water supplies is above the taste threshold, or where there is concern about the safety of the water supply, simple RO systems operating on line pressure have made a major impact. These compact units are usually kitchen installed, and are simple, small, and cheap. For typical line pressure of 400 kPa, 95 percent reduction of TDS is feasible if the inlet concentration is below 2000 mg/ℓ.

Process Water Purification Boiler feed water is a major process application of RO. Scalants and colloids are particularly well rejected by membranes, and TDS is reduced to a level that makes ion exchange or continuous deionization for the residual ions very economical. Even the extremely high quality water required for nuclear power plants can be made from seawater. The ultra-high quality water required for production of electronic microcircuits is usually processed starting with two RO systems operating in series, followed by many other steps.

Process Dewatering Applications RO is useful in many small applications where there is a volume of water containing a small amount of contaminant. RO is often able to recover most of the water at a purity high enough for reuse. The waste is concentrated making its disposal less costly, which generally pays for the recovery process.

Food and Beverage Applications RO achieved modest success in dewatering and concentrating food streams. The first food application pursued by early workers was the dewatering of orange juice prior to freezing. Cheryan [in Noble and Stern (eds.), op. cit., p. 452] describes a proprietary process that achieves high quality and high concentration by removing the flavor-laden phase first, concentrating the sugar stream with tight RO, then at high sugar concentrations using looser membranes to reduce $\Delta\Pi$ (concentrate-permeate). The high sugar permeate from the final stage is recycled through a lower-concentration stage, from which permeate is rejected. Cheryan provides a process schematic on p. 456. Apple-juice concentration has received much attention, but commercial success has been elusive. Other membrane processes are widely used in the juice industry, but for concentration applications, high osmotic pressure and flavor leakage through the membrane are barriers to wider adoption. After many years only a few plants are in operation.

Whey concentration, both of whole whey and ultrafiltration permeate, is practiced successfully, but the solubility of lactose limits the practical concentration of whey to about 20 percent total solids, about a 4× concentration factor. (Membranes do not tolerate solids forming on their surface.) Nanofiltration is used to soften water and clean up streams where complete removal of monovalent ions is either unnecessary or undesirable. Because of the ionic character of most NF membranes, they reject polyvalent ions much more readily than monovalent ions. NF is used to treat "salt whey," the whey expressed after NaCl is added to curd. Nanofiltration permits the NaCl to permeate while retaining the other whey components, which may then be blended with ordinary whey. NF is also used to deacidify whey produced by the addition of HCl to milk in the production of casein.

Basic Principles of Operation RO and NF are pressure-driven processes where the solvent is forced through the membrane by pressure, and the undesired coproducts frequently pass through the membrane by diffusion. The major processes are rate processes, and the relative rates of solvent and solute passage determine the quality of the product. The general consensus is that the solution-diffusion mechanism describes the fundamental mechanism of RO membranes, but a minority disagrees. Fortunately, the equations presented below describe the observed phenomena and predict experimental outcomes regardless of mechanism.

Driving Force For RO and NF, Eq. (22-62) becomes:

$$J = \frac{\mathsf{r}_w}{} (P_f - P_p) - (\Pi_f - \Pi_p) = \frac{\mathsf{r}_w}{} (\Delta P - \Delta\Pi) \qquad (22\text{-}73)$$

where r_w is the water permeability of the membrane, $m^2/Pa{\cdot}s$, and the subscripts f and p refer to feed and permeate. Π is the osmotic pressure, Pa. Since the thickness of the active layer z is almost never known, Eq. (22-73) is usually modified to the form

$$J = \left(\frac{1}{R_m + R_n \cdots}\right)(\Delta P - \Delta\Pi) \qquad (22\text{-}74)$$

where R_m is the membrane resistance, Pa·s/m. Other resistance terms $(R_n \cdots)$ may be added, such as terms for fouling or compaction. Normally, the important terms are the inherent membrane resistance, the driving pressure P, and the osmotic pressure in the feed, Π. For a high rejection RO membrane, the back-pressure and pressure terms for the permeate are insignificant. For most work, the van't Hoff approximation for osmotic pressure gives an adequate estimate:

$$\Pi = \nu n_s RT \qquad (22\text{-}75)$$

where νn_s is the total concentration of ions, $kmol/m^3$ [Eq. (22-71)] and $R = 8.313$ $kPa{\cdot}m^3/kmol{\cdot}K$. This equation should not be used for any unusually high concentration operation, or where accuracy is important.

Salt flux across a membrane is due to effects coupled to water transport, usually negligible, and diffusion across the membrane. Eq. (22-60) describes the basic diffusion equation for solute passage. It is independent of pressure, so as $\Delta P - \Delta\Pi \to 0$, rejection $\to 0$. This important factor is due to the kinetic nature of the separation. Salt passage through the membrane is concentration dependent. Water passage is dependent on $P - \Pi$. Therefore, when the membrane is operating near the osmotic pressure of the feed, the salt passage is not diluted by much permeate water.

The flux equation assumes constant temperature. As T rises, Π rises slowly, but around 25°C the viscosity of water drops enough to produce about a 3 percent rise in flux per °C.

Effects of Operating Variables Figure 22-63 shows trends in effects as various operating variables change in RO. Similar effects apply to NF.

RO and NF Membranes Nanofiltration membranes, sometimes called "loose RO," are more open than RO, and lie between reverse osmosis and ultrafiltration. This definition is not precise. NF membranes are usually negatively charged composite membranes. Donnan exclusion is an important rejection mechanism for charged membranes, and charged NF membranes reject polyvalent anions to a much greater degree than monovalent ions. They are usually tight enough to reject uncharged solutes heavier than a few hundred daltons and can, under ideal conditions, be highly retentive to lactose while passing most monovalent salts in a whey stream. Degrees of ion passage are strongly concentration dependent, with all rejections of charged ions dropping rapidly with increasing ionic strength. $MgSO_4$ rejection may remain high while NaCl rejection drops at around a few thousand ppm.

Methods of Production Modern RO and NF membranes are of two basic types. The more traditional is the asymmetric (skinned) membrane formed by the addition of a nonsolvent to a thin coating of homogeneous polymer solution. As solvent leaves the polymer solution and nonsolvent enters it, the surface polymer precipitates which alters the mechanism of solvent-nonsolvent interchange in the layers below. Thus the top layer, or skin, has a fundamentally different structure. Researchers have learned techniques for preparing membranes with widely differing properties, including some with excellent salt rejection properties. Membranes may be made either in flat sheet or fiber form using this technique. Strathmann [in Porter (ed.), op. cit., pp. 1–60] gives a complete summary.

The second major membrane type is a composite. Starting with a loose asymmetric membrane, usually a UF membrane, a coating is applied which is polymerized in situ to become the salt rejecting membrane. This process is used for most high-performance flat-sheet RO membranes, as well as for many commercial nanofiltration membranes. The chemistry of the leading RO membranes is known, but details on NF membranes are mostly proprietary. It may be inferred from published properties that various chemical approaches are utilized. Further information on composites may be found in Petersen [*J. Membrane Sci.*, **83,** 81–150 (1993)].

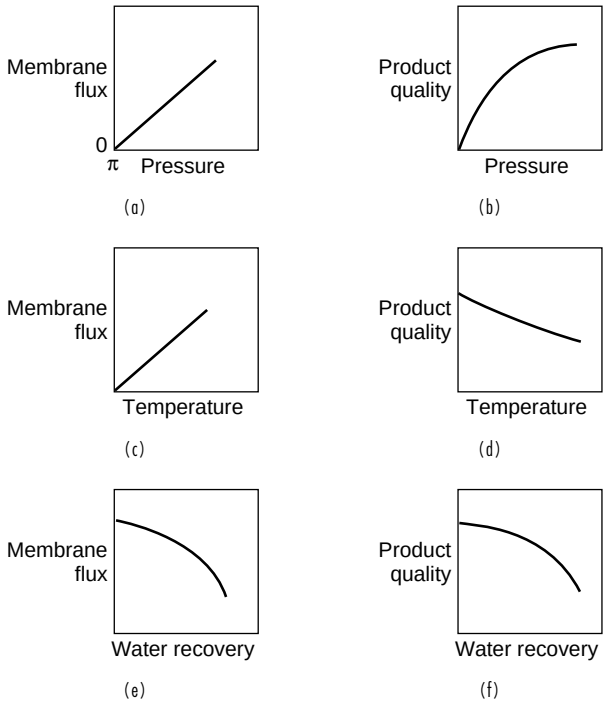


FIG. 22-63 Effects of operating variables on the performance of an RO membrane. (*a*) Water passage increases with pressure, assuming Π is constant. (*b*) Solute rejection rises with pressure, since solvent flux increases and solute diffusion does not. (*c*) Flux rises with temperature because viscosity declines. (*d*) Solute rejection declines with a temperature rise because of the osmotic pressure increase with temperature and because solute passage has a higher activation energy than does solvent passage. (*e*) Flux declines with increasing solute concentration, an osmotic-pressure effect. (*f*) At low-feed velocity past the membrane, solute is polarized at the membrane, while as velocity increases, mass transfer redisperses more of the polarized solute, lowering the effective solute concentration at the membrane. (Rejection is measured between permeate and bulk-feed concentration.) Bulk concentration of salt rises with recovery.

Membrane Characterization Membranes are always rated for flux and rejection. NaCl is always used as one measure of rejection, and for a very good RO membrane, it will be 99.7 percent or more. Nanofiltration membranes are also tested on a larger solute, commonly $MgSO_4$. Test results are very much a function of how the test is run, and membrane suppliers are usually specific on the test conditions. Salt concentration will be specified as some average of feed and exit concentration, but both are bulk values. Salt concentration at the membrane governs performance. Flux, pressure, membrane geometry, and cross-flow velocity all influence polarization and the other variables shown in Fig. 22-63.

Membrane Limitations Chemical attack, fouling, and compaction are prominent problems with RO and NF membranes. Compaction is the most straightforward. It is the result of creep, slow cold flow of the polymer resulting in a loss of water permeability. It is measured by the slope of log flux versus log time in seconds. It is independent of the flux units used and is reported as a slope, sometimes with the minus sign omitted. A slope of –0.001, typical for noncellulosic membranes, means that for every threefold increase in log(time), 10^3 seconds, a membrane looses 10 percent of its flux. Since membranes are rated assuming that the dramatic early decline in permeability has already occurred, the further decline after the first few weeks is very slow. Compaction is specific to pressure, temperature, and envi-

ronment.

Fouling is defined in "Background and Definitions" and is a significant problem in most process applications, and somewhat of a problem in most water applications. RO membranes may be fouled by sparingly soluble scalants which supersaturate at the membrane.

Chemical attack is often a result either of fouling prevention or cleaning in response to fouling. Chlorine and hypochlorite damage most RO and NF membranes, as do oxidants generally (see discussion of chlorine tolerance below).

Process Limitations

Osmotic Pressure In RO, and to a great extent NF, osmotic pressure is a critically important design consideration. A proper thermodynamic treatment of osmotic pressure may be found in Cheryan (op. cit., p. 13). Osmotic pressure is always calculated for the bulk-feed stream. It varies along the membrane train as salt concentration rises. The osmotic pressure that really matters is the one at the membrane, higher by the amount polarization raises the concentration there. As a general rule for a new membrane application, the inlet concentration is limited to about 0.5 N, for which $\Pi \approx 2.5$ MPa, giving a final concentrate Π of 5 MPa for 50 percent conversion. A few systems may be designed at much higher pressure, notably one of Du Pont's hollow fiber bundles, which is rated at 8 MPa. It is rated for 65 percent conversion on ocean water, and can concentrate sucrose to 60 percent using a special technique and membrane. Much of the appeal of NF membranes is their low-pressure operation.

Membrane Chemistry Three chemical families dominate the RO-NF membrane industry. Many other products are made on a small scale, and the field continues to attract significant R&D resources. But three types command most of the market.

Cellulose esters are the oldest. *Cellulose acetate* (CA) blend, a mixture of cellulose acetate (40.1 percent acetyl) and triacetate (43.2 percent acetyl) is the major polymer used; some cellulose triacetate and cellulose acetate-butyrate are used as well. Outstanding features of CA are its known behavior in many applications over many years, its slower fouling rate in some applications, its relative tolerance to chlorine, and foremost, its low cost. Where CA works well, there is little incentive to replace it by other materials. It has outstanding weaknesses including chemical and pH susceptibility, possible biodegradation, high compaction especially at elevated temperature, and poor rejection for organic solutes (due to their high solubility in CA). It is usually made as flat sheet, and occasionally as fibers.

Aromatic polyamide (aramid) membranes are a copolymer of 1-3 diaminobenzene with 1-3 and 1-4 benzenedicarboxylic acid chlorides. They are usually made into fine hollow fibers, 93 μm outer diameter by 43 μm inner diameter. Some flat sheet is made for spirals. These membranes are widely used for seawater desalination and to some extent for other process applications. The hollow fibers are capable of very high-pressure operation and have considerably greater hydrolytic resistance than does CA. Their packing density in hollow-fiber form makes them very susceptible to colloidal fouling (a permeator 8 inches in diameter contains 3 M fibers), and they have essentially no resistance to chlorine.

Cross-linked aromatic polyamides are the third major membrane type. The best known and most successful form has been an interfacially polymerized polyamide formed from 1-3 diaminobenzene and 1,3,5 benzenetricarboxylic acid chloride. This membrane is noted for excellent salt rejection and some degree of chemical resistance, including some resistance to chlorine, but it will not tolerate continuous exposure. The residual negative charge resulting from incomplete reaction and subsequent hydrolysis and ionization of the third acid-chloride group seems to help somewhat in improving its resistance to colloidal fouling. This membrane is made as flat sheet, and can be made in tubular form (13 mm inner diameter).

Chlorine Tolerance Most of the best RO membranes are attacked by oxidants, and they are particularly susceptible to chlorine. A particularly sensitive locus for attack is the amidic hydrogen. Cellulosic membranes are generally less sensitive, and pass the chlorine into the permeate giving downstream biocidal activity, very useful for under-the-sink RO. These factors are largely responsible for CA's survival in RO membranes. Chlorine, whatever its vices, has the virtue of being a known, effective, residual bactericide and a good inhibitor of bacterial growth on membranes (see fouling). It is also very useful in membrane cleaning, because not only does it kill bacteria, it breaks down some membrane deposits.

Chlorine is desirable as a bulk pretreatment biocide for inlet water, but its subsequent removal upstream of the membrane is absolutely necessary and difficult. $NaHSO_3$ is a common additive to dechlorinate before membranes. It is customarily added at 3–5 mg/l, an excess over the stoichiometric requirement. NH_3 is sometimes added to convert the chlorine to chloramine, a much less damaging biocide. Heavy metals present in seawater seem to amplify the damaging effects of chlorine and other oxidants.

Membranes are commonly rated for their chlorine tolerance in "ppm-hours," simply the product of the concentration and the contact time. Tolerance is temperature dependent.

Concentration Polarization Concentration polarization is a function of both flux, which increases the mass rate of material stranded at the membrane and cross-flow velocity, which reduces polarization by enhancing feed-side mass transfer. Polarization is far less of a problem in reverse osmosis and nanofiltration than it is in ultrafiltration or microfiltration, but it cannot be ignored. If cross-flow velocity is insufficient, rejected species concentrate near the membrane to an unacceptable level. The resulting increase in osmotic pressure and the precipitation of sparingly soluble species (scaling) are concerns. Scale inhibitors are normally added to water when they are appropriate and, for these feeds, careful consideration of cross-flow velocity is required. Hollow-fiber modules operate at low flux and at low cross-flow velocity so diffusion is better able to reduce polarization; spirals have much better redispersion rates, but can be overdriven if operated at fluxes above the design values. The equations for polarization are given below in the section describing ultrafiltration.

Rejection Rejection is defined in "Background and Definitions." The highest-rejection membranes are those designed for single-pass production of potable water from the sea. The generally accepted criterion is 99.4 percent rejection of NaCl. Some membranes, notably cellulose triacetate fibers are rated even higher. A whole range of membranes is available as rejection requirements ease, and membranes with excellent chlorine resistance and hydrolytic stability can be made with salt rejection over 90 percent.

Plugging Silt carried into a membrane module may deposit and plug it. Membrane configurations differ markedly in their ability to tolerate suspended solids, with fine hollow fibers fed shell-side being least tolerant, and large bore tubes fed tube-side being most tolerant. Membrane manufacturers use the *silt density index* (SDI) to show the tolerance of their wares for suspended solids. The SDI is an arbitrary test, used to determine the plugging propensity of an RO feed. A 0.45 μm microfiltration membrane, 47 mm in diameter, is used for the test. The feed to be tested is passed through the filter at 30 psi (206 kPa).

The time required for the first 100 ml to pass through the filter is recorded. That is defined as t_0. The flow is continued for 15 minutes, then the time required for an additional 100 ml to pass through the fitter is recorded. That is defined as t_{15}. If the flow has continued throughout the test, that is, the stream has not been reduced to dropwise flow, the SDI is defined as:

$$\text{SDI} = \frac{100(t_{15} - t_0)}{15(t_{15})} = 6.67\,\frac{(t_{15} - t_0)}{(t_{15})} \tag{22-76}$$

If the flow becomes dropwise during the 15 minutes, the formula is instead:

$$\text{SDI} = \frac{100}{(\text{minutes until flow becomes dropwise})} \tag{22-77}$$

Examples: (1) The first 100 ml required 11 seconds, and after 15 minutes of flow, an additional 100 ml required 95 seconds. The SDI would be 5.9 (2) The first 100 ml took 37 seconds, but the flow became dropwise after 4 minutes. The SDI would be 25.

Fouling Fouling is as inevitable as death and taxes. All membranes foul. Prevention and remediation of fouling are major economic and operating concerns in the design of a membrane facility. Scaling results from the precipitation of sparingly soluble species. Colloids deposit on the membrane in spite of cross-flow, and biofouling is

a problem for most feeds. Much can be done to increase the interval at which a membrane unit must be shut down and cleaned. The silt density index is a reasonable, if qualitative, guide to the degree to which colloidal fouling becomes a dominating problem. Biofouling is highly dependent on the feed-biota level and on nutrient levels. Reduction of biological load through pretreatment with chlorine or another biocide is a common practice, and on a pilot scale, microfiltration is being tried. Limited success has come from attempts to maintain anaerobic conditions in the feed. Research in biofouling prevention and remediation is an active area.

Pretreatment For most membrane applications, particularly for RO and NF, pretreatment of the feed is essential. If pretreatment is inadequate, success will be transient. For most applications, pretreatment is location specific. Well water is easier to treat than surface water and that is particularly true for sea wells. A reducing (anaerobic) environment is preferred. If heavy metals are present in the feed even in small amounts, they may catalyze membrane degradation. If surface sources are treated, chlorination followed by thorough dechlorination is required for high-performance membranes [Riley in Baker et al., op. cit., p. 5–29]. It is normal to adjust pH and add antiscalants to prevent deposition of carbonates and sulfates on the membrane. Iron can be a major problem, and equipment selection to avoid iron contamination is required. Freshly precipitated iron oxide fouls membranes and requires an expensive cleaning procedure to remove. Humic acid is another foulant, and if it is present, conventional flocculation and filtration are normally used to remove it. The same treatment is appropriate for other colloidal materials. Ultrafiltration or microfiltration are excellent pretreatments, but in general they are uneconomic.

Process Configuration

Osmotic Pinch Effect Feed is pumped into the membrane train, and as it flows through the membrane array, sensible pressure is lost due to friction effects. Simultaneously, as water permeates, leaving salts behind, osmotic pressure increases. There is no known practical alternative to having the lowest pressure and the highest salt concentration occur simultaneously at the exit of the train, the point where $\Delta P - \Delta\Pi$ is minimized. This point is known as the "osmotic pinch," and it is the point backward from which hydraulic design takes place. A corollary factor is that the permeate produced at the pinch is of the lowest quality anywhere in the array. Commonly, this permeate is below the required quality, so the usual practice is to design around average-permeate quality, not incremental quality. A 1 MPa overpressure at the pinch is preferred, but the minimum brine pressure tolerable is 1.1 times Π.

Brine Staging Velocity past the membrane is important. If too low, polarization is excessive, local Π rises, and rejection declines. Fouling occurs faster. If too high, pressure losses are higher than they need be, and the osmotic pinch is premature. Since the volume of feed declines continuously, the hydraulic design needs periodic rearrangement. This is commonly done as shown in Fig. 22-64, sometimes known as a Christmas tree. This design is commonly used where the fluid is pumped once, as in RO, NF, and gas-separation systems, but not where recirculation is practiced, as in ultrafiltration.

Economics The largest application for RO and NF is water treatment. Brackish water desalination for drinking water is the largest, and seawater desalination is perhaps the best known. Electrodialysis competes with pressure-driven membranes for brackish water applications. Seawater desalination is dominated by evaporation, with membranes an active competitor for midsize plants. There are numerous smaller process applications. The economic examples given are to illustrate the considerable difference between a small process plant and a large seawater RO plant. For the process plant, the cost given is for a skid-mounted self-contained unit for which considerable on-site additions would be required (tanks, piping, utilities, etc.). The seawater economics assume a leveled site but include everything necessary to deliver the product to the site boundary. Brackish water plants are considerably cheaper than seawater plants.

Process Applications The diversity of application for process RO permits only a few generalities. Sugar concentration, wastewater recovery, and beverage uses are a few of the currently popular applications. Taking a fairly standard 100 gpm (6.3 ℓ/s) (based on water permeated) system, a package unit (uninstalled) would cost approximately $90,000 (1995). Standard plant design uses 8-inch multileaf spiral modules. About 25 to 30 percent of the capital cost is for the membranes and housings. This is in line with costs for other membrane processes. Operating costs are predominantly for membrane replacement and power, each in the order of $80/1000 m^3 permeated. Approximately $25/1000 m^3 will be consumed for pretreatment, maintenance, and cleaning. Concentrate disposal costs are highly variable, and capital charges must be added. Spirals are the standard design for process plants, but tubes, plate and frame, and hollow fibers with boreside feed have market niches.

Seawater Desalination Seawater plants use spirals and hollow-fiber modules. Competition between these types is keen, with fibers having the advantage in high-salinity waters: polyamide fibers have higher pressure limits and cellulose triacetate fibers possess very high rejection. Spirals have an edge on cost, robustness, and fouling resistance. Seawater plant economics reflect the costs of high operating pressure, the need to handle and pretreat large quantities of seawater (2–2.5× rated capacity), and so on.

Capital Costs A typical medium-scale RO seawater plant might produce 0.25 m^3/s (6 MGD). For a plant with an open sea intake, seawater salinity of 38 g/l, and conversion of 45 percent, the overall cost would be $26.5 million (1996). A capital breakdown is given in Table 22-18. Capital charges are site specific, and are sensitive to the salinity of the feed. A plant of this size would likely contain six trains. For seawater RO, the best estimate for the slopes of the family of lines in Fig. 22-55 is –0.6 for the equipment and 0.95 for the membranes. Capital charges, shown in Table 22-19, usually dominate the overall economics; the numbers presented are only an example. Seawater economics are based on Shields and Moch, *Am. Desalination Assn. Conf. Monterey CA* (1996).

Operating Costs Annual operating costs for the example in Table 22-18 are shown in Table 22-19. For this 0.25 m^3/s plant, a service factor of 90 percent is assumed.

Energy For the plant described in Table 22-18, the energy consumption is given in Table 22-20. For any simple membrane plant, the power consumption is simply the feed pressure divided by the yield (P/Y) (Pa). Energy consumption is expressed as kWh/m^3, measured as net power fed to the plant divided by net permeate leaving the plant. Energy recovery can be very important in seawater plants, as shown here. Significant losses occur in motors, couplings, pumps, pipes, and

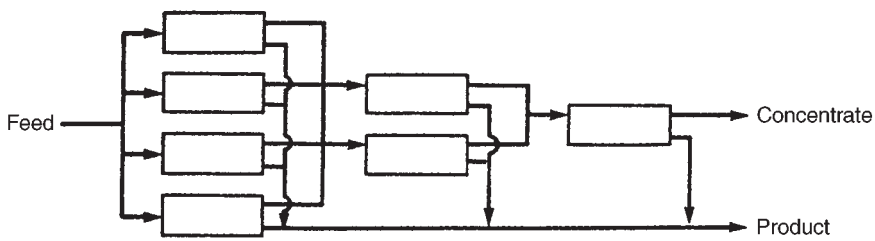


FIG. 22-64 Cascade arrangement for membrane processing to maintain cross-flow velocity as permeate is removed.

TABLE 22-18 RO Seawater Plant, Capital Costs

Item	$000	% of category	% of total capital
Membranes and housings, installed	3,600	21	14
Process equipment	13,700	79	52
Total installed equipment	17,300	100	65
Site development	500	21	2
Intake and outfall structures	1,850	79	7
Subtotal for site costs	2,350	100	9
Construction interest	983	14	4
Contingency	1,572	23	6
A&E fees	3,341	49	13
Working capital	983	14	4
Total indirect capital	6,879	100	26
Total capital employed	26,529		100

TABLE 22-19 RO Seawater Plant, Operating Costs

Item	$000	% of operating cost	% operating + capital	$/m^3 water
Electrical power @ $0.08/kWh	3,163	70	44	0.40
Consumables and chemicals	187	4	3	0.02
Maintenance and parts	482	11	7	0.06
Supervision and labor	265	6	4	0.03
Membrane replacement	390	9	5	0.05
Total	4,487	100	63	0.56
Amortization, 20 years, 8 percent	2,664		37	0.34
Total operating plus capital charges	7,151		100	0.90

manifolds.

ULTRAFILTRATION

Process Description *Ultrafiltration* (UF) is the membrane process which will retain soluble macromolecules and everything larger while passing solvent, ions, and other small soluble species. It is almost always operated with some means of forced convection near the membrane. Conventional dead-end filtration is rarely an option for UF, since most applications behave as if they have a "cake compressibility" factor of 1 in the filtration equation. Cross-flow filtration is practically universal for UF. An illustrative example of UF is its use for whey processing. Whey production exceeds 4×10^7 tons/year worldwide. It is a byproduct of cheese manufacture. Whey is composed of roughly 0.6 percent true proteins, 0.2 percent nonprotein nitrogen, 5 percent lactose, 1 percent salts, some lactic acid, and the balance water at a pH between 3.5 and 6. It contains trace amounts of casein fines and butterfat globules, and a large population of bacteria. UF retains the two principle proteins, alpha-lactalbumin (molar mass 17,000 daltons) and beta lactogloublin (molar mass 36,000 daltons), along with the large casein and butterfat particles and the bacteria. UF passes water, lactose, salts, and nonprotein nitrogen through the membrane into the permeate.

UF is widely used to concentrate oil-in-water emulsions, the byproduct of many metal-working applications, because the membrane retains stable emulsified oil while the water and the very low concentration of dissolved oil and free surfactant pass through it. UF is likewise useful for the concentration of dilute latex. Special membranes are used to remove virus from solution to help achieve the 12-log reduction required for vaccine manufacture. UF is useful for protein recovery in many fermentation operations, from the commodity-scale production of enzymes to small-scale specialty pharmaceutical manufacture.

TABLE 22-20 RO Seawater Plant, Energy Consumption

Item	kWh/m^3	% of total
Low-pressure pumps	0.70	14
High-pressure pumps	5.79	116
Energy recovery turbine	(1.94)	–39
Degasification	0.02	0
Product pump	0.16	3
Plant services	0.28	6
Total energy	5	100

Ultrafiltration may be distinguished from other membrane operations by example: When reverse osmosis is used to process whey, it passes only the water and some of the lactic acid (due to the solubility of lactic acid in RO membranes). Nanofiltration used on whey will pass most of the sodium salts while retaining the calcium salts and most of the lactose. Microfiltration will pass everything except the particulates and the bacteria.

UF Membranes Design of UF membranes prizes high retention, hydrolytic stability, and good process flux. Since fouling is the principal impediment to flux, and membranes which are hydrophilic generally foul less rapidly, there is competition between the truly stable hydrophobic membranes and the less-fouling-prone hydrophilic ones.

Cellulosic Membranes The first commercial UF membranes were made from *cellulose acetate* (CA), with an acetyl content of about 37 percent. They are prized for their low level of interaction with proteins and are still used in other applications where long life is not critical.

Polymeric Membranes Economically important applications required membranes that could operate at higher pH than could CA, for which the optimum is around pH = 5. Many polymeric membranes are now available, most of which have excellent hydrolytic stability. Particularly prominent are polysulfone, polyvinylidene fluoride, polyethersulfone, polyvinyl alcohol-polyethylene copolymers, and acrylic copolymers.

Ceramic Membranes Alumina-based microfiltration membranes and porous carbon substrates are tightened for use as UF membranes usually by depositing a layer of zirconium oxide on the surface.

UF Membranes as a Substrate for RO An important use of UF membranes is as a substrate for composite reverse-osmosis membranes. After the UF membrane (usually polysulfone) is prepared, it is coated with an aqueous solution of an amine, then dipped in an organic solution of an acid chloride to produce an interfacially polymerized membrane coating.

Membrane Characterization The two important characteristics of a UF membrane are its permeability and its retention characteristics. Ultrafiltration membranes contain pores too small to be tested by bubble point. Direct microscopic observation of the surface is difficult and unreliable. The pores, especially the smaller ones, usually close when samples are dried for the electron microscope. **Critical-point drying** of a membrane (replacing the water with a fluid which can be removed at its critical point) is utilized; even though this procedure has complications of its own it has been used to produce a few good pictures.

Water Flux The permeability of a UF membrane is determined by pore size, pore density, and the thickness of the membrane active layer. Water flux is measured in the absence of solute, generally on a newly made or freshly cleaned sample. The test is simple, and involves passing water through the membrane generally in dead-end flow under carefully controlled conditions. In a water flux test, the membrane behaves as a porous medium with the flow described by Darcy's law. Adjustments for viscosity and pressure are made to correct the results to standard conditions, typically the viscosity of water at 25°C and the pressure to 50 psi (343 kPa). The water flux will be many multiples of the process flux when the membrane is being used for a separation. Virgin membrane has a standard water flux of over 1 mm/sec. By the time the membrane is incorporated into a device and used in an application, that flux drops to perhaps 100 μm/s. Process fluxes are much lower.

Molecular Weight Cutoff The best-known method for characterizing UF membranes is molecular weight cutoff. Unfortunately, it is widely misunderstood and has been the source of much error. The concept of *molecular weight cutoff* (MWCO) is powerful and deceptively simple. Ultrafilters retain soluble molecules, so their retention is

measured by seeing which molecules will pass through them. The definition, generally *but not universally* followed is: molecular weight cutoff is the molar mass of the globular protein which is 90 percent retained by the membrane.

There are many complications with interpreting MWCO data. First, UF membranes have a distribution of pore sizes. In spite of decades of effort to narrow the distribution, most commercial membranes are not notably "sharp." What little is known about pore-size distribution in commercial UF membranes fits the Poisson distribution or log-normal distribution. Some pore-size distributions may be polydisperse.

Second, most membrane materials adsorb proteins. Worse, the adsorption is membrane-material specific and is dependent on concentration, pH, ionic strength, temperature, and so on. Adsorption has two consequences: it changes the membrane pore size because solutes are adsorbed near and in membrane pores; and it removes protein from the permeate by adsorption in addition to that removed by **sieving.** Porter (op. cit., p. 160) gives an illustrative table for adsorption of Cytochrome C on materials used for UF membranes, with values ranging from 1 to 25 percent. Because of the adsorption effects, membranes are characterized only when clean. Fouling has a dramatic effect on membrane retention, as is explained in its own section below.

Third, picking the point on the curve of retention versus molar mass where "90 percent" falls is inexact. The retention curve usually bends in a way that makes picking the "90 percent point" somewhat arbitrary.

Fourth, selection of the marker molecule can effect the MWCO measured. Markers for UF membranes are usually protein, but always polymeric. Polymers of the same molar mass can have very different molecular size, and MWCO is more a measure of size than anything else. To further complicate the picture, molecular shape can change in the vicinity of a membrane. One well-known example [Porter (ed.), op. cit., pp. 156–160] is Dextran 250, a branched polysaccharide with molar mass 250 kilodaltons which passes through a 50 kD MWCO membrane. Linear molecules, such as polyacrylic acid, with a given molecular mass passes easily through a membrane that retains a globular protein of the same molecular mass. The definition requires globular proteins, for which many of these effects are mitigated.

When testing a membrane using protein, in keeping with the definition of MWCO, it is necessary to keep the concentration in the feed and the flux very low to minimize polarization effects. Any polarization of the marker at the membrane will alter the measured value, and significant accumulation will result in **autofiltration.** The result is a measurement of the boundary layer rather than the membrane itself. What is needed are conditions in which J/k [see Eq. (22-91)] is close to 1. Reducing the marker concentration to minimize these problems raises the probability that adsorption will become important in reducing the concentration of marker in the permeate. A lack of reproducibility between laboratories is one manifestation of the intractability of the MWCO problem.

Membrane manufacturers require a standard test to maintain batch-to-batch quality. Few use proteins. Materials selected are ones for which the complications are minimized, the probe is simple, fast, and cheap to detect, does not readily biodegrade, and gives results, whatever they are, which are reproducible. There is no standardization of these tests within the industry.

Misunderstandings arise when membrane users assume that MWCO means what it seems to say. The definition implies that a 50 kD membrane will separate a 25 kD material from a 75 kD material. The rule of thumb is that the molecular mass must differ by a factor of ten for a good separation. Special techniques are used to permit the separation of proteins with much smaller mass ratio.

In an ideal world, membranes would contain a very high density of fully uniform, cylindrical pores. It is perhaps natural to envision a membrane as a uniform plane featuring cylindrical holes, challenged by rigid, spherical particles. None of these preconceptions is true. Membrane surfaces may be relatively rough, openings are neither uniform nor cylindrical, and are randomly spaced. A tiny minority of retained species are spherical and rigid; the vast majority is neither. It is perhaps instructive that in spite of the very creative effort invested in "sharp" membranes, their share of the overall membrane market is very small. Practically speaking, ordinary membranes have proven to be adequate for most separations. Very few membranes are used under conditions remotely approaching a test for MWCO. They are usually highly polarized with retention determined more by autofiltration than by inherent properties.

Autofiltration The retention of any material at the surface of the membrane gives rise to the possibility of a secondary or a dynamic membrane being formed. This is a significant problem for fractionation by ultrafiltration because microsolutes are partially retained by almost all retained macrosolutes. The degree of retention is quite case-specific. As a rule of thumb, higher pressure and more polarization results in more autofiltration. Autofiltration is particularly problematic in attempts to fractionate macromolecules.

Process Limitations

Concentration Polarization Throughput data from countless ultrafiltration experiments are shown in two characteristic curves. Figure 22-65 shows flux as a function pressure. Figure 22-66 shows flux as a function of the log of retentate concentration. Figure 22-65 is for a fixed solute concentration. At low transmembrane pressure, Region I, flux is governed by the rate at which solvent passes a porous material—Darcy's law. The magnitude of flux will approximate the water flux if viscosity is the same. Increase the pressure, and at first the flux responds. Soon, however, there is no response to pressure at all (Region III), and in some extreme cases there are reports of a negative response to pressure. This counterintuitive response to an increase in driving force has received considerable attention, and what is going on can be described by looking at the concentration of retained solute stranded at the membrane. It is a given that cross-flow ultrafiltration membrane processes operate at steady state. It isn't unusual for a process to operate for weeks or months at a flux essentially the same as that measured a few minutes after startup. It is therefore apparent that there is no long-term buildup of retained material at the membrane. Therefore, the redispersion of retained material must equal its rate of transport toward the membrane. Flux in the pressure-independent portion of Fig. 22-65 is quantitatively described by making a material balance on the retained solute, and solving the mass-transfer equations for its redispersal. These same equations describe the phenomenon shown in Fig. 22-66, flux at a constant stirring rate but with concentration as a variable.

Because this mass-transfer step is so vital, conventional dead-end operation of ultrafilters is very rare. There are many ways to depolarize a membrane. Cross-flow is by far the most common. Turbulent flow is more common than laminar flow.

The mass-transfer coefficient, k, is contained in the Sherwood number:

$$\mathrm{Sh} = \frac{kd_h}{D} \tag{22-78}$$

For turbulent flow, a correlation attributed to Chilton-Colburn is:

$$\mathrm{Sh} = 0.023\mathrm{Re}^{0.8}\mathrm{Sc}^{0.33} \tag{22-79}$$

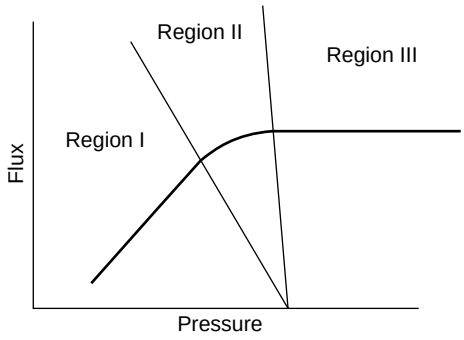


FIG. 22-65 Characteristic curve for flux as a function of pressure for cross-flow membrane processes limited by mass transfer at the membrane.

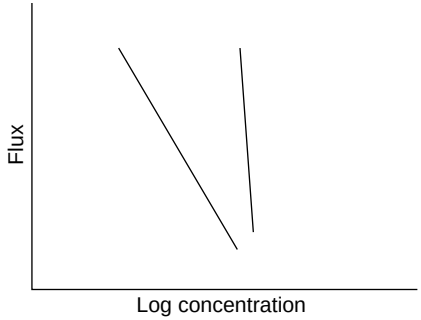


FIG. 22-66 Characteristic curve for flux as a function of feed composition for cross-flow membrane. Right curve is for a higher Sherwood number than the left curve.

$$\mathrm{Sc} = \frac{\nu}{D} \tag{22-80}$$

$$\mathrm{Re} = \frac{Vd}{\nu} \tag{22-81}$$

D is diffusivity, m^2/s, d_h is hydraulic diameter, (4)(cross sectional area)/(wetted perimeter), m, k is the mass-transfer coefficient, m/s, V is the velocity, m/s, and ν is the kinematic viscosity, m^2/s.

For cylindrical flow channels, $d_h = d$, and Re expressed in terms of volumetric flow rate, Q, is:

$$\mathrm{Re} = 4Q/\pi\nu d \tag{22-82}$$

where Q is in m^3/s. Defining J as acting along the x axis, passing from the feed through the membrane into the permeate, and recalling the steady-state stipulation, from Eq. (22-59), the rate of redispersion of retained material from the membrane is:

$$J_{\text{solute}} \approx -N_{\text{solute}} = D\frac{dC}{dx} \tag{22-83}$$

where x is the distance normal to the membrane.

A material balance on solute, ignoring the effects parallel to the membrane, is:

$$J \cdot C_x - J \cdot C_{\text{perm}} - D\frac{dC}{dx} = 0 \tag{22-84}$$

Calling the thickness of the concentration boundary layer, δ, Eq. (22-84) can be integrated to give:

$$J_{\text{solute}} \sim \left(\frac{D}{\delta}\right) \ln\left(\frac{C_{\text{wall}} - C_{\text{perm}}}{C_{\text{bulk}} - C_{\text{perm}}}\right) = k \ln\left(\frac{C_{\text{wall}} - C_{\text{perm}}}{C_{\text{bulk}} - C_{\text{perm}}}\right) \tag{22-85}$$

Since D/δ is the mass-transfer coefficient. For the portion of the operating curve in which flux is invariant, the wall concentration is apparently invariant. The mechanism governing why and how that occurs is the subject of a continuing debate in the literature.

For the usual case when $R = 1$ (total retention of the solute), $C_{\text{perm}} = 0$ and combining these equations gives a general expression for flux in a turbulent-flow membrane system. For any given solute concentration:

$$J \sim J_{\text{solute}} \sim k \sim \frac{Q^{0.8}D^{0.7}}{d^{1.8}\nu^{0.5}} \tag{22-86}$$

Flux is a function of solute concentration as is shown in Fig. 22-66. The exponent on Q is not always found to be 0.8 experimentally.

For laminar flow in a circular tube, the Leveque relationship is:

$$\mathrm{Sh} = 1.62\left(\mathrm{ReSc}\,\frac{d}{l}\right)^{0.33} \tag{22-87}$$

$$k = 1.62\left(\frac{VD^2}{ld}\right)^{0.33} \tag{22-88}$$

$$J \sim J_{\text{solute}} \sim k \sim \left(\frac{QD^2}{ld^3}\right)^{0.33} \tag{22-89}$$

where l is the distance from the channel entrance.

Equations (22-86) and (22-89) are the turbulent- and laminar-flow flux equations for the pressure-independent portion of the ultrafiltration operating curve. They assume complete retention of solute. Appropriate values of diffusivity and kinematic viscosity are rarely known, so an a priori solution of the equations isn't usually possible. Interpolation, extrapolation, even prediction of an operating curve may be done from limited data. For turbulent flow over an unfouled membrane of a solution containing no particulates, the exponent on Q is usually 0.8. Fouling reduces the exponent and particulates can increase the exponent to a value as high as 2. These equations also apply to some cases of reverse osmosis and microfiltration. In the former, the constancy of C_{wall} may not be assumed, and in the latter, D is usually enhanced very significantly by the action of materials not in true solution.

Usually, diffusivity and kinematic viscosity are given properties of the feed. Geometry in an experiment is fixed, thus d and averaged l are constant. Even if values vary somewhat, their presence in the equations as factors with fractional exponents dampens their numerical change. For a continuous steady-state experiment, and even for a batch experiment over a short time, a very useful equation comes from taking the logarithm of either Eq. (22-86) or (22-89) then the partial derivative:

$$\left(\frac{\partial \log J}{\partial \log Q}\right)_{\nu,d,D} = m \tag{22-90}$$

Equation (22-90) is the basis for the ubiquitous plots of log J versus log Q. Such plots are powerful tools for analyzing experimental data. The known range of observed values of m in well-developed turbulent flow is $0.8 < m < 2.0$. For laminar flow, $m = 0.33$ for true solutions, with values up to around 0.8 for systems with particulates. It is important to determine the experimental value, both for design optimization and for prediction of long-term effects. It is important that all values of flux be taken in the pressure-independent region of operation (see Fig. 22-65). High values of m are usually found in systems containing large, dense particles. Polyvinyl chloride latex with particles over 0.5 μm diameter is a classic high-slope example.

The slope of the flux-flow line is an indicator of fouling. In turbulent flow, $m < 0.8$ indicates fouling. A decline in the value of m with time is the most sensitive indicator of fouling. While the slope is difficult to obtain unconfounded by changes in pressure, a well-designed J versus Q experiment yields results with good predictive value for fouling. As a special precaution when using spiral-wound modules Da Costa, Fane, and Wiley [*J. Membrane Sci.*, **87,** 79–98 (1994)] found that while the pressure-drop data in a spiral module behave as if the flow is turbulent, the mass-transfer data are consistent with laminar flow.

Prediction of C_{wall} Equation (22-85) shows a semilog dependency of wall concentration on flux. Experimentally, the dependence of flux on concentration usually deviates significantly from linearity well before the zero-flux intercept extrapolated from data in Fig. 22-66. Experimental data at very low flux are difficult to gather, but usually the flux is much higher than the values extrapolated assuming linearity. The mass-transfer equations predict a mass-transfer coefficient, k, without reference to flux, as they were formulated for nonmembrane systems. This k is used by assumption to predict the wall concentration up to the point at which flux becomes independent of pressure.

$$C_{\text{wall}} - C_{\text{perm}} = (C_{\text{bulk}} - C_{\text{perm}}) \exp(J/k) \tag{22-91}$$

When flux becomes independent of pressure, C_{wall} becomes **constant.** The assumptions underlying the equations, such as constancy of D and especially of ν are unlikely to hold, and other means are needed to determine the true value of C_{wall}. Field [in Howell, Sanchez, and Field, op. cit., pp. 87–95] gives a detailed treatment of this regime.

Osmotic Pressure, Gel Effect, Etc. The reason for the apparent constancy of C_{wall} under usual operating conditions is still tentative.

For many years, it was thought that the macro solute forms a new phase near the membrane—that of a gel or gel-like layer. The model provided good correlations of experimental data and has been widely used. It does not fit known experimental facts. An explanation that fits the known data well is based on osmotic pressure. The van't Hoff equation [Eq. (22-75)] is hopelessly inadequate to predict the osmotic pressure of a macromolecular solution. Using the empirical expression

$$\Pi(C) = \sum_{n=1}^{n=3} a_i C^n \qquad (22\text{-}92)$$

where a_i are experimental constants it is possible to correlate experimental osmotic-pressure data for macro solutes and to predict the concentration at the membrane. Data now confirmed show osmotic pressures high enough to counter the transmembrane driving force [Jonsson, *Desalination,* **51,** 61–77 (1984)]. Other theories of the boundary layer exist, but they have not attracted adherents. In terms of predictive power, both the gel theory and the osmotic-pressure theory provide a framework for correlating data.

Fouling Everything fouls (Fig. 22-67), and in process UF fouling is a major concern. Because of its importance, industrial suppliers of membrane equipment place a major emphasis on understanding, controlling, and preventing fouling. Equipment and process conditions can be specified with confidence for most applications because of the extensive knowledge base accumulated in response to the problem.

Fouling is the term used to describe the loss of throughput of a membrane device as it becomes chemically or physically changed by the process fluid (often by a minor component or a contaminant). A manifestation of fouling in cross-flow UF is that the membrane becomes unresponsive to the hydrodynamic mass transfer which is rate-controlling for most UF. Fouling is different from concentration polarization. Both reduce output, and their resistances are additive. Raising the flow rate in a cross-flow UF will increase flux, as in Eq. (22-90). If the system is badly fouled, $m \sim 0$, and increasing or decreasing flow at constant pressure has little effect on flux. However, raising the pressure may raise flux. For an unfouled system in laminar flow $0.33 < m < 0.8$; for turbulent flow, $0.8 < m < 2$.

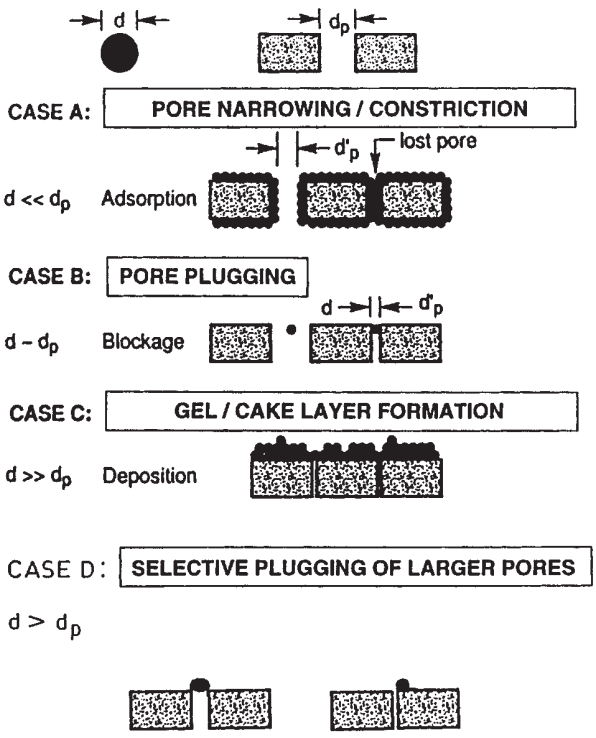


FIG. 22-67 Fouling schematics. Case A—Particles plug narrow pores and narrow larger ones. Case B—Particles plug narrow pores. Case C—Particles form a layer on the membrane. Case D—Particles or debris plug the largest pores. [*Courtesy Elsevier (modified).*]

Fouling affects flux dramatically. The pure water flux through a new UF membrane is commonly tenfold greater than the water flux after the membrane has been exposed to protein. Processing fluxes commonly decline roughly as $J = J_o t^{-n}$ where t is an arbitrary dimensionless time and n is small. J_o is the flux when $t = 1$. Thorough cleaning is required to restore $J = J_o$ as incompletely cleaned membranes foul faster than completely cleaned membranes. Fouling prevention is an important part of process design. Proper selection of membrane, operating conditions, feed pretreatment, startup techniques, and cleaning type and frequency can make a major difference in fouling, thus throughput, thus cost. There can be a startling difference between a well-designed process and a haphazard combination of membrane and process stream. Fouling also strongly influences retention.

Since flow through a porous membrane is always laminar, the volumetric flow through an individual pore is proportional to the fourth power of diameter, as known from the Pouiselle equation. Pore plugging, as in Case D, will dramatically lower flux and significantly increase retention, while Case B will have far less of an effect, lowering flux marginally and probably lowering retention. Even a slight reduction in pore diameter from an adsorption phenomenon (Case A) will have dramatic results. Some commercial membranes are designed with the inevitability of fouling in mind, and their behavior in the first minutes is inferior to their steady-state performance.

Cleaning membranes to restore their efficiency is normal in UF. Food and dairy systems require daily cleaning in any event for hygiene; more frequent cleaning is economically intolerable. A few industrial systems operate for six months between cleanings. Cleaning shortens membrane life, and it is often the major determinant of membrane-replacement frequency.

Among techniques to prevent fouling, pretreatment is widely practiced. Free-oil phases must be removed or stabilized, and whey processing benefits from holding the whey at a mildly elevated temperature for some minutes. Membranes operated at high transmembrane pressure foul much faster. The optimum operating point on Fig. 22-65 is Region II; however it is very difficult to design economical equipment to operate there. Pretreatment is often stream- or site-specific, and it has received little attention in the literature.

Some fouling occurs simply by contact, almost certainly due to adsorption. Some occurs slowly as material is processed, some of that due to trace components in the feed and some due to slow accumulation and rearrangement processes.

Process Configurations Ultrafiltration membranes are produced in four basic forms: tubular, hollow fiber/capillary, flat sheet, and ceramic monolith. Commercial diameter of tubes is 5 to 25 mm. Fibers range from a few mm down to 250 μm. Flat-sheet membrane is most common, made into spiral-wound modules, cassettes, and plate-and-frame devices. Spiral-wound flat sheet is by far the dominant commercial configuration, followed by capillaries in the millimeter range, and then 13 and 25 mm tubes. Spirals have the economic edge, and where they will work they are used. Tubes have the advantage of being tolerant of high solids loadings and of being extremely forgiving of process upsets. The finest fibers are only used for very clean feeds such as protein solutions and water.

The simplest ultrafiltration is the stirred cell, a batch operation. The most complex is a continuous stages-in-series operation incorporating diafiltration. Industrial practice incorporates the full gamut of complexity.

Process Objective UF is used for three principle objectives. First, to **fractionate,** to pass selectively one component through the membrane with the solvent. Second, to **concentrate,** to pass the solvent. These two, while different, are related and it is common to purify and concentrate a component simultaneously. The third objective, quite different, is to **produce a solvent stream** as a product. An example is the operation of an ultrafilter for producing low-cost permeate. An important application of UF is in the automotive industry where UF is used to remove water and microsolutes from huge electrophoretic paint tanks for use in rinsing excess paint (dragout) from

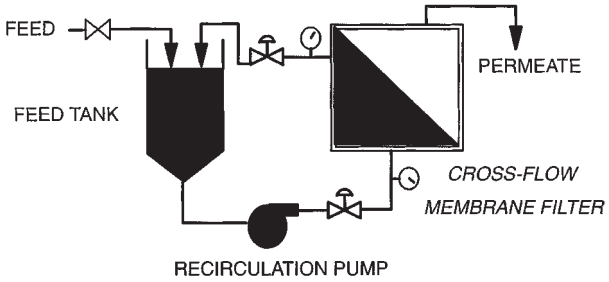


FIG. 22-68 Flow schematic for batch (feed valve closed) or semibatch (feed valve open) operation. (*Courtesy Koch Membrane Systems.*)

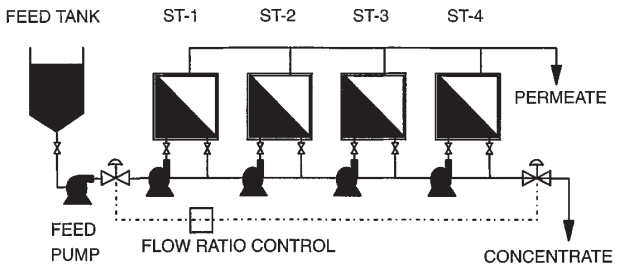


FIG. 22-69 Flow schematic for stages-in-series. In operation, the block valves are open. All pump inlets are connected, but in such a way as to prevent feed bypassing a stage. (*Courtesy Koch Membrane Systems.*)

newly primed auto bodies. Permeate and recovered paint are returned to the paint tank. It is undesirable to concentrate the paint, so the increase in paint solids within the UF loop is maintained below 10 percent.

Batch and Semibatch Straight batch is the least common industrial process, but semibatch is quite common (see Fig. 22-68). In **batch,** the entire quantity to be processed is put in a tank, and a feed from it is pumped across a UF membrane, with the concentrate returned to the tank. Conversion per pass is very low, but with recirculation any desired level of concentration may be obtained. It is the industrial version of the stirred cell. **Semibatch** uses a smaller tank to which fresh feed is introduced continuously. As the process proceeds, the contents of the batch tank become more concentrated with time, and at some point the feed is shut off and the tank contents are concentrated to the desired end point. Batch operation has the advantage of requiring the minimum membrane area, and the disadvantage of requiring the largest tank. Pumping costs are high because it is rarely practical to pressurize the feed tank or locate it at a height, so the circulating loop pressure is lost continuously.

For batch concentration, the yield equation is:

$$Y = \left(\frac{V_o}{V_f}\right)^{R-1} \tag{22-93}$$

Y is fractional yield of retained species, and V_o and V_f are the volume of process fluid at the beginning and end of a batch run, respectively. This equation is valid only when R, retention, is constant.

Diafiltration If a batch process is run so that the permeate is replaced by an equal volume of fresh solvent, unretained solutes are flushed through the system more efficiently. A major use of UF is fractionation, where a solvent, a retained solute and an unretained solute are present. An example is whey, containing water, protein, and lactose. If the retention of protein is 1 and the retention of lactose is 0, the concentration of protein in the retentate rises during UF. The ratio of protein to lactose rises, but the feed concentration of lactose is unchanged in retentate and permeate. Diafiltration dilutes the feed, and permits the concentration of lactose to be reduced. Diafiltration is used to produce high-purity products, and is used to fractionate high-value products. R is always <1 and >0 for every component.

For diafiltration, the yield equation is:

$$Y = \exp\left[\left(\frac{V_D}{V_o}\right)(R-1)\right] \tag{22-94}$$

where V_D is the volume of diafiltration solvent (water) added, equal to the volume of permeate removed.

The combination of diafiltration and batch concentration can be used to fractionate two macrosolutes whose retentions differ by as little as 0.2. It is possible *in principle* to achieve separations that are competitive with chromatography. When tanks and other equipment are considered, as well as the floor space they occupy, the economics of membrane separation of proteins may be attractive [R. van Reis, U.S. Patent 5,256,294 (1993)].

Stages in Series Large-scale UF normally operates in a mode called **stages-in-series** (see Fig. 22-69). Feed is pumped from a feed tank, which in principle can be quite small, to a first recirculating stage. A pipe connects the low-pressure side of this stage to the low-pressure side of another stage. When more than five stages are linked in this manner, the membrane area required drops to within 20 percent of the minimum batch membrane area requirement. The system is self-adjusting and stable. The preferred means of control is to use a volume-ratio controller to regulate the product-exit valve on the last stage. The economic advantages from modular fabrication, reduced tankage, and continuous operation make this the scheme of choice for most large fractionation and concentration operations.

Economic Yield Both in a high-value protein separation and in a low-value commodity concentration, economic yield is vital. Economic yield is defined as the fraction of useful product entering the process that leaves it in salable form. The yield equations used in the industry focus on retention, so they deal only with direct losses through the membrane. These losses result both in direct (product not sold) and indirect costs from a waste stream whose disposal or subsequent use may be more expensive when it is contaminated by macrosolute. There are additional indirect losses, mainly product left in the equipment, particularly that left adhering to the membrane. Costs of cleaning and disposal of this indirect loss, while hard to measure, are usually higher than the cost of product lost through the membrane.

Decoupled Driving Force and Depolarization Needs for improved fractionation motivate designers to reduce autofiltration. Using fluid velocity for depolarization means that hydrodynamic pressure drop will be additive to the transmembrane pressure driving force. Schemes to limit this effect confront a harsh economic reality. Two novel schemes decouple the driving from the depolarizing force.

When fluid flows around a curve in a duct, or when fluid is confined between differentially rotating cylinders, secondary flows called **Taylor vortices** are generated. If a membrane is mounted on a rotating cylinder, these secondary flows minimize polarization independent of driving pressure. The relevant equations are:

$$\mathrm{Ta} = \frac{\omega R g}{\nu}\sqrt{\frac{g}{R}} \tag{22-95}$$

$$\mathrm{Sh} = c\ \mathrm{Ta}^{0.5}\mathrm{Sc}^{0.33} \tag{22-96}$$

where c is an experimental constant, R is the radius of the inner cylinder, g is the gap between inner and outer cylinders, and ω is the angular velocity of the rotating cylinder, radian/s. Ta is the Taylor number. For a fixed device on a given fluid, flux is predicted to be proportional to $\omega^{1/2}$.

By mounting a plate-and-frame membrane assembly atop a torsion-bar spring, membranes may be depolarized by vibrating the stack at a resonant frequency. The membrane moves and the fluid is essentially stationary. At first thought to be ideal for, and limited to, solutions of very high viscosity or solids loading, the devices are now viewed as another economic competitor for a broader range of applications. No adequate theory is available to explain mass transfer in vibrating membrane systems. Some data correlate depolarizing mass transfer with the first power of shear rate over a narrow range of conditions.

Energy Requirements Practically all the energy needed to run an ultrafilter is depolarization energy. The thermodynamic work

required for any UF separation is approximately 0.01 kWh/m^3 of permeate. Energy requirements vary widely by application and economics. Design is a classic trade-off between membrane area and pump related equipment. The range of energy requirements from the easiest to the most difficult for modern designs runs in the magnitude of 0.5 to 5 kWh/m^3 of permeate.

Design UF equipment has considerable variety of design, but the trend is toward more compact, energy efficient, and lower-cost designs. Much of the robustness characteristic of older designs is now available in less costly versions.

Hydraulic Design Looking over a wide spectrum of UF applications, the hydraulic energy delivered to the membrane falls within a characteristic range. At the high extreme, a large-diameter tubular plant operating at very high velocity in order to retard fouling on a stream where long operating cycles between cleanings are valued, power dissipation at the membrane may exceed 150 watts/m^2. A well-designed, relatively large, hydraulically efficient plant will deliver power from electrical source to membrane at 64 percent efficiency. If the flux in the installation is 50 ℓmh, the power consumption of the process is 150/(0.64)(50) = 4.7 kWh/m^3. A large plant designed using less-efficient sanitary standard pumps and spiral-wound membranes could deliver 20 watts/m^2 to the membrane with an energy conversion of 50 percent and a flux of 30 ℓmh. That plant would consume 1.3 kWh/m^3. Very efficient plants for benign feed streams may consume half as much energy.

Module Types Favored Because of their low cost, spiral-wound membranes are the first choice for industrial ultrafiltration. Over the years, the number of applications for which spirals are a good choice has gone from practically none to over 50 percent, owing to very intensive process development and a related extensive modification of the spiral module as it was known in the RO field. When the spiral is not appropriate—examples include feeds where fibers, debris, certain types and loadings of suspended solids, most emulsified oils, etc. are present and too expensive to remove by pretreatment—other module designs are used. Capillary membranes are the usual next choice, and they are in fact preferred for some applications. Then comes open tubes, known for being expensive and practically indestructible. Tubes also have an edge in a few applications, such as apple juice, because they are able to recover more juice before they plug up with pomace. Cassettes are used because of direct scale-up from bench to plant in applications where equipment and operating cost are not paramount. Plate-and-frame modules are still found on occasion.

Economics The general examples section found under "Background and Definitions" is directly applicable to the following.

Capital Costs Package UF units are sold for many applications. Prices vary widely by application, with equipment designed for food and pharmaceutical applications priced higher than general industrial equipment. All package units would include membranes, one or more pumps, a cleaning system, piping, instrumentation, an electrical control panel, and perhaps a process tank, all designed for rapid field installation. A 1996 budget price for a typical industrial spiral or capillary unit containing 100 m^2 of active membrane area, with a process output of the magnitude of 1.0–1.5 ℓ/s is \$250–500/m^2. The replaceable membrane component of that cost is \$30–40/m^2.

UF/MF applications with plant cost of \$10^6 are considered large. In the decade ending in 1995, fewer than ten large plants were sold worldwide in any year. During that decade, the process-membrane industry matured. More vendors for equipment and membranes broadened the applications and lowered the costs. The industry-cost picture is changing fast enough that only broad guidelines are given here. Fresh information from vendors and users is needed if accuracy is required.

UF and MF use energy to depolarize membranes so as to increase flux. As is shown in Fig. 22-55, membranes and mechanical equipment are traded off to achieve an overall economic minimum. Three things can drive a design toward the use of more membranes and less mechanical equipment: cheaper membranes, very high flux, and very low flux. The availability of lower-cost membranes is easiest to understand. In the five years ending in 1995, the cost of both membrane area and membrane housings was driven down by competition. Pumps, pipes, and other peripheral equipment also declined, but not as much. By the principles of Fig. 22-55, this pushed the optimum design point to the right. Membrane costs maintained their *slope* but came down in *position*. Neither high-flux applications (potable water for example, average design flux for UF is 125 ℓmh, and for MF it is 185 ℓmh) or very low flux (polyvinylalcohol, average design flux 5.8 ℓmh) are very responsive to mechanical energy applied at the membrane. In the case of water, there is little to depolarize, and most systems operate in Region I of Fig. 22-13. Polyvinylalcohol is so viscous that it is, or becomes, laminar in a spiral module. The pressure drop through a spiral limits the velocity and forces the economics toward plants with high-area and moderate-pumping packages.

In the case of whey, paint, and other midflux process fluids, mechanical energy at the membrane surface produces a larger dividend. For these applications, pumping for depolarization is much more important economically, but the trend toward lower-cost membranes has nonetheless shifted systems toward more membrane area.

TABLE 22-21 Capital-Cost Distribution for Components in Large UF/MF Plants

Cost distribution	% of total, range
Membranes and membrane housings	17–40
Pumps, motors, etc.	15–9
Pipes, valves, and framework	35–31
Cleaning system	18–10
Control panel	15–10

In 1996, a \$1M plant would process: 6 ℓ/s of polyvinylalcohol (UF), 17 ℓ/s of whey (UF), 35 ℓ/s dextrose (MF), or 108 ℓ/s water (MF or UF).

During 1990–1995, capital costs for large UF/MF plants broke down into the ranges shown in Table 22-21.

Operating Costs Operating expenses again span a considerable range, but there are fairly consistent operating norms (Table 22-22). A few very high flux MF applications with fluxes of up to 500 ℓmh are just starting to become commercial. These applications use large pumps to maintain output. It is not yet know whether these cost estimates will apply to those plants.

TABLE 22-22 Operating-Cost Range for Large UF/MF Plants

Expense item	Range of variable commonly encountered
Energy consumption	0.5–5 kWh/m^3 permeated
Cleaning chemicals and lost product	\$10–100/m^2 membrane installed-year
Membrane replacement	1–5 years at \$20–40 m^2; 10–20 years at \$200/m^2
Operating, cleaning, and maintenance labor	2–3% of installed capital
Maintenance materials	0.6–0.06% of installed capital

MICROFILTRATION

Process Description Microfiltration (MF) separates particles from true solutions, be they liquid or gas phase. Alone among the membrane processes, microfiltration may be accomplished without the use of a membrane. The usual materials retained by a microfiltration membrane range in size from several μm down to 0.2 μm. At the low end of this spectrum, very large soluble macromolecules are retained by a microfilter. Bacteria and other microorganisms are a particularly important class of particles retained by MF membranes. Among membrane processes, dead-end filtration is uniquely common to MF, but cross-flow configurations are often used.

Brief Examples Microfiltration is the oldest and largest membrane field. It was important economically when other disciplines were struggling for acceptance, yet because of its incredible diversity and lack of large applications, it is the most difficult to categorize. Nonetheless, it has had greater membrane sales than all other membrane applications combined throughout most of its history. The early

success of microfiltration was linked to an ability to separate microorganisms from water, both as a way to detect their presence, and as a means to remove them. Both of these applications remain important.

Laboratory Microfiltration membranes have countless laboratory uses, such as recovering biomass, measuring particulates in water, clarifying and sterilizing protein solutions, and so on. There are countless examples for both general chemistry and biology, especially for analytical procedures. Most of these applications are run in dead-end flow, with the membrane replacing a more conventional medium such as filter paper.

Medical MF membranes provide a convenient, reliable means to sterilize fluids without heat. Membranes are used to filter injectable fluids during manufacture. Sometimes they are inserted into the tube leading to a patient's vein.

Process Membrane microfiltration competes with conventional filtration, particularly with diatomaceous earth filtration in general-process applications. A significant advantage for membrane MF is the absence of a diatomaceous earth residue for disposal. Membranes have captured most of the final filtration of wine (displacing asbestos), are gaining market share in the filtration of gelatin and corn syrup (displacing diatomaceous earth), are employed for some of the cold pasteurization of beer, and have begun to be used in the pasteurization of milk. Wine and beer filtration operate dead-end; gelatin, corn syrup, and milk are cross-flow operations. MF is used to filter all fluid reactants in the manufacture of microcircuits to ensure the absence of particulates, with point-of-use filters particularly common.

Gas Phase Microfiltration plays an important and unique role in filtering gases and vapors. One important example is maintaining sterility in tank vents, where incoming air passes through a microfilter tight enough to retain any microorganisms, spores, or viruses. A related application is the containment of biological activity in purge gases from fermentation. An unrelated application is the filtration of gases, even highly reactive ones, in microelectronics fabrication to prevent particulates from contaminating a chip.

Downstream Processing Microfiltration plays a significant role in downstream processing of fermentation products in the pharmaceutical and bioprocessing industry. Examples are clarification of fermentation broths, sterile filtration, cell recycle in continuous fermentation, harvesting mammalian cells, cell washing, mycelia recovery, lysate recovery, enzyme purification, vaccines, and so forth.

MF Membranes Microfiltration is a mature field that has proliferated and subdivided. The scope and variety of MF membranes far exceeds that in any other field. A good overview is given by Strathmann [in Porter (ed.), op. cit., pp. 1–78]. MF membranes may be classified into those with tortuous pores or those with capillary pores. Tortuous-pore membranes are far more common, and are spongelike structures. The pore openings in MF are much larger than those in any other membrane. Surface pores may be observed by electron microscope, but tortuous pores are much more difficult to observe directly. Membranes may be tested by bubble-point techniques. Many materials not yet useful for tighter membranes are made into excellent MF membranes. Retention is the primary attribute of an MF membrane, but important as well are permeability, chemical and temperature resistance, dirt capacity (for dead-end filters), FDA-USP approval, inherent strength, adsorption properties, wetting behavior, and service life.

Membrane-production techniques listed below are applicable primarily or only to MF membranes. In addition, the Loeb-Sourirjain process, used extensively for reverse osmosis and ultrafiltration membranes, is used for some MF membranes.

Membranes from Solids Membranes may be made from microparticles by sintering or agglomeration. The pores are formed from the interstices between the solid particles. The simplest of this class of membrane is formed by sintering metal, metal oxide, graphite, ceramic, or polymer. Silver, tungsten, stainless steel, glass, several ceramics, and other materials are made into commercial membranes. Sintered metal may be coated by TiO_2 or zirconium oxide to produce MF and UF membranes. Membranes may be made by the careful winding of microfibers or wires.

Ceramic Ceramic membranes are made generally by the sol-gel process, the successive deposition of ever smaller ceramic precursor spheres, followed by firing to form multitube monoliths. The diameter of the individual channels is commonly about 2 to 6 mm. Monoliths come in a variety of shapes and sizes. A 19-channel design is common. One manufacturer makes large monoliths with square channels.

Track-Etched Track-etched membranes (Fig. 22-70) are now made by exposing a thin polymer film to a collimated beam of radiation strong enough to break chemical bonds in the polymer chains. The film is then etched in a bath which selectively attacks the damaged polymer. The technique produces a film with photogenic pores, whose diameter may be varied by the intensity of the etching step. Commercially available membranes have a narrow pore size distribution and are reportedly resistant to plugging. The membranes have low flux, because it is impossible to achieve high pore density without sacrificing uniformity of diameter.

Chemical Phase Inversion Symmetrical phase-inversion membranes (Fig. 22-71) remain the most important commercial MF membranes produced. The process produces tortuous-flow membranes. It involves preparing a concentrated solution of a polymer in a solvent. The solution is spread into a thin film, then precipitated through the slow addition of a nonsolvent, usually water, sometimes from the vapor phase. The technique is impressively versatile, capable of producing fairly uniform membranes whose pore size may be varied within broad limits.

Thermal Phase Inversion Thermal phase inversion is a technique which may be used to produce large quantities of MF membrane economically. A solution of polymer in poor solvent is prepared at an elevated temperature. After being formed into its final shape, a sudden drop in solution temperature causes the polymer to precipitate. The solvent is then washed out. Membranes may be spun at high rates using this technique.

Stretched Polymers MF membranes may be made by stretching

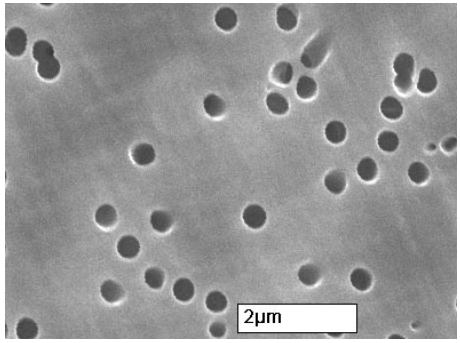


FIG. 22-70 Track-etched 0.4 μm polycarbonate membrane. (*Courtesy Millipore Corporation.*)

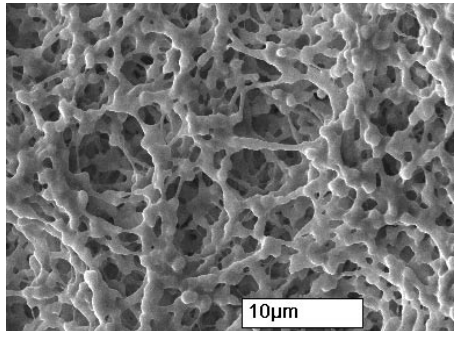


FIG. 22-71 Chemical phase inversion 0.45 μm polyvinylidene fluoride membrane. (*Courtesy Millipore Corporation.*)

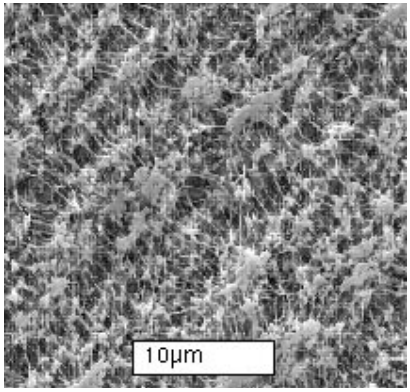


FIG. 22-72 Stretched polytetrafluoroethylene membrane. (*Courtesy Millipore Corporation.*)

(Fig. 22-72). Semicrystalline polymers, if stretched perpendicular to the axis of crystallite orientation, may fracture in such a way as to make reproducible microchannels. Best known are Goretex® produced from Teflon®, and Celgard® produced from polyolefin. Stretched polymers have unusually large fractions of open space, giving them very high fluxes in the microfiltration of gases, for example. Most such materials are very hydrophobic.

Membrane Characterization MF membranes are rated by flux and pore size. Microfiltration membranes are uniquely testable by direct examination, but since the number of pores that may be observed directly by microscope is so small, microscopic pore size determination is mainly useful for membrane research and verification of other pore-size-determining methods. Furthermore, the most critical dimension may not be observable from the surface. Few MF membranes have neat, cylindrical pores. Indirect means of measurement are generally superior. Accurate characterization of MF membranes is a continuing research topic for which interested parties should consult the current literature.

Bubble Point Large areas of microfiltration membrane can be tested and verified by a bubble test. Pores of the membrane are filled with liquid, then a gas is forced against the face of the membrane. The Young-Laplace equation, $\Delta P = (4\gamma \cos \Theta)/d$, relates the pressure required to force a bubble through a pore to its radius, and the interfacial surface tension between the penetrating gas and the liquid in the membrane pore. γ is the surface tension (N/m), d is the pore diameter (m), and P is transmembrane pressure (Pa). Θ is the liquid-solid contact angle. For a fluid wetting the membrane perfectly, $\cos \Theta = 1$.

By raising the gas pressure on a wet membrane until the first bubble appears, the largest pore may be identified, and its size computed. This is a good test to run on a membrane apparatus used to sterilize a fluid, since bacteria larger than the identified largest pore (or leak) cannot readily penetrate the assembly. Pore-size distribution may also be run by bubble point. Bubble-point testing is particularly useful in assembled microfilters, since the membrane and all seals may be verified. Periodic testing insures that the assembly retains its integrity. Diffusional flow of gas is a complication in large MF assemblies. It results from gas dissolving in pore liquid at the high-pressure side, and desorbing at the low-pressure side If the number of pores and the average pore length are known, the effect can be computed. Special protocols are used when this method is used for critical applications. Detail is provided in ASTM F316-86, "Standard test method for pore size characteristics of membrane filters by bubble point and mean flow pore test." The bubble-point test may also be run using two liquids. Because interfacial surface tensions of liquids can be quite low, this technique permits measurements on pores as small as 10 nm.

Charged Membranes The use of tortuous-flow membranes containing a positive electrical charge may reduce the quantity of negatively charged particles passing even when the pore size is much larger than the particle. The technique is useful for making prefilters or layered membranes that withstand much higher solids loadings before becoming plugged.

Bacteria Challenge Membranes are further tested by challenge with microorganisms of known size: their ability to retain all of the organisms is taken as proof that all pores are smaller than the organism. The best-known microorganism for pore-size determination is *Pseudomonas diminuta,* an asporogenous gram-negative rod with a mean diameter of 0.3 μm. Membranes with pore size smaller than that are used to ensure sterility in many applications. Leahy and Sullivan [*Pharmaceutical Technology,* **2**(11), 65 (1978)] provide details of this validation procedure.

Membrane thickness is a factor in microbial retention. Tortuous-pore membranes rated at 0.22 μm typically have surface openings as large as 1 μm (Fig. 22-71). Narrower restrictions are found beneath the surface. In challenge tests, *P. diminuta* organisms are found well beneath the surface of an 0.2 μm membrane, but not in the permeate.

Latex Latex particles of known size are available as standards. They are useful to challenge MF membranes.

Process Configuration As befits a field with a vast number of important applications and a history of innovation, there are countless variations on how an MF process is run.

Dead-end versus Cross-flow Conventional filtration is usually run dead-end, and is facilitated by amendments that capture the particulates being removed. Membranes have very low dirt capacity, so only applications with very low solids to be removed are run in conventional dead-end flow. A rough upper limit to solids content is about 0.5 percent; streams containing <0.1 percent are almost always processed by dead-end devices. Since dead-end membrane equipment is much less expensive than cross-flow, great ingenuity is applied to protecting the critical membrane pores by structured prefilters to remove larger particles and debris. The feed may also be pretreated. It is common practice to dispose of the spent membrane rather than clean it. The membrane may be run inverted. A review of dead-end membrane filtration is given by Davis and Grant [in Ho and Sirkar (eds.), op. cit., pp. 461–479].

Cross-flow is the usual case where cake compressibility is a problem. Cross-flow microfiltration is much the same as cross-flow ultrafiltration in principle. In practice, the devices are often different. As with UF, spiral-wound membranes provide the most economical configuration for many large-scale installations. However, capillary devices and cassettes are widely employed, especially at smaller scale. A detailed description of cross-flow microfiltration had been given by Murkes and Carlsson [*Crossflow Filtration,* Wiley, NY (1988)].

Membrane Inverted Most membranes have larger openings on one face than on the other. Common practice is to run the tightest face against the feed in order to avoid plugging of the backing by particles. The rationale is that anything that makes it past the "skin" will have relatively unimpeded passage into the backing and out with the permeate. For very low solids this convention is reversed, the rationale being that the porous backing provides a trap for particulates, rather like filter aid.

If the complete passage of soluble macromolecules is required, a highly polarized membrane is an advantage. The upside-down membrane hinders the back diffusion of macrosolutes. Countering the tendency of the retained particulates to "autofilter" soluble macrosolutes, the inhibition of back diffusion raises the polarization and thus the passage of macrosolutes such as proteins. The particulates are physically retained by the membrane. Blinding and plugging can be controlled if the membrane is backwashed frequently. This technique has been demonstrated at high solids loadings in an application where high passage of soluble material is critical, the microfiltration of beer [Wenten, Rasmussen, and Jonsson, *North Am. Membrane Soc. Sixth Annual Meeting,* Breckenridge, CO (1994)].

Liquid Backpulse Solid membranes are backwashed by forcing permeate backward through the membrane. Frequent pulsing seems to be the key.

Air Backflush A configuration unique to microfiltration feeds the process stream on the shell side of a capillary module with the permeate exiting the tube side. The device is run as an intermittent dead-end filter. Every few minutes, the permeate side is pressurized with air. First displacing the liquid permeate, a blast of air pushed back-

ward through the membrane pushes off the layer of accumulated solids. The membrane skin contacts the process stream, and while being backwashed, the air simultaneously expands the capillary and membrane pores slightly. This momentary expansion facilitates the removal of imbedded particles.

Process Limitations The same sorts of process limitations affecting UF apply to MF. The following section will concentrate on the differences.

Concentration Polarization The equations governing cross-flow mass transfer are developed in the section describing ultrafiltration. The velocity, viscosity, density, and channel-height values are all similar to UF, but the diffusivity of large particles (MF) is orders-of-magnitude lower than the diffusivity of macromolecules (UF). It is thus quite surprising to find the fluxes of cross-flow MF processes to be similar to, and often higher than, UF fluxes. Two primary theories for the enhanced diffusion of particles in a shear field, the inertial-lift theory and the shear-induced theory, are explained by Davis [in Ho and Sirkar (eds.), op. cit., pp. 480–505], and Belfort, Davis, and Zydney [*J. Membrane. Sci.*, **96,** 1–58 (1994)]. While not clear-cut, shear-induced diffusion is quite large compared to Brownian diffusion except for those cases with very small particles or very low cross-flow velocity. The enhancement of mass transfer in turbulent-flow microfiltration, a major effect, remains completely empirical.

Fouling Fouling affects MF as it affects all membrane processes. One difference is that the fouling effect caused by deposition of a foulant in the pores or on the surface of the membrane can be confounded by a rearrangement or compression of the solids cake which may form on the membrane surface. Also, the high, open space found in tortuous-pore membranes makes them slower to foul and harder to clean.

Equipment Configuration Since the early days when membrane was available only in flat-sheet form, the variety of offerings of various geometry and fabricated filter component types has grown geometrically. An entire catalog is devoted just to list the devices incorporating membranes whose area ranges from less than 1 cm^2 up to 3 m^2. Microfiltration has grown to maturity selling these relatively small devices. Replacement rather than reuse has long been the custom in MF, and only with later growth of very large applications, such as water, sewage, and corn sweeteners, has long membrane life become an economic necessity on a large scale.

Conventional Designs Designs familiar from other unit operations are also used in microfiltration. Cartridge-filter housings may be fitted with pleated MF membrane making a high-area dead-end membrane filter. Plate-and-frame type devices are furnished with MF sheet stock, and are common in some applications. Capillary bundles with tube-side feed are used for cross-flow applications, and are occasionally used in dead-end flow. A few tubular membranes are used. Spiral-wound modules are becoming increasingly important for process applications where economics are paramount. Belt filters have been made using MF membrane.

Ceramics Ceramic microfilters for commercial applications are almost always employed as tube-side feed multitube monoliths. They are also available as flat sheet, single tubes, discs, and other forms primarily suited to lab use. They are used for a few high-temperature applications, in contact with solvents, and particularly at very high pH.

Cassettes *Cassette* is a term used to describe two different cross-flow membrane devices. The less-common design is a usually large stack of membrane separated by a spacer, with flow moving in parallel across the membrane sheets. This variant is sometimes referred to as a **flat spiral,** since there is some similarity in the way feed and permeate are handled. The more common cassette has long been popular in the pharmaceutical and biotechnical field. It too is a stack of flat-sheet membranes, but the membrane is usually connected so that the feed flows across the membrane elements in series to achieve higher conversion per pass. Their popularity stems from easy direct scale-up from laboratory to plant-scale equipment. Their limitation is that fluid management is inherently very limited and inefficient. Both types of cassette are very compact and capable of automated manufacture.

Representative Process Applications

Pharmaceutical Removal of suspended matter is a frequent application for MF. Processes may be either clarification, in which the main product is a clarified liquid, or solids recovery. Separating cells or their fragments from broth is the most common application. Clarification of the broth in preparation for product recovery is the usual objective, but the primary goal may be recovery of cells. Cross-flow microfiltration competes well with centrifugation, conventional filtration by rotary vacuum filter or filter press and decantation. MF delivers a cleaner permeate, an uncontaminated, concentrated cell product which may be washed in the process, and generally gives high yields. There is no filter-aid disposal problem. Microfiltration has higher capital costs than the other processes, although total cost may be lower. The recovery of penicillin is an example of a process for which cross-flow microfiltration is generally accepted.

Water and Wastewater Microfiltration is beginning to be applied to large-scale potable-water treatment. Its major advantage is positive removal of cryptosporidium and giardia cysts, and its major disadvantage is cost. MF is used in a few large sewage-treatment facilities, where its primary advantage is that it permits a major reduction in the physical size of the facility.

Chemical MF is used in several applications to recover caustic values from cleaning or processing streams. An example is the caustic solution used to clean dairy evaporators, which may be cleaned for reuse by passing it through a microfilter. Significant savings in caustic purchase and disposal costs provide the incentive. Acids are also recovered and reused. Ceramic microfilters are most commonly used in these applications.

Food and Dairy Microfiltration has many applications in the food and dairy industries. An innovative dairy application uses MF membranes to remove bacteria as a nonthermal means of disinfection for milk. A special flow apparatus maintains a carefully controlled transmembrane pressure as the milk flows across the membrane. The concentrate contains the bacteria and spores, as well as any fat. The concentrate may be heat sterilized and recombined with the sterile permeate. In another milk application, some success is reported in separating fat from milk or other dairy streams by cross-flow microfiltration instead of centrifugation. Transmembrane pressure must be kept very low to prevent fat penetration into the membrane. In the food industry, MF membranes are replacing diatomaceous earth filtration in the processing of gelatin. The gelatin is passed with the permeate, but the haze producing components are retained. UF may be used downstream to concentrate the gelatin.

Flow Schemes The outline of batch, semibatch, and stages-in-series is given in the section describing ultrafiltration. Diafiltration is also described there. All these techniques are common in MF, except for stages-in-series, used rarely. MF features uses of special techniques to control transmembrane pressure in some applications. An example is one vendor's device for the microfiltration of milk. In most devices the permeate simply leaves by the nearest exit, but for this application the permeate is pumped through the device in such a way as to duplicate the pressure drop in the concentrate side, thus maintaining a constant transmembrane-pressure driving force. In spite of the low-pressure driving force, the flux is extremely high.

Limitations Some applications which seem ideal for MF, for example the clarification of apple juice, are done with UF instead. The reason is the presence of deformable solids which easily plug and blind an MF membrane. The pores of an ultrafiltration membrane are so small that this plugging does not occur, and high fluxes are maintained. UF can be used because there is no soluble macromolecule in the juice that is desired in the filtrate. There are a few other significant applications where MF seems obvious, but is not used because of deformable particle plugging.

Economics Microfiltration may be the triumph of the Lilliputians; nonetheless, there are a few large-industrial applications. Dextrose plants are very large, and as membrane filtration displaces the precoat filters now standard in the industry, very large membrane microfiltration equipment will be built.

Site Size Most MF processes require a smaller footprint than competing processes. Reduction in total-area requirements are sometimes a decisive economic advantage for MF. It may be apparent that

the floor-space costs in a pharmaceutical facility are high, but municipal facilities for water and sewage treatment are often located on expensive real estate, giving MF an opportunity despite its higher costs otherwise.

Large Plants The economics of microfiltration units costing about 10^6 is treated under ultrafiltration. When ceramic membranes are used, the cost optimum may shift energy consumption upward to as much as 10 kWh/m^3.

Disposables For smaller MF applications, short membrane life is a traditional characteristic. In these applications, costs are dominated by the disposables, and an important characteristic of equipment design is the ease, economy, and safety of membrane replacement.

Hygiene and Regulation Almost unique to MF is the influence of regulatory concerns in selection and implementation of a suitable microfilter. Since MF is heavily involved with industries regulated by the Food and Drug Administration, concerns about process stability, consistency of manufacture, virus reduction, pathogen control, and material safety loom far larger than is usually found in other membrane separations.

GAS-SEPARATION MEMBRANES

Process Description Gas-separation membranes separate gases from other gases. Some gas filters, which remove liquids or solids from gases, are microfiltration membranes. Gas membranes generally work because individual gases differ in their solubility and diffusivity through nonporous polymers. A few membranes operate by sieving, Knudsen flow, or chemical complexation.

Selective gas permeation has been known for generations, and the early use of palladium silver-alloy membranes achieved sporadic industrial use. Gas separation on a massive scale was used to separate U^{235} from U^{238} using porous (Knudsen flow) membranes. An upgrade of the membranes at Oak Ridge cost $1.5 billion. Polymeric membranes became economically viable about 1980, introducing the modern era of gas-separation membranes. H_2 recovery was the first major application, followed quickly by acid gas separation (CO_2/CH_4) and the production of N_2 from air.

Three basic mechanisms can be used for membranes in gas separation. They are types (*b*), (*c*), and (*d*) in Fig. 22-47. Membranes of type (*d*) are by far the dominant type.

The more permeable component is called the *fast gas,* so it is the one enriched in the permeate stream. Permeability through polymers is the product of solubility and diffusivity. The diffusivity of a gas in a membrane is inversely proportional to its kinetic diameter, a value determined from zeolite cage exclusion data (see Table 22-23 after Breck, *Zeolite Molecular Sieves,* Wiley, NY, 1974, p. 636).

Leading Examples These applications are commercial, some on a very large scale. They illustrate the range of application for gas-separation membranes. Unless otherwise specified, all use polymeric membranes.

Hydrogen Hydrogen recovery was the first large commercial membrane gas separation. Polysulfone fiber membranes became available in 1980 at a time when H_2 needs were rising, and these novel membranes quickly came to dominate the market. Applications include recovery of H_2 from ammonia purge gas, and extraction of H_2 from petroleum cracking streams. Hydrogen once diverted to low-quality fuel use is now recovered to become ammonia, or is used to desulfurize fuel, etc. H_2 is the fast gas.

Carbon Dioxide-Methane Much of the natural gas produced in the world is coproduced with an acid gas, most commonly CO_2 and/or H_2S. While there are many successful processes for separating the gases, membrane separation is a commercially successful competitor, especially for small installations. The economics work best for feeds with very high or very low CH_4 content. Methane is a slow gas; CO_2, H_2S, and H_2O are fast gases.

Oxygen-Nitrogen Because of higher solubility, in many polymers, O_2 is faster than N_2 by a factor of 5. Water is much faster still. Since simple industrial single-stage air compressors provide sufficient pressure to drive an air-separating membrane, moderate purity N_2 (95–99.5%) may be produced in low to moderate quantities quite economically by membrane separation. (Argon is counted as part of the nitrogen.) An O_2-enriched stream is a coproduct, but it is rarely of economic value. The membrane process to produce O_2 as a primary product has a limited market.

Helium Helium is a very fast gas, and may be recovered from natural gas through the use of membranes. More commonly, membranes are used to recover He after it has been used and become diluted.

Gas Dehydration Water is extremely permeable in polymer membranes. Dehydration of air and other gases is a growing membrane application.

Vapor Recovery Organic vapors are recovered from gas streams using highly permeable rubbery polymer membranes which are generally unsuitable for permanent gas separations because of poor selectivity. The high sorption of vapors in these materials makes them ideal for stripping and recovering vapors from gases.

Competing Processes Membranes are not the only way to make these separations, neither are they generally the dominant way. In many applications, membranes compete with cryogenic distillation and with pressure-swing adsorption; in others, physical absorption is the dominant method. The growth rate for membrane capacity is higher than that for any competitor.

Basic Principles of Operation Gas-separation literature often

TABLE 22-23 Kinetic Diameters for Important Gases

Penetrant	He	H_2	NO	CO_2	Ar	O_2	N_2	CO	CH_4	C_2H_4	Xe	C_3H_8
Kinetic dia, nm	0.26	0.289	0.317	0.33	0.34	0.346	0.364	0.376	0.38	0.39	0.396	0.43

TABLE 22-24 Gas-Permeation Units

Quantity	Engineering units	Literature units	SI units
Permeation rate	Standard cubic feet/minute		kmol/s
Permeation flux	ft^3/ft^2·day	cm/sec (STP)	kmol/m^2·s
Permeability	ft^3·ft/ft^2·day·psi	Barrers	kmol/m·s·Pa
Permeance	ft^3/ft^2·day·psi	Barrers/cm	kmol/m^2·s·Pa

TABLE 22-25 Barrer Conversion Factors

Quantity	Multiply	By	To get
Permeability	Barrers	3.348×10^{-19}	kmol/m·s·Pa
Permeability	Barrers	4.810×10^{-8}	ft^3(STP)/ft·psi·day
Permeance	Barrers/cm	3.348×10^{-17}	kmol/m^2·s·Pa
Permeance	Barrers/cm	1.466×10^{-6}	ft^3(STP)/ft^2·psi·day

TABLE 22-26 Industry-Specific Gas Measures

Industry-unit	How measured	Cubic feet per pound mole	kmol per mscf
STP, Mscf	1000 ft^3 at 32°F	359.3	1.262
Gas industry, Mscf	1000 ft^3 at 60°F	379.8	1.194
Air industry, Mnsf	1000 ft^3 at 70°F	387.1	1.172

uses nomenclature derived from distillation, a practice that will generally be followed here. L is the molar feed rate, V is the molar permeate rate, R is the molar residue ($L - V$). Mole fractions of components i, j, in the feed-residue phase will be x_i, x_j . . . and in the permeate phase y_i, y_j. . . . Stage cut, Θ, is permeate volume/feed volume, or V/L.

Basic Equations In "Background and Definitions," the basic equation for gas permeation was derived with the major assumptions noted. Equation (22-62) may be restated as:

$$J_i \sim N_i = (\rho_i/z)(p_{i,\text{feed}} - p_{i,\text{permeate}}) \tag{22-97}$$

where ρ_i is the permeability of component i through the membrane, J_i is the flux of component i through the membrane for the *partial pressure difference* (Δp) of component i. z is the effective thickness of the membrane. By choosing units appropriately, $J = \rho\Delta p$.

A similar equation may be written for a second component, j, and any additional number of components, employing partial pressures:

$$J_j = (\rho_j/z)(p_{j,\text{feed}} - p_{j,\text{permeate}}) \tag{22-98}$$

The total pressure is the sum of the partial pressures:

$$P_{\text{feed}} = \sum (p_{\text{feed}})_{i,j,\ldots} \tag{22-99}$$

$$P_{\text{permeate}} = \sum (p_{\text{permeate}})_{i,j,\ldots} \tag{22-100}$$

For simplicity, consider a two component system. The volume fraction of a component is

$$x_i = \frac{p_{\text{feed}}}{P_{\text{feed}}} \tag{22-101}$$

$$y_i = \frac{p_{\text{permeate}}}{P_{\text{permeate}}} \tag{22-102}$$

When two species are permeating through a membrane, the ratio of their fluxes can be written following Eqs. (22-97) and (22-98) as:

$$\frac{J_i}{J_j} = \frac{\dfrac{\rho_i}{z}(p_{i,\text{feed}} - p_{i,\text{permeate}})}{\dfrac{\rho_i}{z}(p_{j,\text{feed}} - p_{j,\text{permeate}})} \tag{22-103}$$

Recalling Eq. (22-63), and restating it in the nomenclature for gas membranes:

$$\alpha = \frac{y_i/y_j}{x_i/x_j} \tag{22-104}$$

Defining the pressure ratio $\Phi = P_{\text{feed}}/P_{\text{permeate}}$ and applying Eqs. (22-99) through (22-102) gives:

$$\frac{J_i}{J_j} = \alpha\left[\frac{x_i - (y_i/\Phi)}{x_j - (y_j/\Phi)}\right] \tag{22-105}$$

Combining these equations and rearranging, the permeate composition may be solved explicitly:

$$y_i = \left(\frac{\Phi}{2}\right)\left[x_i + \frac{1}{\Phi} + \frac{1}{\alpha - 1} - \sqrt{\left(x_i + \frac{1}{\Phi} + \frac{1}{\alpha - 1}\right)^2 - \frac{4\alpha x_i}{(\alpha - 1)\Phi}}\right] \tag{22-106}$$

Equation (22-106) gives a permeate concentration as a function of the feed concentration at a stage cut, $\Theta = 0$, To calculate permeate composition as a function of Θ, the equation may be used iteratively if the permeate is unmixed, such as would apply in a test cell. The calculation for real devices must take into account the fact that the driving force is variable due to changes on both sides of the membrane, as partial pressure is a point function, nowhere constant. Using the same caveat, permeation rates may be calculated component by component using Eq. (22-98) and permeance values. For any real device, both concentration and permeation require iterative calculations dependent on module geometry.

Driving Force Gas moves across a membrane in response to a difference in chemical potential. Partial pressure is sufficiently proportional to be used as the variable for design calculations for most gases of interest, but fugacity must be used for CO_2 and usually for H_2 at high pressure. Gas composition changes as a gas passes along a membrane. As the fast gas passes through the membrane, x_i drops. Total pressure on the upstream side of the membrane drops because of frictional losses in the device. Frictional losses on the permeate side will affect the permeate pressure. The partial pressure of a component in the permeate may thus rise rapidly. Permeation rate is a point function, dependent on the difference in partial pressures at a point on the membrane. Many variables affect point partial pressures, among them are membrane structure, module design, and permeate gas-sweep rates. Juxtaposition of feed and permeate is a function of permeator design, and a rapid decline in driving force may result when it is not expected (see "Membrane System Design Features"). An additional complication may arise in a few cases from the Joule-Thompson effect during expansion of a gas through a membrane changing the temperature. High-pressure CO_2 is an example.

Plasticization Gas solubility in the membrane is one of the factors governing its permeation, but the other factor, diffusivity, is not always independent of solubility. If the solubility of a gas in a polymer is too high, plasticization and swelling result, and the critical structure that controls diffusion selectivity is disrupted. These effects are particularly troublesome with condensable gases, and are most often noticed when the partial pressure of CO_2 or H_2S is high. H_2 and He do not show this effect This problem is well known, but its manifestation is not always immediate.

Limiting Cases Equation (22-106) has two limiting cases for a binary system. First, when $\alpha \gg \phi$. In this case, selectivity is no longer very important.

$$y_i \cong x_i \frac{P_{\text{feed}}}{P_{\text{permeate}}} = x_i\Phi \tag{22-107}$$

Module design is very important for this case, as the high α may result in high permeate partial pressure. An example is the separation of H_2O from air.

Conversely, when $\Phi \gg \alpha$, pressure ratio loses its importance, and permeate composition is:

$$y_i \cong \frac{x_i\alpha}{[1 + x_i(\alpha - 1)]} \tag{22-108}$$

Module design for this case is of lesser importance.

Selectivity and Permeability

State of the Art A desirable gas membrane has high separating power (α) and high permeability to the fast gas, in addition to critical requirements discussed below. The search for an ideal membrane produced copious data on many polymers, neatly summarized by Robeson [*J. Membrane Sci.*, **62,** 165 (1991)]. Plotting log permeability versus log selectivity (α), an "upper bound" is found (see Fig. 22-73) which all the many hundreds of data points fit. The data were taken between 20–50°C, generally at 25 or 35°C.

The lower line in Fig. 22-73 shows the upper bound in 1980. Although no breakthrough polymers have been reported in the past few years, it would be surprising if these lines remain the state of the art forever.

The upper-bound line connects discontinuous points, but polymers exist near the bound for separations of interest. Whether these will be available as membranes is a different matter. A useful membrane requires a polymer which can be fabricated into a device having an active layer around 50 nm thick. At this thickness, membrane properties may vary significantly from bulk properties, although not by a factor of 2.

The data reported are *permeabilities,* not *fluxes.* Flux is propor-

TABLE 22-27 High-Performance Polymers for O_2/N_2*

Polymer	α (O_2/N_2)	ρ (O_2)—Barrers
Poly (trimethylsilylpropyne)	2.0	4000
Tetrabromo Bis A polycarbonate	7.47	1.36
Poly (tert-butyl acetylene)	3.0	300
Vectra polyester	15.3	0.00046
Poly (triazole)	9.0	1.2
Polypyrrolone	6.5	7.9

*Polymers that are near the upper bound and their characteristics.

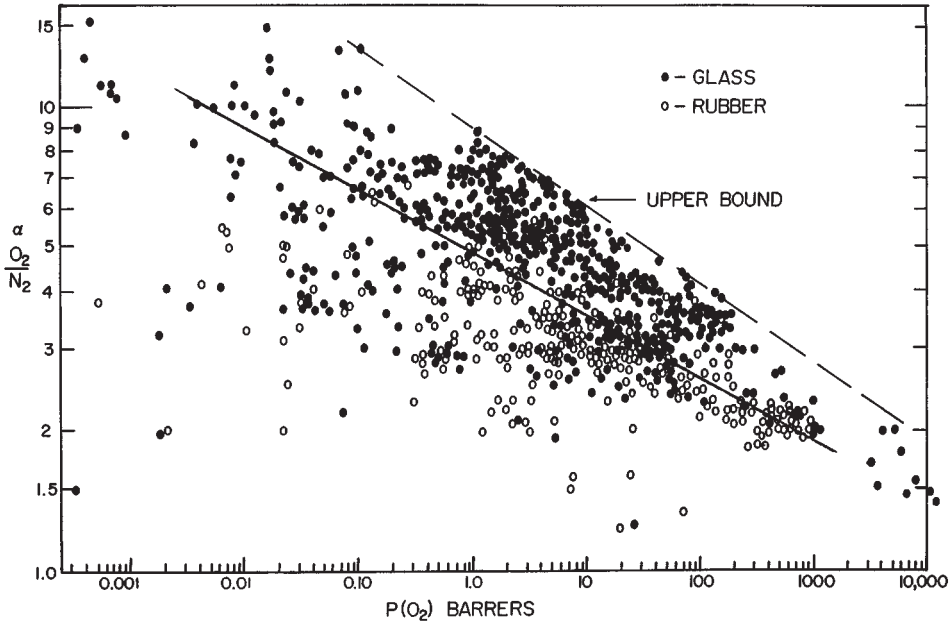


FIG. 22-73 Plot of separation factor versus permeability for many polymers, O_2/N_2. Abscissa—"Fast Gas Permeability, $\rho(O_2)$ Barrers." Ordinate—"Selectivity, α (O_2/N_2)."

tional to permeability/thickness. The separations designer must deal with real membranes, for which thickness is determined by factors outside the designer's control. It is vital that flux data are used in design.

Glassy polymers are significantly overrepresented in the high-selectivity region near the upper bound, and rubbery polymers are overrepresented at the high-permeability end, although the highest-permeability polymer discovered, poly(trimethylsilylpropyne) is glassy. Most of the polymers with interesting properties are noncrystalline. Current membrane-materials research is strongly focused on glassy materials and on attempts to improve diffusivity, as it seems more promising than attempts to increase solubility [Koros, *North Am. Membrane Soc. Sixth Annual Meeting,* Breckenridge, CO (1994)].

Robeson [*J. Membrane Sci.,* **62,** 165 (1991); *Polymer,* **35,** 4970 (1994)] has determined upper-bound lines for many permeant pairs in hundreds of polymers. These lines may be drawn from Eq. (22-109) and the data included in Table 22-28. These values will give ρ_i in Barrers; α is dimensionless. Robeson [op.cit., (1991); op. cit., (1994)] lists high-performance polymers for most of these gas pairs, like Table 22-28.

$$\log \rho_i = \log k - m \log \alpha_{ij} \qquad (22\text{-}109)$$

Temperature Effects A temperature increase in a polymer membrane permits larger segmental motions in the polymer, producing a dramatic increase in diffusivity. Countering this is a decrease in solubility. It increases the size of the gaps in the polymer matrix, decreasing diffusivity selectivity. The net result is that for a glassy polymer, permeability rises while selectivity declines. For organic permeants in rubbery polymers, this trend is often reversed.

Plasticization and Other Time Effects Most data from the literature, including those presented above are taken from experiments where one gas at a time is tested, with α calculated as a ratio of the two permeabilities. If either gas permeates because of a high-sorption coefficient rather than a high diffusivity, there may be an increase in the permeability of all gases in contact with the membrane. Thus, the α actually found in a real separation may be much lower than that calculated by the simple ratio of permeabilities. The data in the literature do not reliably include the plasticization effect. If present, it results in the sometimes slow relaxation of polymer structure giving a rise in permeability and a dramatic decline in selectivity.

Other Caveats Transport in glassy polymers is different from transport in rubbery ones. In glassy polymers, there are two sites in which sorption may occur, and the literature dealing with dual-mode sorption is voluminous. The simplest case describes behavior when the downstream pressure is zero. It is of great help in understanding the theory but of limited value in practice. There are concerns about permeation of mixtures in glassy polymers with reports of crowding out and competitive sorption. Practical devices are built and operated for many streams, and the complications are often minor. But taking data independently determined for two pure gases and dividing them to obtain α in the absence of other facts is risky.

TABLE 22-28 Upper-Bound Coordinates for Gas Pairs

Gas pair	log k	m
He/N_2	4.0969	1.0242
H_2/N_2	4.7236	1.5275
He/CH_4	3.6991	0.7857
H_2/CH_4	4.2672	1.2112
O_2/N_2	5.5902	5.800
He/O_2	3.6628	1.295
H_2/O_2	4.5534	2.277
CO_2/CH_4	6.0309	2.6264
He/H_2	2.9823	4.9535
He/CO_2	2.8482	1.220
H_2/CO_2	3.0792	1.9363

Gas-Separation Membranes

Organic Organic polymer membranes are the basis for almost all commercial gas-separation activity. Early membranes were cellulose esters and polysulfone. These membranes have a large installed base. New installations are dominated by specialty polymers designed for the purpose, including some polyimides and halogenated polycarbonates. In addition to skinned membranes, composites are made from "designer" polymers, requiring as little as 2 g/1000 m^2. The rapid rise of N_2/O_2 membranes in particular is the result of stunning improvements in product uniformity and quality. A few broken fibers in a

100 m^2 module results in the module's being scrapped.

Caulked Membrane manufacturing defects are unavoidable, and pinholes are particularly deleterious in gas-separation membranes. A very effective remedy is to **caulk** the membrane by applying a highly permeable, very thin topcoat over the finished membrane. While the coating will have poor selectivity, it will plug up the gross leaks while impairing the fast gas permeance only slightly. Unless the as-cast membrane is almost perfect, caulking dramatically improves membrane performance.

Metallic Palladium films pass H_2 readily, especially above 300°C. α for this separation is extremely high, and H_2 produced by purification through certain Pd alloy membranes is uniquely pure. Pd alloys are used to overcome the crystalline instability of pure Pd during heating-cooling cycles. Economics limit this membrane to high-purity applications.

Advanced Materials Experimental membranes have shown remarkable separations between gas pairs such as O_2/N_2 whose kinetic diameters (see Table 22-23) are quite close. Most prominent is the carbon molecular sieve membrane, which operates by ultramicroporous molecular sieving (see Fig. 22-48*c*). Preparation of large-scale permeators based on ultramicroporous membranes has proven to be a major challenge.

Catalytic A catalytic-membrane reactor is a combination heterogeneous catalyst and permselective membrane that promotes a reaction, allowing one component to permeate. Many of the reactions studied involve H_2. Membranes are metal (Pd, Ag), nonporous metal oxides, and porous structures of ceramic and glass. Falconer, Noble, and Sperry [in Noble and Stern (eds.), op. cit., pp. 669–709] review status and potential developments.

Membrane System Design Features For the rate process of permeation to occur, there must be a driving force. For gas separations, that force is partial pressure (or fugacity). Since the ratio of the component fluxes determines the separation, the partial pressure of each component at each point is important. There are three ways of driving the process: Either high partial pressure on the feed side (achieved by high total pressure), or low partial pressure on the permeate side, which may be achieved either by vacuum or by introduction of a sweep gas. Both of the permeate options have negative economic implications, and they are less commonly used.

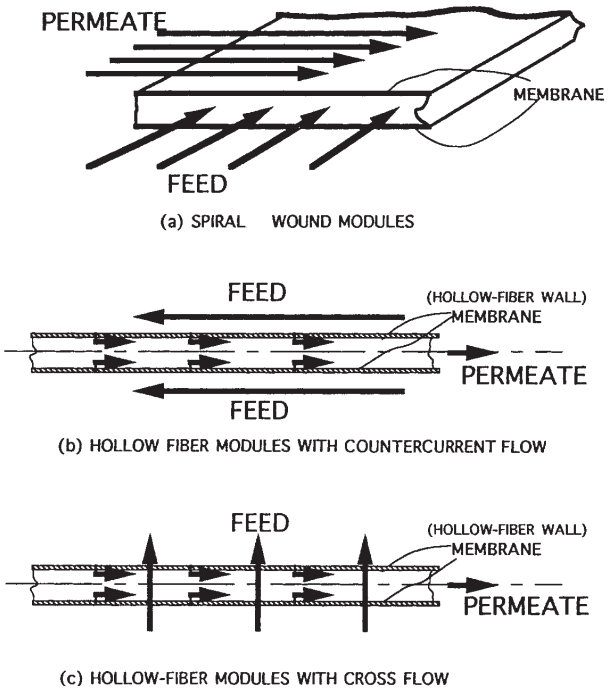


FIG. 22-74 Flow paths in gas permeators. (*Courtesy Elsevier.*)

Figure 22-74 shows three of the principal operating modes for gas membranes. A critical issue is the actual partial pressure of permeant at a point on the membrane. Flow arrangements for the permeate are very important in determining the efficiency of the separation, in rough analogy to the importance of arrangements in heat exchangers.

Spiral membranes are the usual way to form flat sheet into modules. They have the characteristic that the feed and the permeate move at right angles. Since the membrane is always cast on a porous support, point-permeate values are influenced by the substrate.

Hollow-fiber membranes may be run with shell-side or tube-side feed, cocurrent, countercurrent or in the case of shell-side feed and two end permeate collection, co- and countercurrent. Not shown is the scheme for feed inside the fiber, common practice in lower-pressure separations such as air.

The design of the membrane device will influence whether the membrane is operating near its theoretical limit. Sengupta and Sirkar [in Noble and Stern (eds.), op. cit., pp. 499-552] treat module design thoroughly (including numerical examples for most module configurations) and provide an extensive bibliography.

For a hollow-fiber device running with shell-side feed with the membrane on the outside, Giglia et al. [*Ind. Eng. Chem Research,* **29,** 1239–1248 (1991)] analyzed the effect of membrane-backing porosity on separation efficiency. The application is production of N_2 from air, the desired result being the lowest possible O_2 content in the retentate at a given stage cut. The modules used were operated cocurrent and countercurrent. If the porous-membrane backing prevented the permeate from mixing with the gas adjacent to the membrane, a result approximating cross-flow is expected. For the particular membrane structure used, the experimental result for cocurrent flow was quite close to the calculated cocurrent value, while for countercurrent flow, the experimental data were between the values calculated for the crosscurrent model and the countercurrent model. For a membrane to be commercially useful in this application, the mass transfer on the permeate side must exceed the crosscurrent model.

Air is commonly run with tube-side feed. The permeate is run countercurrent with the separating skin in contact with the permeate. (The feed gas is in contact with the macroporous back side of the membrane.) This configuration has proven to be superior, since the permeate-side mass-transfer problem is reduced to a minimum, and the feed-side mass-transfer problem is not limiting.

Partial Pressure Pinch An example of the limitations of the partial pressure pinch is the dehumidification of air by membrane. While O_2 is the fast gas in air separation, in this application H_2O is faster still. Special dehydration membranes exhibit α = 20,000. As gas passes down the membrane, the partial pressure of H_2O drops rapidly in the feed. Since the H_2O in the permeate is diluted only by the O_2 and N_2 permeating simultaneously, p_{H2O} rises rapidly in the permeate. Soon there is no driving force. The commercial solution is to take some of the dry air product and introduce it into the permeate side as a countercurrent sweep gas, to dilute the permeate and lower the H_2O partial pressure. It is in effect the introduction of a leak into the membrane, but it is a controlled leak and it is introduced at the optimum position.

Fouling Industrial streams may contain condensable or reactive components which may coat, solvate, fill the free volume, or react with the membrane. Gases compressed by an oil-lubricated compressor may contain oil, or may be at the water dew point. Materials that will coat or harm the membrane must be removed before the gas is treated. Most membranes require removal of compressor oil. The extremely permeable poly(trimethylsilylpropyne) may not become a practical membrane because it loses its permeability rapidly. Part of the problem is pore collapse, but it seems extremely sensitive to contamination even by diffusion pump oil and gaskets [Robeson, op. cit., (1994)].

A foulinglike problem may occur when condensable vapors are left in the residue. Condensation may result which in the best case results in blinding of the membrane, and in the usual case, destruction of the membrane module. Dew-point considerations must be part of any gas-membrane design exercise.

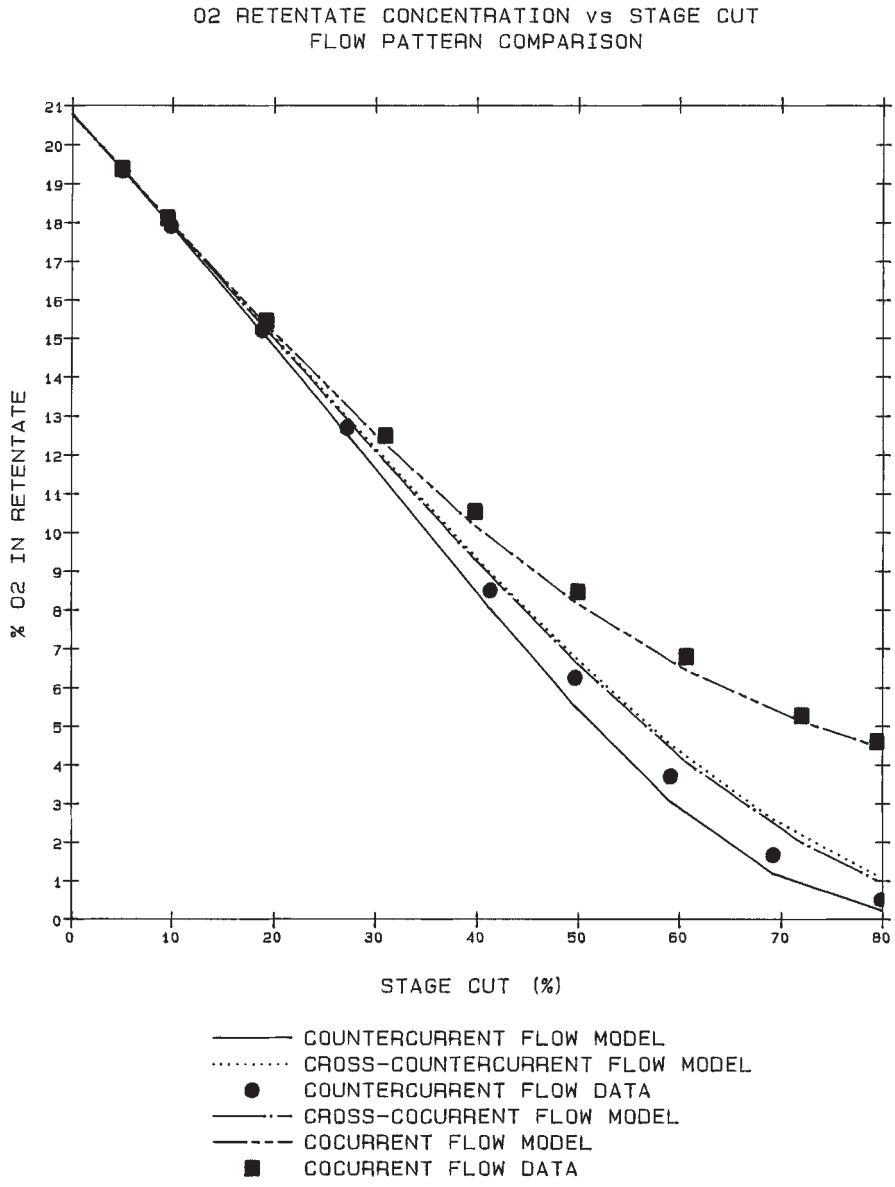


FIG. 22-75 Air fractionation by membrane. O_2 in retentate as a function of feed fraction passed through the membrane (stage cut) showing the different result with changing process paths. Process has shell-side feed at 690 kPa (abs) and 298 K. Module comprised of hollow fibers, diameter 370 μm od × 145 μm id × 1500 mm long. Membrane properties $\alpha = 5.7$ (O_2/N_2), permeance for $O_2 = 3.75 \times 10^{-6}$ Barrer/cm. (*Courtesy Innovative Membrane Systems/ Praxair.*)

Modules and Housings Modern gas membranes are packaged either as hollow-fiber bundles or as spiral-wound modules. The former uses extruded hollow fibers. Tube-side feed is preferable, but it is limited to about 1.5 MPa. Higher-pressure applications are usually fed on the shell side. A large industrial permeator contains fibers 400 μm by 200 μm i.d. in a 6-inch shell ten feet long. Flat-sheet membrane is wound into spirals, with an 8- by 36-inch permeator containing 25 m^2 of membrane. Both types of module are similar to those illustrated in "Background and Definitions." Spiral modules are useful when feed flows are very high and especially in vapor-permeation applications. Otherwise, fiber modules have a large and growing share of the market.

Energy Requirements The thermodynamic minimum energy requirement to separate a metric ton of N_2 from air and compress it to atmospheric pressure at 25°C is independent of separation method, 20.8 MJ or 5.8 kWh. In practice, a cryogenic distillation plant requires twice this energy, and it produces a very pure product as a matter of course. The membrane process requires somewhat more energy than distillation at low purity and much more energy at high purity. Membranes for O_2-reduced air are economical and are a rapidly growing application, but not because of energy efficiency. Figure 22-75 may be used to estimate membrane energy requirements. From the required purity, locate the stage cut on either of the countercurrent flow curves. The compressor work required is calculated using the pressure and the term (product flow rate)/$(1 - \Theta)$. The N_2-rich product is produced at pressure, and the O_2-enriched permeate is vented. For

example, if gas is required containing 97 percent inerts, assume the product composition would be 96 percent N_2, 2 percent O_2, 1 percent Ar and 3 percent O_2, giving a calculated molar mass of 28.2. One tonne would thus contain 35.4 kmol. For 98 percent inerts, Fig. 22-75 shows a stage cut of 67 percent when operating at 690 kPa (abs) and 25°C. Therefore, 35.5/(1 − 0.67) = 108 kmol of air are required as feed. The adiabatic compression of 108 kmol of air from atmospheric pressure and 300K (it would subsequently be cooled to 273 + 25 = 298K) requires 192 kWh. Assuming 75 percent overall compressor + driver efficiency, 256 kWh are required. For comparison, a very efficient, large N_2 distillation plant would produce 99.99 percent N_2 at 690 kPa for 113 kWh/metric ton. The thermodynamic minimum to separate (N_2 + Ar) and deliver it at the given P and T is 72 kWh.

Economics It is ironic that a great virtue of membranes, their versatility, makes economic optimization of a membrane process very difficult. Designs can be tailored to very specific applications, but each design requires a sophisticated computer program to optimize its costs. Spillman [in Noble and Stern (eds)., op. cit., pp. 589–667] provides an overall review and numerous specific examples including circa 1989 economics.

Rules of Thumb With a few notable exceptions such as H_2 through Pd membranes, membrane separations are not favored when a component is required at high purity. Often, membranes serve these needs by providing a moderate purity product which may be inexpensively upgraded by a subsequent process. Increasing the purity of N_2 by the introduction of H_2 or CH_4 to react with unwanted O_2 is a good example. Unless permeates are recycled, high product purity is accompanied by lower product recovery.

Pressure ratio (Φ) is quite important, but transmembrane ΔP matters as well. Consider the case of a vacuum permeate ($\Phi = \infty$): The membrane area will be an inverse function of P. Φ influences separation and area, transmembrane ΔP influences area.

In a binary separation, the highest purity of integrated permeate occurs at $\Theta = 0$. Purity decreases monotonically until it reaches the feed purity at $\Theta = 1$. In a ternary system, the residue concentration of the gas with the intermediate permeability will reach a maximum at some intermediate stage cut.

Concentration polarization is a significant problem only in vapor separation. There, because the partial pressure of the penetrant is normally low and its solubility in the membrane is high, there can be depletion in the gas phase at the membrane. In other applications it is usually safe to assume bulk gas concentration right up to the membrane.

Another factor to remember is that for $\alpha = 1$, or for $\Phi = 1$, or for $(1/\Theta) = 1$ there is no separation at all. Increasing any of the quantities as defined make for a better separation, but the improvement is diminishing in all cases as the value moves higher. An example of the economic tradeoff between permeability and α is illustrated in Fig. 22-76 where the economics are clearly improved by sacrificing selectivity for flux.

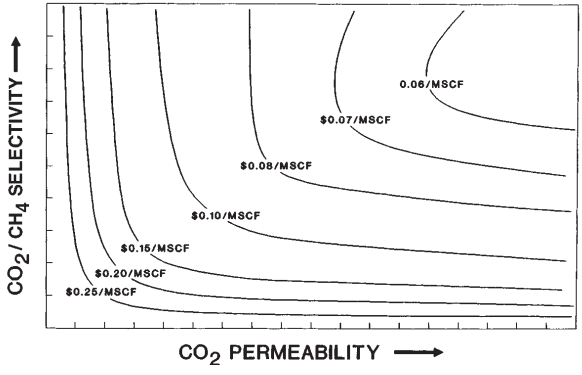


FIG. 22-76 Constant-cost lines as a function of permeability and selectivity for CO_2/CH_4. Cellulose-acetate membrane "mscf" is one thousand standard cubic feet. (*Courtesy W. R. Grace.*)

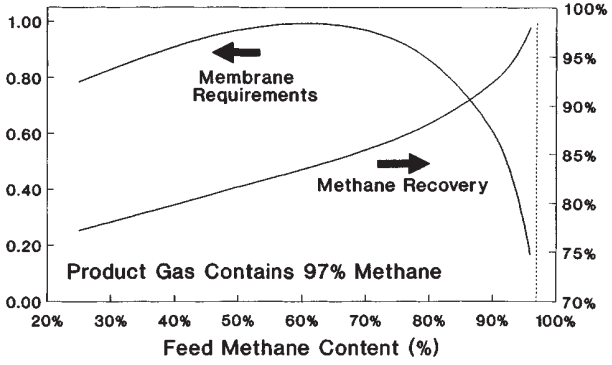


FIG. 22-77 Influence of feed purity on total membrane area when the residue gas at fixed purity is the product. Feed-gas volume is constant. CO_2/CH_4 cellulose-acetate membrane, $\alpha = 21$. (*Courtesy W. R. Grace.*)

Compression If compression of either feed or permeate is required, it is highly likely that compression capital and operating costs will dominate the economics of the gas-separation process. In some applications, pressure is essentially "free," such as when removing small quantities of CO_2 from natural gas. The gas is often produced at pressure, but is compressed for transmission anyway, and since the residue constitutes the product, it continues downstream at pressure. H_2 frequently enters the separation process at pressure, an advantage for membranes. Unlike CH_4, the H_2 is in the permeate, and recompression may be a significant cost. A relative area cure for CO_2/CH_4 is shown in Fig. 22-77. When the permeate is the product (H_2, CO_2) the increasing membrane area shown in Fig. 22-78 is largely the effect of more gas to pass through the membrane, since the curve is based on a constant volume of feed gas, not a constant output of H_2. The facts of life in compressor economics are in painful opposition to the desires of the membrane designer. Pressure ratios higher than six become expensive; vacuum is very expensive, and scale is important. Because of compressor economics, staging membranes with recompression is unusual. Designers can assume that a flow sheet that mixes unlike streams or reduces pressure through a throttling valve will increase cost in most cases.

Product Losses Account must be taken of the product loss, the slow gas in the permeate (such as CH_4), or the fast gas in the residue (such as H_2). Figure 22-79 illustrates the issue for a membrane used to purify natural gas from 93 percent to pipeline quality, 98 percent. In the upper figure, the gas is run through a permeator bank operating as a single stage. For the membrane and module chosen, the permeate contains 63 percent CH_4. By dividing the same membrane area into

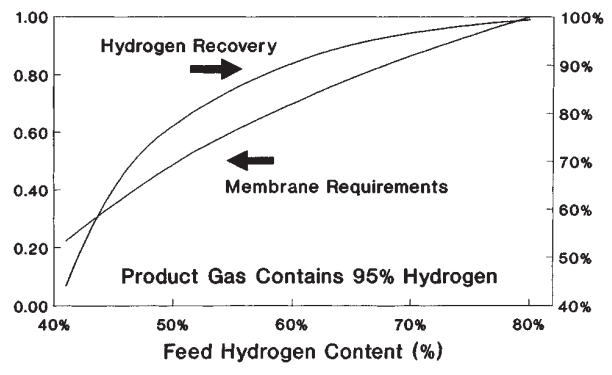
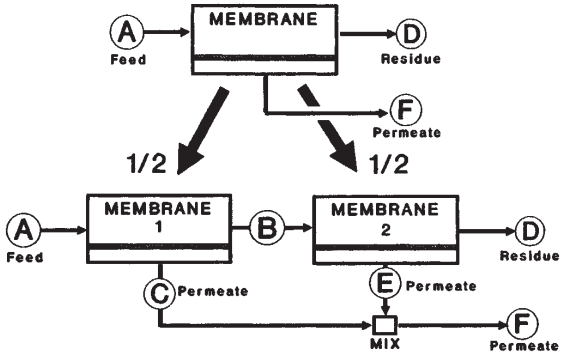


FIG. 22-78 Influence of feed purity on total membrane area when the permeate gas at fixed purity is the product. Feed-gas volume is constant. H_2/CH_4 cellulose-acetate membrane, $\alpha = 45$. (*Courtesy W. R. Grace.*)



		A	B	C	D	E	F
CO2	%	7.0	3.6	43.9	2.0	27.3	36.6
CH4	%	93.0	96.2	56.1	98.0	72.7	63.4
RATE	Ratio	1.00	0.92	0.08	0.86	0.06	0.14
PRESS	psia	860	860	15	860	15	15

FIG. 22-79 Effect on permeate of dividing a one-stage separation into two equal stages having the same total membrane area. Compositions of A, D, and F are equal for both cases. (*Courtesy W. R. Grace.*)

two stages, two permeates (or more) may be produced, one of which may have significantly higher economic value than the single mixed permeate. In fact, where CH_4 is involved, another design parameter is the local economic value of various waste streams as fuel.

Membrane Replacement Membrane replacement is a significant cost factor, but membrane life and reliability are now reasonable. Membranes are more susceptible to operating upsets than more traditional equipment, but their field-reliability record in properly engineered, properly maintained installations is good to excellent. In N_2 separations, membrane life is very long.

Competing Technologies The determination of which separation technique is best for a specific application is a dynamic function of advances in membranes and several other technologies. At this writing, very small quantities of pure components are best obtained by purchase of gas in cylinders. For N_2, membranes become competitive at moderate flow rates where purity required is <99.5 percent. At higher flow rates and higher purity, *pressure swing adsorption* (PSA) is better (see Sec. 16: "Adsorption and Ion Exchange"). At still higher volumes, delivered liquid N_2, pipeline N_2, or on-site distillation will be superior. For O_2, membranes have little economic importance. The problem is the economic cost of using vacuum on the permeate side, or the equally unattractive prospect of compressing the feed and operating at low stage cut. For H_2, membranes are dominant when the feed is at high pressure, except for high purity (excepting Pd noted above) and very large volume. Higher purity or lower feed pressure favor PSA. Very high volume favors cryogenic separation. For CH_4, membranes compete at low purity and near pipeline (98 percent) purity, but distillation and absorption are very competitive at large scale and for intermediate CO_2 contamination levels.

Membranes are found as adjuncts to most conventional processes, since their use can improve overall economics in cases where membrane strength coincides with conventional process weakness.

PERVAPORATION

Process Description **Pervaporation** is a separation process in which a liquid mixture contacts a nonporous permselective membrane. One component is transported through the membrane preferentially. It evaporates on the downstream side of the membrane leaving as a vapor. The name is a contraction of permeation and evaporation. Permeation is induced by lowering partial pressure of the permeating component, usually by vacuum or occasionally with a sweep gas. The permeate is then condensed or recovered. Thus, three steps are necessary: Sorption of the permeating components into the membrane, diffusive transport across the nonporous membrane, then desorption into the permeate space, with a heat effect. Pervaporation membranes are chosen for high selectivity, and the permeate is often highly purified.

In the flow schematic (Fig. 22-80), the condenser controls the vapor pressure of the permeating component. The vacuum pump, as shown, pumps both liquid and vapor phases from the condenser. Its major duty is the removal of noncondensibles. Early work in pervaporation focused on organic-organic separations. Many have been demonstrated; few if any have been commercialized. Still, there are prospects for some difficult organic separations.

An important characteristic of pervaporation that distinguishes it from distillation is that it is a rate process, not an equilibrium process. The more permeable component may be the less-volatile component. Pervaporation has its greatest utility in the resolution of azeotropes, as an adjunct to distillation. Selecting a membrane permeable to the minor component is important, since the membrane area required is roughly proportional to the mass of permeate. Thus pervaporation devices for the purification of the ethanol-water azeotrope (95 percent ethanol) are always based on a hydrophilic membrane.

Pervaporation membranes are of two general types. **Hydrophilic membranes** are used to remove water from organic solutions, often from azeotropes. **Hydrophobic membranes** are used to remove organic compounds from water. The important operating characteristics of hydrophobic and hydrophilic membranes differ. Hydrophobic membranes are usually used where the solvent concentration is about

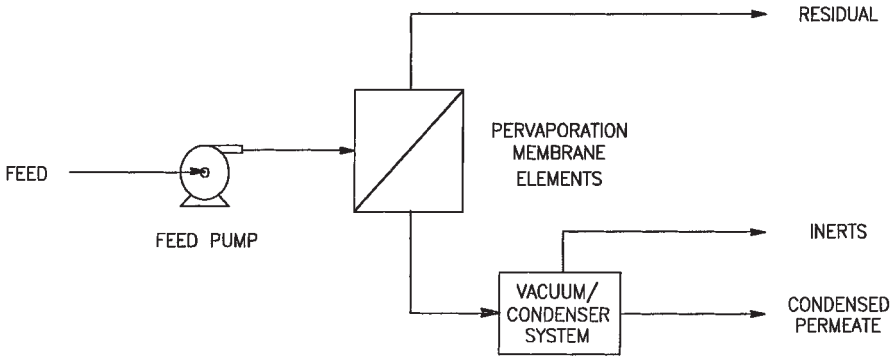


FIG. 22-80 Simplified flow schematic for a pervaporation system. Heated feed enters from left through a feed pump. Heaters in a recirculating feed loop may be required (not shown). Stripped liquid exits at the top of the pervaporation membrane. Vapor exits at the bottom to a condenser. Liquid and noncondensibles are removed under vacuum. (*Courtesy Hoechst Celanese.*)

6 percent or less—above this value, other separations methods are usually cheaper unless the flow rate is small. At low-solvent levels the usual membrane (silicone rubber) is not swollen appreciably, and movement of solvent into the membrane makes depletion of solvent in the boundary layer (concentration polarization) an important design problem. Hydrophilic pervaporation membranes operate such that the upstream portion is usually swollen with water, while the downstream face is low in water concentration because it is being depleted by vaporization. Fluxes are low enough (<5 kg/m²·hr) that boundary layer depletion (liquid side) is not limiting.

The simplifying assumptions that make Fick's law useful for other processes are not valid for pervaporation. The activity gradient across the membrane is far more important than the pressure gradient. Equation (22-110) is generally used to describe the pervaporation process:

$$J_i = -D_i C \frac{d \ln a_i}{dz} \qquad (22\text{-}110)$$

where a_i is the activity coefficient of component *i*.

This equation is not particularly useful in practice, since it is difficult to quantify the relationship between concentration and activity. The Flory-Huggins theory does not work well with the cross-linked semi-crystalline polymers that comprise an important class of pervaporation membranes. Neel (in Noble and Stern, op. cit., pp. 169–176) reviews modifications of the Stefan-Maxwell approach and other equations of state appropriate for the process.

A typical permeant-concentration profile in a pervaporation membrane is shown in Fig. 22-81. The concentration gradient at the permeate (vapor side) of the hydrophilic membrane is usually rate controlling. Therefore the downstream pressure (usually controlled by condenser temperature) is very important for flux and selectivity. Since selectivity is the ratio of fluxes of the components in the feed, as downstream pressure increases, membrane swelling at the permeate interface increases, and the concentration gradient at the permeate interface decreases. The permeate flux drops, and the more swollen membrane is less selective. A rise in permeate pressure may result in a drastic drop in membrane selectivity. This effect is diminished at low water concentrations, where membrane swelling is no longer dominant. In fact, when the water concentration drops far enough, permeate backpressure looses its significance. (See Fig. 22-82.)

For rubbery membranes (hydrophobic), the degree of swelling has less effect on selectivity. Thus the permeate pressure is less critical to the separation, but it is critical to the driving force, thus flux, since the vapor pressure of the organic will be high compared to that of water.

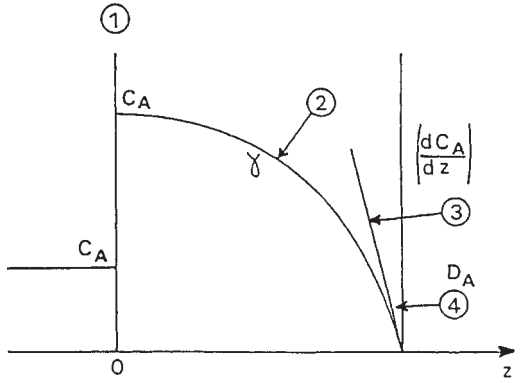


FIG. 22-81 Permeant-concentration profile in a pervaporation membrane. 1—Upstream side (swollen). 2—Convex curvature due to concentration-dependent permeant diffusivity. 3—Downstream concentration gradient. 4—Exit surface of membrane, depleted of permeant, thus unswollen. (*Courtesy Elsevier.*)

Definitions Following the practice presented under "Gas-Separation Membranes," distillation notation is used. Literature articles often use mass fraction instead of mole fraction, but the substitution of one to the other is easily made.

$$\beta \equiv \frac{y_i}{x_i} \qquad (22\text{-}111)$$

where β is the enrichment factor. β is related to α, [Equation (22-104)] the separation factor by

$$\beta = \frac{\alpha}{1 + (\alpha - 1)x_i} \qquad \alpha = \frac{\beta(1 - x_i)}{1 - x_i\beta} \qquad (22\text{-}112)$$

α is larger than β, and conveys more meaning when the membrane approaches the ideal. β is preferred in pervaporation because it is easier to use in formulations for cost, yield, and capacity. In fact, note that neither factor is constant, and that both generally change with x_i and temperature.

Operational Factors In industrial use, pervaporation is a continuous-flow single-stage process. Multistage cascade devices are unusual. Pervaporation is usually an adjunct separation, occasionally a principal one. It is used either to break an azeotrope or to concentrate a minor component. Large stand-alone uses may develop in areas

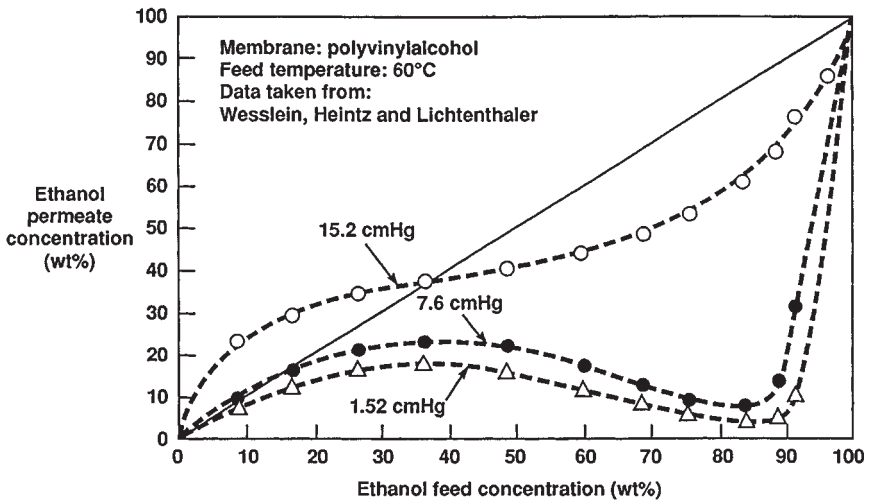


FIG. 22-82 Pervaporation schematic for ethanol-water. The illustration shows the complex behavior for a simple system at three pressures. Only the region above 90 percent is of commercial interest. (*Courtesy Elsevier.*)

where distillation is at a disadvantage, such as with closely boiling components, but these developments, have not yet been made. Notable exceptions occur when a stream is already fairly pure, such as a contaminated water source, or isopropanol from microelectronics fabrication washing containing perhaps 15 percent water.

In continuous flow, the feed will begin with concentration ($x_{i,\text{feed}}$) and be stripped until it reaches some desired ($x_{i,\text{residue}}$). If significant mass is removed from the feed, it will cool, since the general rule for liquids is that the latent heat exceeds the specific heat per °C by two orders of magnitude (more for water). So the membrane has a concentration gradient and a temperature gradient both across it and along it. Pervaporation is a complex multigradient process.

The term β is not constant for some important separations. Even worse, it can exhibit maxima that make analytic treatment difficult. Operating diagrams are often used for preliminary design rather than equations. Because of the very complex behavior in the membrane as concentrations change, all design begins with an experiment. For water removal applications, design equations often mispredict the rate constants as the water content of the feed approaches zero. The estimates tend to be lower than the experimental values, which would lead to overdesign. Therefore it is necessary to obtain experimental data over the entire range of water concentrations encountered in the separation. Once the kinetic data are available, heat transfer and heat capacity are the problem. It is general practice to pilot the separation on a prototype module to measure the changes due to thermal effects. This is particularly true for water as the permeant, given its high latent heat.

For removal of an organic component from water, swelling of the organophillic membrane would result in a higher flux and lower α. At organic levels below about 10 percent, that has not been a major problem. In most applications, boundary-layer mass-transfer limitations become limiting. Pilot data must therefore be taken with hydrodynamic similarity to the module that will be used and the actual organic permeation rate may become limited by the boundary layer. In organic-organic pervaporation, membrane swelling is a major concern.

Vapor Feed A variant on pervaporation is to use vapor, rather than liquid, as a feed. While the resulting process could be classified along with gas-separation membranes, it is customarily regarded as pervaporation.

The residue at the top of a distillation column is a vapor, so there is logic in using it as the feed to a membrane separator. Weighed against the obvious advantage are disadvantages of vapor handling (compressors cost more than pumps) and equipment size to handle the larger vapor volume. When the more volatile component permeates, heat must be added to maintain superheat. The vapor feed technique has been used in a few large installations where the advantages outweigh the disadvantages.

Leading Examples

Dehydration The growing use of isopropanol as a clean-rinse fluid in microelectronics produces significant quantities of an 85–90 percent isopropanol waste. Removing the water and trace contaminants is required before the alcohol can be reused. Pervaporation produces a 99.99 percent alcohol product in one step. It is subsequently polished to remove metals and organics. In Europe, dehydration of ethanol is the largest pervaporation application. For the very large ethanol plants typical of the United States, pervaporation is not competitive with thermally integrated distillation.

Organic from Water An area where pervaporation may become important is in flavors, fragrances, and essential oils. Here, high-value materials with unique properties are recovered from aqueous or alcohol solutions.

Pollution Control Pervaporation is used to reduce the organic loading of a waste stream, thus effecting product recovery and a reduction in waste-treatment costs. An illustration is a waste stream containing 11 percent (wt) *n*-propanol. The residue is stripped to 0.5 percent and 96 percent of the alcohol is recovered in the permeate as a 45 percent solution. This application uses a hydrophobic, rubbery membrane. The residue is sent to a conventional waste-treatment plant.

Pervaporation Membranes Pervaporation has a long history, and many materials have found use in pervaporation experiments. Cellulosic-based materials have given way to polyvinyl alcohol and blends of polyvinyl alcohol and acrylics in commercial water-removing membranes. These membranes are typically solution cast (from water) on ultrafiltration membrane substrates. It is important to have enough cross linking in the final polymer to avoid dissolution of the membrane in use. A very thin membrane with little penetration into the UF substrate is required. The substrate can be a problem, as it provides significant pressure drop to the vapor passing through it which, as mentioned above, has serious ramifications for flux and separation efficiency. Many new membranes are under development. Ion-exchange membranes, and polymers deposited by or polymerized by plasma, are frequently mentioned in the literature.

Modules Every module design used in other membrane operations has been tried in pervaporation. One unique requirement is for low hydraulic resistance on the permeate side, since permeate pressure is very low (0.1–1 Pa). The rule for near-vacuum operation is the bigger the channel, the better the transport. Another unique need is for heat input. The heat of evaporation comes from the liquid, and intermediate heating is usually necessary. Of course economy is always a factor. Plate-and-frame construction was the first to be used in large installations, and it continues to be quite important. Some smaller plants use spiral-wound modules, and some membranes can be made as capillary bundles. The capillary device with the feed on the inside of the tube has many advantages in principle, such as good vapor-side mass transfer and economical construction, but it is still limited by the availability of membrane in capillary form.

SELECTION OF BIOCHEMICAL SEPARATION PROCESSES

General References: Albertsson, *Partition of Cell Particles and Macromolecules,* 3d ed., John Wiley & Sons, New York, 1986. Belter, Cussler, and Hu, *Bioseparations,* Wiley Interscience, New York, 1988. Cooney and Humphrey (eds.), *Comprehensive Biotechnology,* vol. 2, Pergamon, Oxford, 1985. Janson and Ryden (eds.), *Protein Purification,* VCH, New York, 1989. Scopes, *Protein Purification,* 2d ed., Springer-Verlag, New York, 1987. Stephanopoulos (ed.), *Biotechnology,* 2d ed., vol. 3, VCH, Weinheim, 1993. Walter, Brooks, and Fisher (eds.), *Partitioning in Aqueous Two-Phase Systems,* Academic Press, Orlando, FL, 1985.

GENERAL BACKGROUND

The biochemical industry derives its products from two primary sources. Natural products are yielded by plants, animal tissue, and fluids, and obtained via fermentation from bacteria, molds and fungi, and from mammalian cells. Products can also be obtained by recombinant methods through the insertion of foreign DNA directly into the hosting microorganism to allow overproduction of the product in this unnatural environment. The range of bioproducts is enormous, and the media in which they are produced are generally complex and ill-defined, containing many unwanted materials in addition to the desired product. The product is invariably at low concentration. The goals of downstream processing operations include removal of these unwanted impurities, bulk-volume reduction with concomitant concentration of the desired product, and, for protein products, transfer of the protein to an environment where it will be stable and active, ready for its intended application. This requires on average three to six separate processing steps. Some of the purification methods in general use are shown in Fig. 22-83 [Bonnerjea et al., *Bio/Technology,* **4,** 954–958 (1986)] which indicates the average stage at which different methods are used in the downstream processing train. A general strategy for downstream processing of biological materials and the types of operations that may be used in the different steps is shown in Fig. 22-84 [see also Ho, in M. R. Ladisch et al. (eds.), *Protein Purification from Molecular Mechanisms to Large-Scale Processes,* ACS Symp. ser.

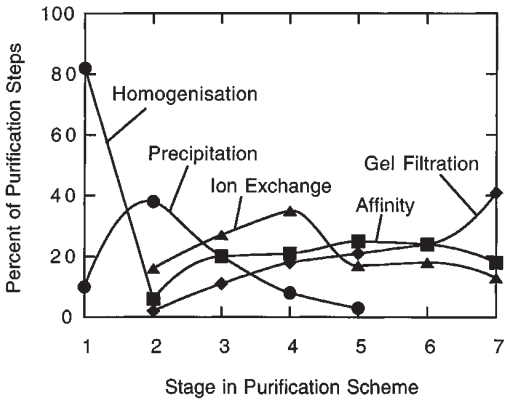


FIG. 22-83 Frequency of use of purification methods at different stages in purification schemes published in the literature. (*Adapted from Bonnerjea et al., op. cit.*)

427, ACS, Washington DC, 1990, pp. 14–34]. Section 24 in this handbook provides a general discussion of biochemical engineering.

Low-molecular-weight products, generally secondary metabolites such as alcohols, carboxylic and amino acids, antibiotics, and vitamins, can be recovered using many of the standard operations such as liquid-liquid extraction, adsorption and ion-exchange, described elsewhere in this handbook. Proteins require special attention, however, as they are sufficiently more complex, their function depending on the integrity of a delicate three-dimensional tertiary structure that can be disrupted if the protein is not handled correctly. For this reason, this section focuses primarily on protein separations. Cell separations, as a necessary part of the downstream processing sequence, are also covered.

Techniques used in bioseparations depend on the nature of the product (i.e., the unique properties and characteristics which provide a "handle" for the separation), and on its state (i.e., whether soluble or insoluble, intra- or extracellular, etc.). All early isolation and recovery steps remove whole cells, cellular debris, suspended solids, and colloidal particles, concentrate the product, and, in many cases, achieve some degree of purification, all the while maintaining high yield. For intracellular compounds, the initial harvesting of the cells is important

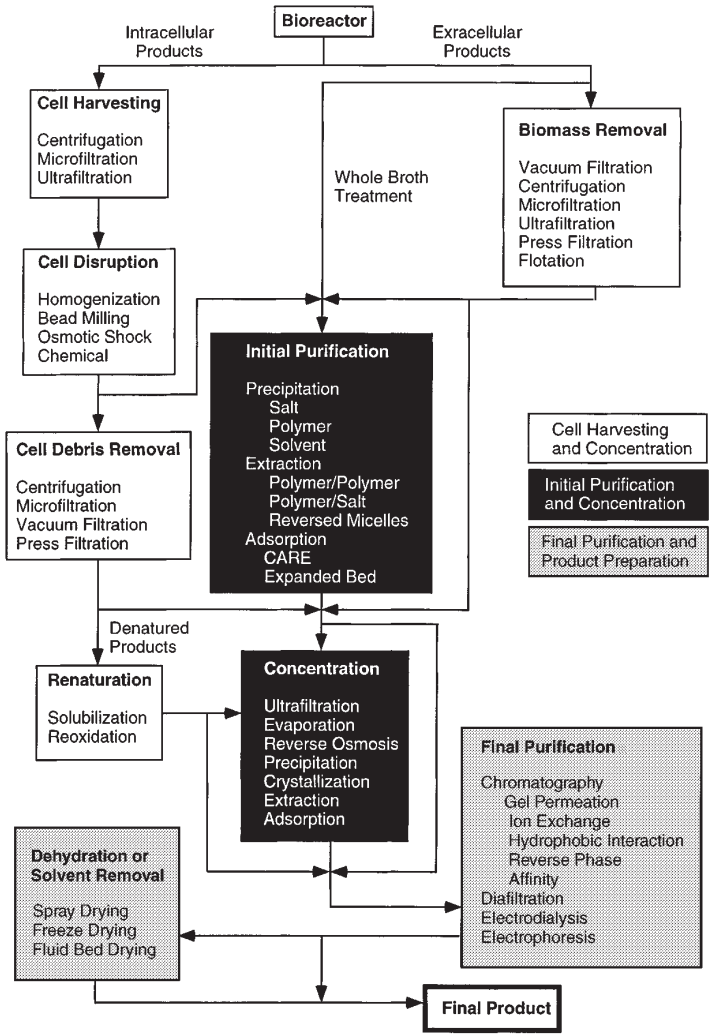


FIG. 22-84 General stages in downstream processing for protein production indicating representative types of operations used at each stage.

for their concentration prior to release of the product. Following this phase, a range of purification steps is employed to remove the remaining impurities and enhance the product purity; this purification phase, in turn, is followed by polishing steps to remove the last traces of contaminating components and process-related additions (e.g., buffer salts, detergents, etc.), and to prepare the product for storage and/or distribution. The prevention and/or avoidance of contamination is another important goal of downstream processing.

Even for good yields of 80 to 95 percent per step, the overall yield can be poor for any process that requires a large number of steps. Thus, careful consideration must be given to optimization of the process in terms of both the unit operations themselves, and their sequencing. It is usually desirable to reduce the process volume early in the downstream processing, and to remove any components that can be removed fairly easily (particulates, small solutes, large aggregates, nucleic acids, etc.) so as not to overly burden the more refined separation processes downstream. Possible shear and temperature damage, and deactivation by endogenous proteases must be considered in the selection of separation processes.

The purification of proteins to be used for therapeutic purposes presents more than just the technical problems associated with the separation process. Owing to the complex nature and intricate three-dimensional structure, the routine determination of protein structure as a quality-control tool, particularly in its final medium for use, is not well established. In addition, the complex nature of the human immune system allows for even minor quantities of impurities and contaminants to be biologically active. Thus, regulation of biologics production has resulted in the concept of the process defining the product since even small and inadvertent changes in the process may affect the safety and efficacy of the product. Indeed, it is generally acknowledged that even trace amounts of contaminants introduced from other processes, or contaminants resulting from improper equipment cleaning can compromise the product. From a regulatory perspective, then, operations should be chosen for more than just efficiency. The consistency of the unit operation, particularly in the face of potentially variable feed from the culture/fermentation process, is the cornerstone of the process definition. Operations that lack robustness or are subject to significant variation should not be considered. Another aspect of process definition is the ability to quantify the operation's performance. Finally, the ease with which the equipment can be cleaned in a verifiable manner should play a role in unit-operation selection.

In the development of new products, optimization of the fermentation medium for titer only often ignores the consequences of the medium properties on subsequent downstream processing steps such as filtration and chromatography. It is imperative, therefore, that there be effective communication and understanding between workers on the upstream and downstream phases of the product development if rational trade-offs are to be made to ensure overall optimality of the process. One example is to make the conscious decision, in collaboration with those responsible for the downstream operations, whether to produce a protein in an unfolded form or in its native folded form; the purification of the aggregated unfolded proteins is simpler than that of the native protein, but the refolding process itself to obtain the product in its final form may lack scalability.

INITIAL PRODUCT HARVEST AND CONCENTRATION

The initial processing steps are determined to a large extent by the location of the product species, and generally consist of cell/broth separation and/or cell-debris removal. For products retained within the biomass during production, it is first necessary to concentrate the cell suspension before homogenization or chemical treatment to release the product. Clarification to remove the suspended solids is the process goal at this stage.

Regardless of the location of the protein and its state, cell separation needs to be inexpensive, simple, and reliable, as large amounts of fermentation-broth dilute in the desired product may be handled. The objectives are to obtain a well-clarified supernatant and solids of maximum dryness, avoiding contamination by using a contained operation. Mechanical methods, almost exclusively centrifugation and cross-flow filtration, are preferred for cell separations [Datar and Rosen, in Stephanopoulos (ed.), op. cit., pp. 369–503].

Intracellular products can be present either as folded, soluble proteins, or as dense masses of unfolded protein (inclusion bodies). For these products, it is first necessary to concentrate the cell suspension before effecting release of the product. Filtration can result in a suspension of cells that can be of any desired concentration up to 15–17 percent, and that can be diafiltered into the desired buffer system. In contrast, the cell slurry that results from centrifugation will either be that of a dry mass (requiring resuspension but substantially free of residual broth, i.e., from a tubular bowl centrifuge) or a wet slurry (containing measurable residual broth and requiring additional resuspension). During the separation, conditions which result in cell lysis (such as extremes in temperature) must be avoided. In addition, while soluble protein is generally protected from shear and external proteolysis, these proteins are still subject to thermal denaturation.

For extracellular products, which are invariably water-soluble, the goal is the removal of whole cells (clarification) and, in the case of typical protein products, the removal of dissolved low-molecular-weight compounds. This must be done under relatively gentle conditions to avoid undesired denaturation of the product. Again, either filtration or centrifugation can be applied. Filtration results in a cell-free supernatant with dilution associated with the diafiltration of the final cell slurry. Centrifugation, regardless of the mode, will result in a small amount of cells in the centrate, but there is no dilution of the supernatant. During the process development careful studies should be conducted to examine the effects of pH and ionic strength on the yield, as cells and cell debris may retain the product through charge interactions. If the broth or cell morphology does not allow for filtration or if dry cell mass is required, tubular-bowl centrifugation is typically utilized. It should be noted that plant and animal cells cannot sustain the same degree of applied shear as microbial cells, and thus cross-flow filtration or classical centrifugation may not be applicable. Alternatives using low-shear equipment under gentle conditions are often employed in these situations.

For whole broths the range of densities and viscosities encountered affect the concentration factor that can be attained in the process, and can also render cross-flow filtration uneconomical because of the high pumping costs, and so on. Often, the separation characteristics of the broth can be improved by broth conditioning using physiocochemical or biological techniques, usually of a proprietary nature. The important characteristics of the broth are rheology and conditioning.

Centrifugation Centrifugation relies on the enhanced sedimentation of particles of density different from that of the surrounding medium when subjected to a centrifugal-force field [Axelsson, in Cooney and Humphrey (eds.), op. cit., pp. 325–346] (see also Sec. 18: "Liquid-Solid Operations and Equipment"). Advantages of centrifugal separations are that they can be carried out continuously and have short retention times, from a fraction of a second to seconds, which limit the exposure time of sensitive biologicals to shear stresses. Yields are high, provided that temperature and other process conditions are adequately controlled. They have small space requirements, and an adjustable separation efficiency makes them a versatile unit operation. They can be completely closed to avoid contamination, and, in contrast to filtration, no chemical external aids are required that can contaminate the final product. The ability now to contain the aerosols typically generated by centrifuges adds to their operability and safety.

Sedimentation rates must be sufficiently high to permit separation, and can be enhanced by modifying solution conditions to promote the aggregation of proteins or impurities. An increase in precipitation of the contaminating species can often be accomplished by a reduction in pH, or an elevation in temperature. Flocculating agents, which include polyelectrolytes, polyvalent cations, and inorganic salts, can cause a 2000-fold increase in sedimentation rates. Some examples are polyethylene imine, EDTA, and calcium salts. Cationic bioprocessing aids (cellulosic or polymeric) reduce pyrogen, nucleic acid, and acidic protein loads which can foul chromatography columns. The removal of these additives both during centrifugation and subsequent processing must be clearly demonstrated.

There are many different types of centrifuges, classified according to the way in which the transport of the sediment is handled. The

selection of a particular centrifuge type is determined by its capacity for handling sludge; the advantages and disadvantages of various separator types are discussed by Axelsson [in Cooney and Humphrey (eds.), op. cit., pp. 325–346]. Solids-retaining centrifuges are operated in a semibatch mode, as they must be shut down periodically to remove the accumulated solids; they are primarily used when solids concentrations are low, and have found application during the clarification and simultaneous separation of two liquids. In solids-ejecting centrifuges, the solids are removed intermittently either through radial slots or axially while the machine is running at full speed. These versatile machines can be used to handle a variety of feeds, including yeast, bacteria, mycelia, antibiotics, enzymes, and so on. Solids-discharging nozzle centrifuges have a large capacity, and can accommodate up to 30 percent solids loading. Decanter centrifuges consist of a drum, partly cylindrical and partly conical, and an internal screw conveyor for transport of the solids, which are discharged at the conical end; liquids are discharged at the cylindrical end. Levels within the drum are set by means of external nozzles.

Continuous-flow units, the scroll decanter and disk-stack centrifuges, are easiest to use from an operational perspective; shutdown of the centrifuge during the processing of a batch is not expected. While the disk-stack centrifuge enjoys popularity as a process instrument within the pharmaceutical and biotechnology industries, the precise timing of solids ejection and continuous high-speed nature of the device make for complex equipment and frequent maintenance. It is often used to harvest cells, since the solids generated are substantially wet and could lead to measurable yield losses in extracellular product systems. For intracellular product processing, the wet cell sludge is easily resuspended for use in subsequent processing.

The tubular bowl, in contrast, is a semibatch processing unit owing to the limited solids capacity of the bowl. The use of this unit requires shutdown of the centrifuge during the processing of the batch. The semibatch nature of these centrifuges can thus greatly increase processing-cycle times. The introduction of disposable sheets to act as bowl liners has significantly impacted turnaround times during processing. The dry nature of the solids generated makes the tubular-bowl centrifuge well-suited for extracellular protein processing, since losses to the cell sludge are minimal. In contrast, the dry, compact nature of the sludge can make the cells difficult to resuspend. This can be problematic for intracellular protein processing where cells are homogenized in easily clogged, mechanical disrupters.

Filtration Cross-flow filtration (microfiltration includes cross-flow filtration as one mode of operation in "Membrane Separation Processes" which appears earlier in this section) relies on the retention of particles by a membrane. The driving force for separation is pressure across a semipermeable membrane, while a tangential flow of the feed stream parallel to the membrane surface inhibits solids settling on and within the membrane matrix (Datar and Rosen, loc. cit.).

Microfiltration is used for the removal of suspended particles, recovery of cells from fermentation broth, and clarification of homogenates containing cell debris. Particles removed by microfiltration typically average greater than 500,000 nominal molecular weight [Tutunjian, in Cooney and Humphrey (eds.), op. cit., pp. 367–381; Gobler, in Cooney and Humphrey (eds.), op. cit., pp. 351–366]. Ultrafiltration focuses on the removal of low-molecular-weight solutes and proteins of various sizes, and operates in the less than 100,000 nominal-molecular-weight cutoff range [Le and Howell, in Cooney and Humphrey (eds.), op. cit., pp. 383–409]. Both operations consist of a concentration segment (of the larger particles) followed by diafiltration of the retentate [Tutunjian, in Cooney and Humphrey (eds.), op. cit., pp. 411–437].

Generally, the effectiveness of the separation is determined not by the membrane itself, but rather by the formation of a secondary or dynamic membrane caused by interactions of the solutes and particles with the membrane. The buildup of a gel layer on the surface of an ultrafiltration membrane owing to rejection of macromolecules can provide the primary separation characteristics of the membrane. Similarly, with colloidal suspensions, pore blocking and bridging of pore entries can modify the membrane performance, while molecules of size similar to the membrane pores can adsorb on the pore walls, thereby restricting passage of water and smaller solutes. Media containing poorly defined ingredients may contain suspended solids, colloidal particles, and gel-like materials that prevent effective microfiltration. In contrast to centrifugation, specific interactions can play a significant role in membrane-separation processes.

The factors to consider in the selection of cross-flow filtration include the cross-flow velocity, the driving pressure, the separation characteristics of the membrane (permeability and pore size), size of particulates relative to the membrane pore dimensions, and the hydrodynamic conditions within the flow module. Again, since particle-particle and particle-membrane interactions are key, broth conditioning (ionic strength, pH, etc.) may be necessary to optimize performance.

Selection of Cell-Separation Unit Operation The unit operation selected for cell separations can depend on the subsequent separation steps in the train. In particular, when the operation following cell separation requires cell-free feed (e.g. chromatography), filtration is used, since centrifugation is not absolute in terms of cell separation. In addition, if cells are to be stored (i.e., they contain the desired product) because later processing is more convenient (e.g., only two-shift operation, facility campaigns equipment with other products, batch is too big for single pass in equipment), it is generally better to store the cells as a frozen concentrate rather than a paste, since the concentrate thaws more completely, avoiding small granules of unfrozen cell solids that can foul homogenizers, columns, and filters. Here the retentate from filtration is desired, although the wet cell mass from a disc stack-type centrifuge may be used.

Centrifugation is generally necessary for complex media used to make natural products, for, while the media components may be sifted prior to use, they can still contain small solids that can easily foul filters. The medium to be used should be tested on a filter first to determine the fouling potential. Some types of organisms, such as filamentous organisms may sediment too slowly owing to their larger cross sections, and are better treated by filtration (mycelia have the potential to easily foul tangential-flow units; vacuum-drum filtration using a filter aid, e.g., diatomaceous earth, should also be considered). Often the separation characteristics of the broth can be improved by broth conditioning using physicochemical or biological techniques, usually of a proprietary nature.

Regardless of the machine device, centrifuges are typically maintenance-intensive. Filters can be cheaper in terms of capital and maintenance and should be considered first unless centrifugal equipment already exists. Small facilities (<1000 liters) use filtration, since centrifugation scale-down is constrained by equipment availability. Comparative economics of the two classes of operations are discussed by Datar and Rosen (loc. cit.).

Cell Disruption Intracellular protein products are present as either soluble, folded proteins or inclusion bodies. Release of folded proteins must be carefully considered. Active proteins are subject to deactivation and denaturation, and thus require the use of "gentle" conditions. In addition, due consideration must be given to the suspending medium; lysis buffers are often optimized to promote protein stability and protect the protein from proteolysis and deactivation. Inclusion bodies, in contrast, are protected by virtue of the protein agglomeration. More stressful conditions are typically employed for their release, which includes going to higher temperatures if necessary. For "native" proteins, gentler methods and temperature control are required.

The release of intracellular protein product is achieved through rupture of the cell walls, and release of the protein product to the surrounding medium, through either mechanical or nonmechanical means, or through chemical, physical, or enzymatic lysis [Engler, in Cooney and Humphrey (eds.), op. cit., pp. 305–324; Schutte and Kula, in Stephanopoulos (ed.), op. cit., pp. 505–526]. Mechanical methods use pressure, as in the Manton/APV-Gaulin/French Press, or the Microfluidizer, or mechanical grinding, as in ball mills, the latter being used typically for flocs and usually only for natural products. Nonmechanical means include use of desiccants or solvents, while cell lysis can also be achieved through physical means (osmotic shock, freeze/thaw cycles), chemical (detergents, chaotropes) or enzymatic (lysozyme, phages).

In pressure-based homogenizers, cells suspended in an aqueous

medium are forced at high velocity through a narrow, adjustable gap between a valve and its seat at pressures in excess of 50 MPa. Product release, which generally follows first-order kinetics, occurs through impingement of the high-velocity cell-suspension jet on the stationary surfaces, and possibly also by the high-shear forces generated during the acceleration of the liquid through the gap. While sufficiently high pressures can be attained using commercially available equipment to ensure good release in a single pass, the associated adiabatic temperature increases (~1.8°C/1000 psig) may cause unacceptable activity losses for heat-labile proteins. Further denaturation can occur on exposure to the lysis medium. Thus, multiple passes may be preferred, with rapid chilling of the processed-cell suspension between passes. The number of passes and the heat removal ability should be carefully optimized. The efficiency of the process depends on the homogenizing pressure and the choice of the valve unit, for which there are many designs available. Materials of construction are important to minimize erosion of the valve, to provide surface resistance to aggressive cleaning agents and disinfectants, and to permit steam cleaning and sanitization.

The release of inclusion bodies, in contrast, may follow a different strategy. Since inclusion bodies are typically recovered by centrifugation, it is often advantageous to send the lysate through the homogenizer with multiple passes to decrease the particle size of the cell debris. Since the inclusion bodies are much denser than the cell debris, the debris, now much reduced in size, can be easily separated from the inclusion bodies by centrifugation at low speeds. The inclusion bodies may be resuspended and centrifuged multiple times (often in the presence of low concentrations of denaturants) to clean up these aggregates. Since the inclusion bodies are already denatured, temperature control is not as important as in the case of native proteins.

In high-speed-agitation ball mills, cells suspended with beads are agitated by disks rotating at high speed. Ball mills have longer residence times than the pressure homogenizers, and are susceptible to channeling and shedding of the ball material.

Chemical lysis, or solubilization of the cell wall, is typically carried out using detergents such as Triton X-100, or the chaotropes urea, and guanidine hydrochloride. This approach does have the disadvantage that it can lead to some denaturation or degradation of the product. While favored for laboratory cell disruption, these methods are not typically used at the larger scales. Enzymatic destruction of the cell walls is also possible, and as more economical routes to the development of appropriate enzymes are developed, this approach could find industrial application. Again, the removal of these additives is an issue.

Physical methods such as osmotic shock, in which the cells are exposed to high salt concentrations to generate an osmotic pressure difference across the membrane, can lead to cell-wall disruption. Similar disruption can be obtained by subjecting the cells to freeze/thaw cycles, or by pressurizing the cells with an inert gas (e.g., nitrogen) followed by a rapid depressurization. These methods are not typically used for large-scale operations.

On homogenization, the lysate may drastically increase in viscosity due to DNA release. This can be ameliorated to some extent using multiple passes to reduce the viscosity. Alternatively, precipitants or nucleic acid digesting enzymes can be used to remove these viscosity-enhancing contaminants.

For postlysis processing, careful optimization must be carried out with respect to pH and ionic strength. Often it is necessary to do a buffer exchange. Cell debris can act as an ion exchanger and bind proteins ionically, thus not allowing them to pass through a filtration device or causing them to be spun out in a centrifuge. Once optimal conditions are found, these conditions can be incorporated in the lysis buffer by either direct addition (if starting from cell paste) or diafiltration (if starting from a cell concentrate).

Protein Refolding The products of recombinant DNA technology are frequently not produced in their native, biologically active form, because the foreign hosts in which they are produced lack the appropriate apparatus for the folding of the proteins. Thus, the overproduced proteins are generally recovered as refractile or inclusion bodies, or aggregates, typically 1–3 μm in size, and all cysteine residues are fully reduced. It is necessary at some stage in the processing to dissolve the aggregates and then refold them to obtain the desired biologically active product [Cleland and Wang, in Stephanopoulos (ed.), op. cit., pp. 527–555].

Advantages of inclusion bodies in the production stage are their ease of separation by centrifugation following cell disruption because of their size and density, and their provision of excellent initial-purification possibilities, as long as impurities are not co-purified to any significant extent with the inclusion bodies. They also provide a high expression level and prevent endogenous proteolysis. There can be, however, significant product loss during protein refolding to the active form.

Following cell disruption, and washing, the pellet is solubilized through the disruption of hydrogen and ionic bonds, and hydrophobic interactions by the addition of chaotropes such as guanidine hydrochloride (4–9 M), urea (7–8 M), sodium thiocyanate (4–9 M), or detergents such as Triton X-100 or sodium dodecyl sulfate. This step may also require the breaking of all incorrectly formed intramolecular disulfide bonds through the addition of appropriate reducing agents (e.g., beta mercaptoethanol). To permit proper refolding of the protein, it is necessary to reduce the chaotrope concentration either by dilution, or by solvent exchange using dialysis against a buffer (poor scale-up potential), diafiltration using the desired buffers, or electrodialysis (good scale-up potential). High-protein concentrations can lead to aggregate formation, while if the concentration is too low, the volumes to be processed become inhibitive. Subsequently, oxidation of the cysteine residues is needed to allow for correct disulfide bond formation in the native protein.

INITIAL PURIFICATION

In initial purification steps the goal is to obtain concentration with partial purification of the product, which is recovered either as a precipitate (precipitation), a solution in a second phase (liquid-liquid extraction), or adsorbed to solids (adsorption, chromatography).

Precipitation Precipitation of products, impurities or contaminants can be induced by the addition of solvents, salts, or polymers to the solution, by increasing temperature, or by adjusting the solution pH (Scopes, op. cit., pp. 41–71; Ersson et al., in Janson and Ryden, op. cit., pp. 3–32). This operation is used most often in the early stages of the separation sequence, particularly following centrifugation, filtration, and/or homogenization steps. Precipitation is often carried out in two stages, the first to remove bulk impurities and the second to precipitate and concentrate the target protein. Generally, amorphous precipitates are formed, owing to occlusion of salts or solvents, or to the presence of impurities.

Salts can be used to precipitate proteins by "salting out" effects. The effectiveness of various salts is determined by the Hofmeister series, with anions being effective in the order citrate > $PO_4^{=}$ > $SO_4^{=}$ > CH_3COO^- > Cl^- > NO_3^-, and cations according to NH_4^+ > K^+ > Na^+ (Ersson et al., op. cit., p. 10; Belter et al., op. cit., pp. 221–236). Salts should be inexpensive owing to the large quantities used in precipitation operations. Ammonium sulfate is the most commonly used precipitant. Drawbacks to this approach include low selectivity, high sensitivity to operating conditions, and downstream complications associated with salt removal and disposal of the high-nitrogen-content stream. Generally, aggregates formed on precipitation with ammonium sulfate are fragile, and are easily disrupted by shear. Thus, these precipitation operations are, following addition of salt, often aged without stirring before being fed to a centrifuge by gravity feed or using low-shear pumps (e.g., diaphragm pumps).

The organic solvents most commonly used for protein precipitation are acetone and ethanol (Ersson et al., op. cit.). These solvents can cause some denaturation of the protein product. Temperatures below 0°C can be used, since the organic solvents depress the freezing point of the water. The precipitate formed is often an extremely fine powder that is difficult to centrifuge and handle. With organic solvents, in-line mixers are preferred, as they minimize solvent-concentration gradients, and regions of high-solvent concentrations, which can lead to significant denaturation and local precipitation of undesired components typically left in the mother liquors. In general, precipitation with organic solvents at lower temperature increases yield and reduces

denaturation. It is best carried out at ionic strengths of 0.05–0.2 M.

Water-soluble polymers and polyelectrolytes (e.g., polyethylene glycol, polyethylene imine polyacrylic acid) have been used successfully in protein precipitations, and there has been some success in affinity precipitations wherein appropriate ligands attached to polymers can couple with the target proteins to enhance their aggregation. Protein precipitation can also be achieved using pH adjustment, since proteins generally exhibit their lowest solubility at their isoelectric point. Temperature variations at constant salt concentration allow for fractional precipitation of proteins.

Precipitation is typically carried out in standard cylindrical tanks with low-shear impellers. If in-line mixing of the precipitating agent is to be used, this mixing is employed just prior to the material entering the aging tank. Owing to their typically poor filterability, precipitates are normally collected using a centrifugal device.

Extraction Partitioning of the desired protein to a second phase in liquid-liquid extraction operations can be achieved using two-phase aqueous polymer systems (Albertsson, op. cit.), reversed micellar systems [Kelley and Hatton, in Stephanopoulos (ed.), op. cit., pp. 593–616], or phase-separated micellar solutions [Pryde and Phillips, *Biochem. J.*, **233,** 525–533 (1986)]. Organic solvents more typically identified with solvent-extraction operations cannot be used here because of protein solubility constraints, and because they lead to protein denaturation and degradation. Aqueous two-phase polymer systems are good for unclarified broths since particles tend to collect at the interface between the two phases, making their removal very efficient. They can also be used early on in the processing train for initial bulk-volume reduction and partial purification. These processes have not been applied widely as yet, owing both to a general lack of experience with these phase systems, and the need to remove phase-forming reagents (polymers, salts, detergents) from the products.

The basis for the separation is that when two polymers, or a polymer and certain salts, are mixed together in water, they are incompatible, leading to the formation of two immiscible but predominantly aqueous phases, each rich in only one of the two components [Albertsson, op. cit.; Kula, in Cooney and Humphrey (eds.), op. cit., pp. 451–471]. A phase diagram for a polyethylene glycol (PEG)-Dextran, two-phase system is shown in Fig. 22-85. Proteins are known to distribute unevenly between these phases. This uneven distribution can be used for the selective concentration and partial purification of the products. Partitioning between the two phases is controlled by the polymer molecular weight and concentration, protein net charge and size, and hydrophobic and electrostatic interactions. Affinity ligands covalently bonded to one of the phase-forming polymers have been found to be effective in enhancing dramatically the selectivity and partitioning behavior.

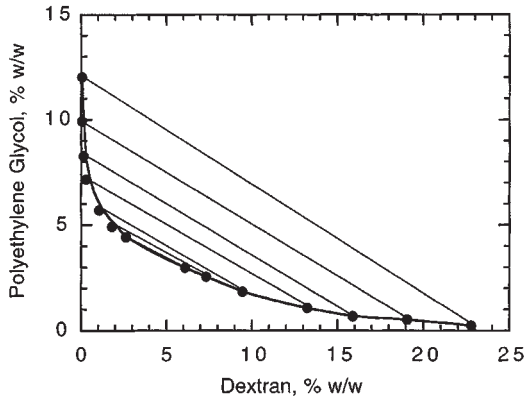


FIG. 22-85 Phase diagram for a PEG/Dextran, biphasic, aqueous-polymer system used in liquid-liquid extraction operations for protein separations. (*Albertsson,* Partition of Cell Particles and Macromolecules, *3d ed., Copyright © 1986. Reprinted by permission of John Wiley & Sons, Inc.*)

Product recovery from these systems can be accomplished by either changes in temperature or system composition. Composition changes can be affected by dilution, back extraction and micro- and ultrafiltration. As the value of the product decreases, recovery of the polymer may take on added significance. A flow diagram showing one possible configuration for the extraction and product and polymer recovery operations is shown in Fig. 22-86 [Greve and Kula, *J. Chem. Tech. Biotechnol.*, **50,** 27–42 (1991)]. The phase-forming polymer and salt are added directly to the fermentation broth. The cells or cell debris and contaminating proteins report to the salt-rich phase and are discarded. Following pH adjustment of the polymer-rich phase, more salt is added to induce formation of a new two-phase system in which the product is recovered in the salt phase, and the polymer can be recycled. In this example, disk-stack centrifuges are used to enhance the phase-separation rates. Other polymer recycling options include

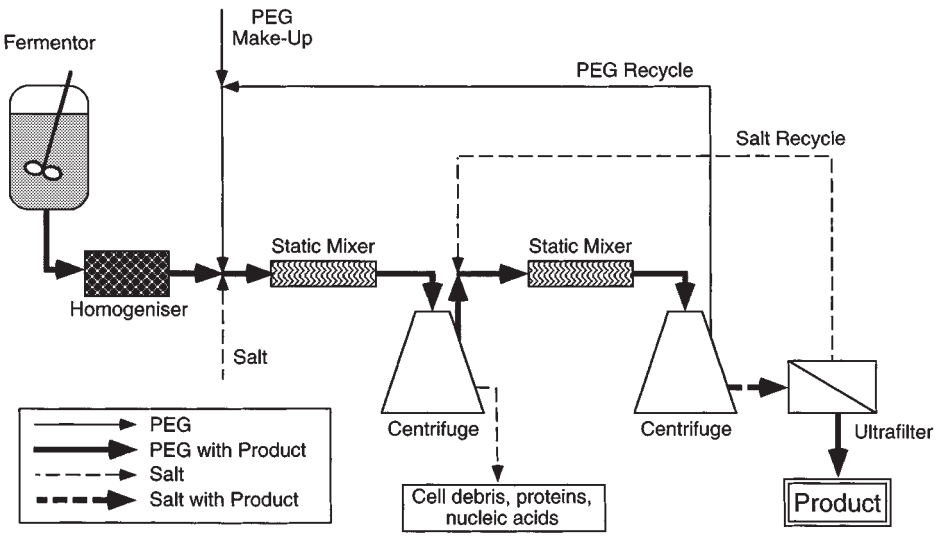


FIG. 22-86 Process scheme for protein extraction in aqueous two-phase systems for the downstream processing of intracellular proteins, incorporating PEG and salt recycling. [*Reprinted from Kelly and Hatton in Stephanopoulos (ed.), op. cit.; adapted from Greve and Kula, op. cit.*]

extraction with a solvent or supercritical fluid, precipitation, or diafiltration. Electrodialysis can be used for salt recovery and recycling.

Reversed micellar solutions can also be used for the selective extraction of proteins (Kelley and Hatton, op. cit.). In these systems, detergents soluble in an oil-phase aggregate to stabilize small water droplets having dimensions similar to those of the proteins to be separated. These droplets can host hydrophilic species such as proteins in an otherwise inhospitable organic solvent, thus enabling these organic phases to be used as protein extractants. Factors affecting the solubilization effectiveness of the solvents include charge effects, such as the net charge determined by the pH relative to the protein isoelectric point, charge distribution and asymmetry on the protein surface, and the type (anionic or cationic) of the surfactant used in the reversed micellar phase. Ionic strength and salt type affect the electrostatic interactions between the proteins and the surfactants, and also affect the sizes of the reversed micelles. Attachment of affinity ligands to the surfactants has been demonstrated to lead to enhancements in extraction efficiency and selectivity [Kelley et al., *Biotech. Bioeng.*, **42,** 1199–1208 (1993)].

Product recovery from reversed micellar solutions can often be attained by simple back extraction, by contacting with an aqueous solution having salt concentration and pH that disfavors protein solubilization, but this is not always a reliable method. Addition of cosolvents such as ethyl acetate or alcohols can lead to a disruption of the micelles and expulsion of the protein species, but this may also lead to protein denaturation. These additives must be removed by distillation, for example, to enable reconstitution of the micellar phase. Temperature increases can similarly lead to product release as a concentrated aqueous solution. Removal of the water from the reversed micelles by molecular sieves or silica gel has also been found to cause a precipitation of the protein from the organic phase.

Aqueous-detergent solutions of appropriate concentration and temperature can phase separate to form two phases, one rich in detergents, possibly in the form of micelles, and the other depleted of the detergent (Pryde and Phillips, op. cit.). Proteins distribute between the two phases, hydrophobic (e.g., membrane) proteins reporting to the detergent-rich phase and hydrophilic proteins to the detergent-free phase. Indications are that the size-exclusion properties of these systems can also be exploited for viral separations. These systems would be handled in the same way as the aqueous two-phase systems.

On occasion, for extracellular products, cell separation can be combined with an initial volume reduction and purification step using liquid-liquid extraction. This is particularly true for low-molecular-weight products, and has been used effectively for antibiotic and vitamin recovery. Often scroll decanters can be used for this separation. The solids are generally kept in suspension (which requires that the solids be denser than heavy phase), while the organic phase, which must be lighter than water (cells typically sink in water) is removed. Experience shows that scrolls are good for handling the variability seen in fermentation feedstock. Podbielniak rotating-drum extraction units have been used often, but only when solids are not sticky, gummy or flocculated, as they can get stuck in perforations of the concentric drums, but will actually give stages to the extraction in short-residence time (temperature-sensitive product). The Karr reciprocating-plate column can handle large volumes of whole-broth materials efficiently, and is amenable to ready scale-up from small laboratory-scale systems to large plant-scale equipment.

Adsorption Adsorption (see also Sec. 16: "Adsorption and Ion Exchange") can be used for the removal of pigments and nucleic acids, for example, or can be used for direct adsorption of the desired proteins. Stirred-batch or expanded-bed operations allow for presence of particulate matter, but fixed beds are not recommended for unclarified broths owing to fouling problems. These separations can be effected through charge, hydrophobic, or affinity interactions between the species and the adsorbent particles, as in the chromatographic steps outlined below. The adsorption processes described here are different from those traditionally ascribed to chromatography in that they do not rely on packed-bed operations.

In *continuous affinity recycle extraction* (CARE) operations, the adsorbent beads are added directly to the cell homogenate and the mixture is fed to a microfiltration unit. The beads loaded with the desired solute are retained by the membrane, and the product is recovered in a second stage by changing the buffer conditions to disfavor binding.

Stable expanded-bed operations promise the ability to handle whole broths efficiently, all the while maintaining plug-flow characteristics. Magnetically stabilized fluidized beds have been shown to work effectively for bioproduct separations, but are not yet used commercially. A commercially available process uses well-designed beads of appropriate densities and sizes to enable bed fluidization and stable operation without appreciable recirculation.

Membrane Processes Membrane processes are also used; diafiltration is convenient for the removal of small contaminating species such as salts and smaller proteins, and can be combined with subsequent steps to concentrate the protein. Provided that proper membrane materials have been selected to avoid protein-membrane interactions, diafiltration using ultrafiltration membranes is typically straightforward, high-yielding and capital-sparing. These operations can often tolerate the concentration of the desired protein to its solubility limit, maximizing process efficiency.

FINAL PURIFICATION AND PRODUCT FORMULATION

The final purification steps are responsible for the removal of the last traces of impurities. The volume reduction in the earlier stages of the separation train are necessary to ensure that these high-resolution operations are not overloaded. Generally, chromatography is used in these final stages. Electrophoresis can also be used, but since it is rarely found in process-scale operations, it is not addressed here. The final product preparation may require removal of solvent and drying, or lyophilization, of the product.

Chromatography Chromatography is the most widely used downstream processing operation because of its versatility, high selectivity and efficiency, in addition to its adequate scale-up potential based on wide experience in the biochemical processing industries. As familiarity is gained with other techniques such as liquid-liquid extraction they will begin to find more favor in the early stages of the separation train, but are unlikely to replace chromatography in the final stages where high purities are needed.

Chromatography is a fixed-bed adsorption operation, in which a column filled with chromatographic packing materials is fed with the mixture of components to be separated. Apart from gel-permeation chromatography, in the most commonly practiced industrial processes the solutes are adsorbed strongly to the packing materials until the bed capacity has been reached. The column may then be washed to remove impurities in the interstitial regions of the bed prior to elution of the solutes. This latter step is accomplished by using buffers or solvents which weaken the binding interaction of the proteins with the packings, permitting their recovery in the mobile phase. Different elution strategies (isocratic, gradient elution) can be used to ensure adequate separation of the species to be resolved. In gel-permeation chromatography (discussed below), and in high-performance liquid chromatography, the principle of operation is different in that it is the differential migration of the various components owing to their different affinities for the packing materials that allows the species to be separated.

Advantages of chromatography for protein separations include the large number of possible chemical interactions resulting from variations in the frequency and distribution of the amino-acid side chains on the surfaces of the proteins, and the availability of a wide array of different adsorption media. Chromatography has high efficiency and selectivity, and adequate scale-up potential.

Types of Chromatography Practiced Separation of proteins using chromatography can exploit a range of different physical and chemical properties of the proteins and the chromatography adsorption media [Janson and Ryden, op. cit.; Scopes, op. cit.; Egerer, in Finn and Prave (eds.), *Biotechnology Focus 1,* Hanser Publishers, Munich, 1988, pp. 95–151]. Parameters that must be considered in the selection of a chromatographic method include composition of the reaction mixture, the chemical structure and stability of the components, the electric charge at a defined pH value and the isoelectric point of the proteins, the hydrophilicity and hydrophobicity of the

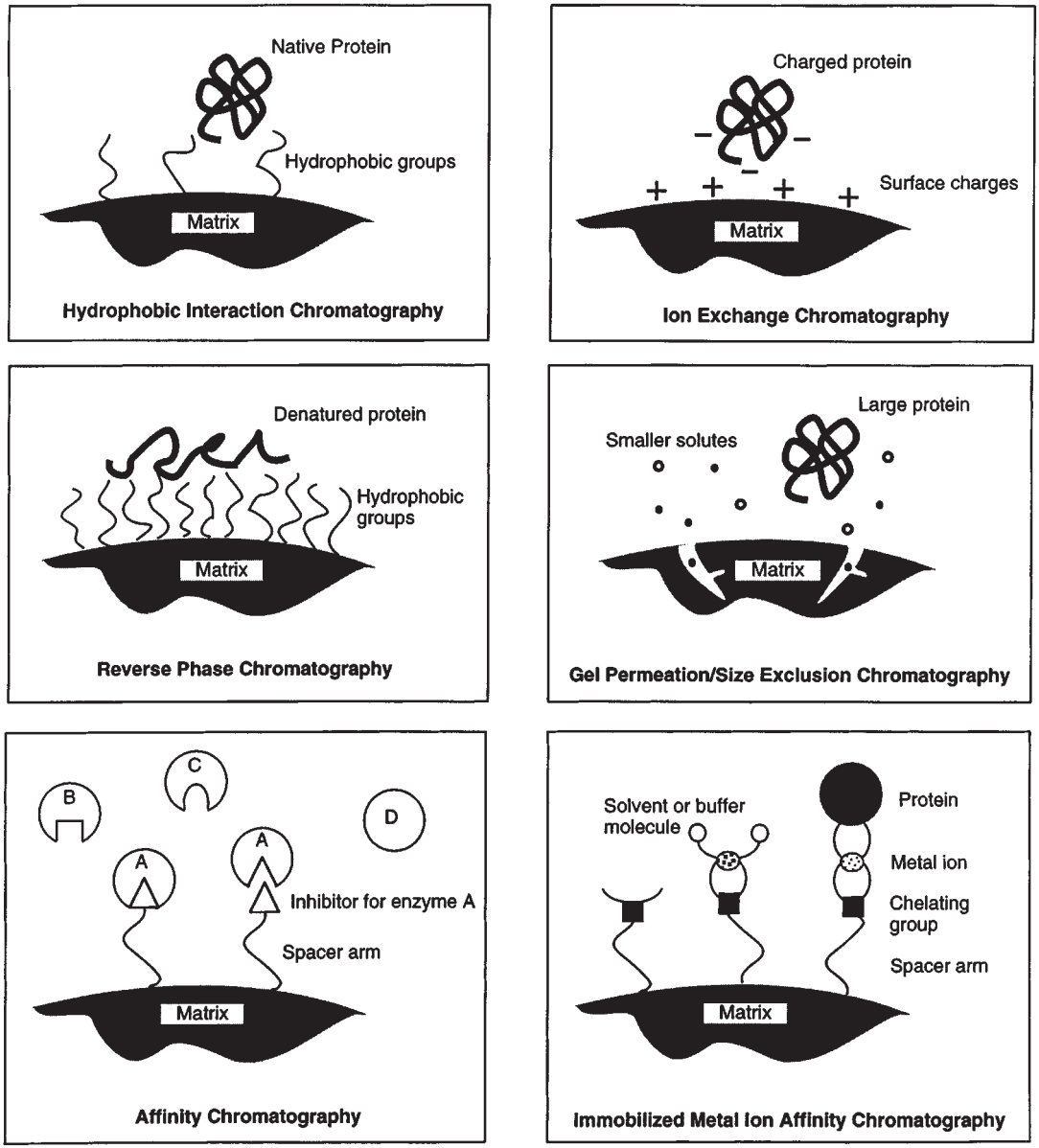


FIG. 22-87 Schematic illustration of the chromatographic methods most commonly used in downstream processing for protein recovery.

components, and molecular size. The different types of interactions are illustrated schematically in Fig. 22-87.

Ion-exchange chromatography relies on the coulombic attraction between the ionized functional groups of proteins and oppositely charged functional groups on the chromatographic support. It is used to separate the product from contaminating species having different charge characteristics under well-defined eluting conditions, and for concentration of the product, owing to the high-adsorptive capacity of most ion-exchange resins, and the resolution attainable. It is used effectively at the front end of a downstream processing train for early volume reduction and purification.

The differences in sizes and locations of hydrophobic pockets or patches on proteins can be exploited in *hydrophobic interaction chromatography* (HIC) and *reversed-phase chromatography* (RPC); discrimination is based on interactions between the exposed hydrophobic residues and hydrophobic ligands which are distributed evenly throughout an hydrophilic porous matrix. As such, the binding characteristics complement those of other chromatographic methods, such as ion-exchange chromatography.

In HIC, the hydrophobic interactions are relatively weak, often driven by salts in moderate concentration (1 to 2 M), and depend primarily on the exposed residues on or near the protein surface; preservation of the native, biologically active state of the protein is an important feature of HIC. Elution can be achieved differentially by decreasing salt concentration or increasing the concentration of polarity perturbants (e.g., ethylene glycol) in the eluent.

Reversed-phase chromatography relies on significantly stronger hydrophobic interactions than in HIC, which can result in unfolding and exposure of the interior hydrophobic residues, i.e., leads to protein denaturation and irreversible inactivation; as such, RPC depends

on total hydrophobic-residue content. Elution is effected by organic solvents applied under gradient conditions.

Ligands for both HIC and RPC are straight chain alkanes or simple aromatic compounds. Increasing the carbon number and the graft density of the ligands on the support surface leads to increasing strength of interaction and passing from HIC to RPC mode of operation. Raising the temperature increases the hydrophobic interactions at the temperatures commonly encountered in biological processing.

HIC is most effective during the early stages of a purification strategy and has the advantage that sample pretreatment such as dialysis or desalting after salt precipitation is not usually required. It is also finding increased use as the last high-resolution step to replace gel filtration. It is a group-separation method, and generally 50 percent or more of extraneous impurities are removed. This method is characterized by high-adsorption capacity, good selectivity, and satisfactory yield of active material.

Despite the intrinsically nonspecific nature of ion-exchange and reversed-phase/hydrophobic interactions, it is often found that chromatographic techniques based on these interactions can exhibit remarkable resolution; this is attributed to the dynamics of multisite interactions being different for proteins having differing surface distributions of hydrophobic and/or ionizable groups.

Gel-permeation chromatography separates proteins nominally on the basis of size only, where the effective size of the protein is determined by its geometry and solvation characteristics. Smaller proteins are able to penetrate the pore volumes of the beads, and are therefore retained relative to the larger proteins, which remain in the fast-flowing fluid in the interstitial regions of the bed. Such ideal behavior is rarely observed, however, as proteins can interact adsorptively with the gel matrix, thus affecting their relative elution behaviors. Industrially, gel-permeation chromatography is used for desalting, removing low-molecular-weight impurities, and removal of desired product oligomers. It is used in the latter stages of the separation sequence, often as a final "polishing" step.

Protein affinity chromatography can be used for the separation of an individual compound, or a group of structurally similar compounds from crude-reaction mixtures, fermentation broths, or cell lysates by exploiting very specific and well-defined molecular interactions between the protein and affinity groups immobilized on the packing-support material. Examples of affinity interactions include antibody-antigen, hormone-receptor, enzyme-substrate/analog/inhibitor, metal ion-ligand, and dye-ligand pairs. Monoclonal antibodies are particularly effective as biospecific ligands for the purification of pharmaceutical proteins. Affinity chromatography may be used for the isolation of a pure product directly from crude fermentation mixtures in a single chromatographic step. Immunosorbents should not be subjected to crude extracts, however, as they are particularly susceptible to fouling and inactivation. Affinity chromatography does not find wide use on the process scale because of its high cost, if a protein ligand such as A or G is to be used.

Immobilized metal ion affinity chromatography (IMAC) relies on the interaction of certain amino-acid residues, particularly histidine, cysteine, and tryptophan, on the surface of the protein with metal ions fixed to the support by chelation with appropriate chelating compounds, invariably derivatives of iminodiacetic acid. Commonly-used metal ions are Cu^{2+}, Zn^{2+}, Ni^{2+} and Co^{2+}. Despite its relative complexity in terms of the number of factors which influence the process, IMAC is beginning to find industrial applications. The choice of chelating group, metal ion, pH, and buffer constituents will determine the adsorption and desorption characteristics. Elution can be effected by several methods, including pH gradient, competitive ligands, organic solvents, and chelating agents.

Following removal of unbound materials in the column by washing, the bound substances are recovered by changing conditions to favor desorption. A gradient or stepwise reduction in pH is often suitable. Otherwise, one can use competitive elution with a gradient of increasing concentration. IMAC eluting agents include ammonium chloride, glycine, histamine, histidine, or imidazol. Inclusion of a chelating agent such as EDTA in the eluent will allow all proteins to be eluted indiscriminately along with the metal ion.

Chromatographic Development The basic concepts of chromatographic adsorption separations are described elsewhere in this handbook. Proteins differ from small solutes in that the large number of charged and/or hydrophobic residues on the protein surface provide multiple binding sites, which ensure stronger binding of the proteins to the adsorbents, as well as some discrimination based on the surface distribution of amino-acid residues. The proteins are recovered by elution with a buffer that reduces the strength of this binding and permits the proteins to be swept out of the column with the buffer solution. In isocratic elution, the buffer concentration is maintained constant during the elution period. Since the different proteins may have significantly different adsorption isotherms, the recovery may not be complete, or it may take excessive processing time to recover all proteins from the column. In gradient elution operations, the composition of the mobile phase is changed during the process to decrease the binding strength of the proteins successively, the more loosely bound proteins being removed first before the eluent is strengthened to enable recovery of the more strongly adsorbed species. The change in eluent composition can be gradual and continuous, or it can be stepwise. Industrially, in large-scale columns it is difficult to maintain a continuous gradient owing to difficulties in fluid distribution, and thus stepwise changes are almost universally used. In some adsorption modes, the protein can be recovered by the successive addition of competing compounds to displace the adsorbed proteins. In all cases, the product is eluted as a Gaussian (to a first approximation) peak, with some possible overlap between adjacent product peaks.

Displacement chromatography relies on a different mode of elution. Here a displacer which is more strongly adsorbed than any of the proteins is introduced with the mobile phase. As the displacer concentration front develops, it pushes the proteins ahead of itself. The more strongly adsorbed proteins then act as displacers for the less strongly bound proteins, and so on. This leads to the development of a displacer train in which the different molecules are eluted from the column in abutting rectangular peaks in the order of their interaction strength with the adsorption sites of the column. Despite its apparent process advantages, displacement chromatography has not yet become an accepted industrial operation, primarily because of lack of suitable displacers, and possible contamination of the protein product with these displacers.

For efficient adsorption it is advisable to equilibrate both the column and the sample with the optimum buffer for binding. Prior to this, the column must be cleaned to remove tightly bound impurities by increasing the salt concentration beyond that used in the product-elution stages. At the finish of cleaning operation the column should be washed with several volumes of the starting buffer to remove remaining adsorbed material. In desorption, it is necessary to drive the favored binding equilibrium for the adsorbed substance from the stationary to the mobile phase. Ligand-protein interactions are generally a combination of electrostatic, hydrophobic, and hydrogen bonds, and the relative importance of each of these and the degree of stability of the bound protein must be considered in selecting appropriate elution conditions; frequently compromises must be made. Gradient elution often gives good results.

Changes in pH or ionic strength are generally nonspecific in elution performance; ionic-strength increases are effective when the protein binding is predominantly electrostatic, as in IEC. Polarity changes are effective when hydrophobic interactions play the primary role in protein binding. By reducing the polarity of the eluting mobile phase, this phase becomes a more thermodynamically favorable environment for the protein than adsorption to the packing support. A chaotropic salt (KSCN, KCNO, KI in range 1–3 M) or denaturing agent (urea, guanidine HCl; 3–4 M) in the buffer can also lead to enhanced desorption. For the most hydrophobic proteins (e.g., membrane proteins) one can use detergents just below their critical micelle concentrations to solubilize the proteins and strip them from the packing surface.

Specific elution requires more selective eluents. Proteins can be desorbed from ligands by competitive binding of the eluting agent (low concentration 5–100 mM) either to the ligand or to the protein. Specific eluents are most frequently used with group-specific adsorbents since selectivity is greatly increased in the elution step. The effectiveness of the elution step can be tailored using a single eluent, pulses of different eluents, or eluent gradients. These systems are

generally characterized by mild desorption conditions. If the eluting agent is bound to the protein, it can be dissociated by desalting on a gel-filtration column or by diafiltration.

Column Packings The quality of the separation obtained in chromatographic separations will depend on the capacity, selectivity, and hydraulic properties of the stationary phase, which usually consists of porous beads of hydrophilic polymers filled with the solvent. The xerogels (e.g., cross-linked dextran) shrink and swell depending on solvent conditions, while aerogels have sizes independent of solution conditions. A range of materials is used for the manufacture of gel beads, classified according to whether they are inorganic, synthetic, or polysaccharides. The most widely used materials are based on neutral polysaccharides and polyacrylamide. Cellulose gels, such as cross-linked dextran, are generally used as gel-filtration media, but can also be used as a matrix for ion exchangers. The primary use of these gels is for desalting and buffer exchange of protein solutions, as nowadays, fractionation by gel filtration is performed largely with composite gel matrices. Agarose, a low-charge fraction of the seaweed polysaccharide agar, is a widely used packing material.

Microporous gels made by point cross-linking dextran or polyacrylamides are used for molecular-sieve separations such as size-exclusion chromatography and gel filtration, but are generally too soft at the porosities required for efficient protein chromatography. Macroporous gels are most often obtained from aggregated and physically cross-linked polymers. Examples include agarose, macroreticular polyacrylamide, silica, and synthetic polymers. These gels are good for ion-exchange and affinity chromatography, as well as for other adsorption chromatography techniques. Composite gels, in which the microporous gel is introduced into the pores of macroreticular gels, combine the advantages of both types.

High matrix rigidity is offered by porous silica, which can be derivatized to enhance its compatibility with proteins, but it is unstable at alkaline pH. Hydroxyapatite particles have high selectivity for a wide range of proteins and nucleic acids.

Sequencing of Chromatography Steps The sequence of chromatographic steps used in a protein purification train should be designed such that the more robust techniques are used first, to obtain some volume reduction (concentration effect) and to remove major impurities that might foul subsequent units; these robust units should have high chemical and physical resistance to enable efficient regeneration and cleaning, and should be of low material cost. These steps should be followed by the more sensitive and selective operations, sequenced such that buffer changes and concentration steps between applications to chromatographic columns are avoided. Frequently, ion-exchange chromatography is used as the first step. The elution peaks from such columns can be applied directly to hydrophobic-interaction chromatographic columns or to a gel-filtration unit, without the need for desalting of the solution between applications. These columns can also be used as desalting operations, and the buffers used to elute the columns can be selected to permit direct application of the eluted peaks to the next chromatographic step.

Factors to be considered in making the selection of chromatography processing steps are cost, sample volume, protein concentration and sample viscosity, degree of purity of protein product, presence of nucleic acids, pyrogens, and proteolytic enzymes. Ease with which different types of adsorbents can be washed free from adsorbed contaminants and denatured proteins must also be considered.

Lyophilization and Drying After the last high-performance purification steps it is usually necessary to prepare the finished product for special applications. For instance, final enzyme products are often required in the form of a dry powder to provide for stability and ease of handling, while pharmaceutical preparations also require high purity, stability during formulation, absence of microbial load, and extended shelf life. This product-formulation step may involve drying of the final products by freeze drying, spray drying, fluidized-bed drying, or crystallization (Golker, in Stephanopoulos, op. cit., pp. 695–714).

Freeze drying, or lyophilization, is normally reserved for temperature-sensitive materials such as vaccines, enzymes, microorganisms, and therapeutic proteins, as it can account for a significant portion of total production cost. This process is characterized by three distinct steps, beginning with freezing of the product solution, followed by water removal by sublimation in a primary drying step, and ending with secondary drying by heating to remove residual moisture.

Freezing is carried out on cooled plates in trays or with the product distributed as small particles on a drum cooler; by dropping the product solution in liquid nitrogen or some other cooling liquid; by cospraying with liquid CO_2 or liquid nitrogen; or by freezing with circulating cold air. The properties of the freeze-dried product, such as texture and ease of rehydration, depend on the size and shape of the ice crystals formed, which in turn depend on the degree of undercooling. It is customary to cool below the lowest equilibrium eutectic temperature of the mixture, although many multicomponent mixtures do not exhibit eutectic points. Freezing should be rapid to avoid effects from local concentration gradients. Removal of water from solution by the formation of ice crystals leads to changes in salt concentration and pH, as well as enhanced concentration of the product, in the remaining solution; this in turn can enhance reaction rates, and even reaction order can change, resulting in cold denaturation of the product. With a high initial protein concentration the freeze concentration factor and the amount of ice formed will be reduced, resulting in greater product stability. For aseptic processing, direct freezing in the freeze-drying plant ensures easier loading of the solution after filtration than if transferred separately from remote freezers.

In the primary drying step, heat of sublimation is supplied by contact, conduction, or radiation to the sublimation front. It is important to avoid partial melting of the ice layer. Many pharmaceutical preparations dried in ampoules are placed on heated shelves. The drying time depends on the quality of ice crystals, indicating the importance of controlling the freezing process; smaller crystals offer higher interfacial areas for heat and mass transfer, but larger crystals provide pores for diffusion of vapor away from the sublimation front.

A high percentage of water remains after the sublimation process, present as adsorbed water, water of hydration or dissolved in the dry amorphous solid; this is difficult to remove. Usually, shelf-temperature is increased to 25 to 40°C and chamber pressure is lowered as far as possible. This still does not result in complete drying, however, which can be achieved only by using even higher temperatures, at which point thermally induced product degradation can occur.

Excipients can be used to improve stability and prevent deterioration and inactivation of biomolecules through structural changes such as dissociation from multimeric states into subunits, decrease in α-helical content accompanied by an increase in β-sheet structure, or complete unfolding of helical structure. These are added prior to the freeze-drying process. Examples of these protective agents include sugars, sugar derivatives, and various amino acids, as well as polymers such as dextran, polyvinyl pyrrolidone, hydroxyethyl starch, and polyethylene glycol. Some excipients, the **lyoprotectants,** provide protection during freezing, drying, and storage, while others, the **cryoprotectants,** offer protection only during the freezing process.

Spray drying can use up to 50 percent less energy than freeze-drying operations and finds application in the production of enzymes used as industrial catalysts, as additives for washing detergents, and as the last step in the production of single-cell protein. The product is usually fed to the dryer as a solution, a suspension, or a free-flowing wet substance. Spray drying is an adiabatic process, the energy being provided by hot gas (usually hot air) at temperatures between 120 and 400°C. Product stability is assured by a very short drying time in the spray-drying equipment, typically in the subsecond to second range, which limits exposure to the elevated temperatures in the dryer. Protection can be offered by addition of additives (e.g., galactomannan, polyvinyl pyrrolidone, methyl cellulose, cellulose).

The spray-drying process requires dispersion of the feed as small droplets to provide a large heat and mass-transfer area. The dispersion of liquid is attained using rotating disks, different types of nozzles or ultrasound, and is affected by interfacial tension, density, and dynamic viscosity of the feed solution, as well as the temperature and relative velocities of the liquid and air in the mixing zone. Rotating-disk atomizers operate at 4000 to 50,000 rpm to generate the centrifugal forces needed for dispersion of the liquid phase; typical droplet sizes of 25 to

950 μm are obtained. These atomizers are specially suitable for dispersing suspensions that would tend to clog nozzles.

For processing under aseptic conditions, the spray drier must be connected to a filling line that allows aseptic handling of the product.

INTEGRATION OF FERMENTATION AND DOWNSTREAM PROCESSING OPERATIONS

Traditionally, the upstream fermentation and cell culture processes have been viewed as being distinct from the subsequent downstream processing and purification steps, and the two different sets of processes have been optimized individually. In some instances, careful consideration of the conditions used in the fermentation process, or manipulation of the genetic makeup of the host, can simplify and even eliminate some unit operations in the downstream processing sequence [Kelley and Hatton, *Bioseparation*, **1,** 303–349 (1991)]. Some of the advances made in this area are the engineering of strains of *Escherichia coli* to allow the inducible expression of lytic enzymes capable of disrupting the wall from within for the release of intracellular protein products, the use of secretion vectors for the expression of proteins in bacterial production systems, and protein synthesis to include a peptide or protein fusion to confer unique properties to the product to facilitate subsequent downstream processing. The cell culture medium can be selected to avoid components that can hinder subsequent purification procedures. Integration of the fermentation and initial separation/purification steps in a single operation can also lead to enhanced productivity, particularly when the product can be removed as it is formed to prevent its proteolytic destruction by the proteases which are frequently the by-product of fermentation processes. The introduction of a solvent directly to the fermentation medium (e.g., phase-forming polymers), the continuous removal of products using ultrafiltration membranes, or the use of continuous fluidized-bed operations are examples of this integration.