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Basic Approaches to Separation. Analysis and Classification of Methods According to Underlying Transport Characteristics

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Basic Approaches to Separation. Analysis and Classification of Methods According to Underlying Transport Characteristics

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Abstract

We note the loss of opportunities in the historical fragmentation of separation science, and give arguments for an increased unification of approaches in the future. The complexities of classifying separation methods are discussed, and it is suggested that the science of taxonomy must be invoked to make comprehensive advances toward realistic polythetic classifications. Some basic elements of a classificatory system are described in terms of the type of displacement leading to separation and the profile of the driving force leading to relative displacement. The driving forces may be continuous (c) or discontinuous (d), arising in external fields and interfacial interactions, respectively. Flow may be integral to the separation (F) by its occurrence parallel (F(=)) or perpendicular (F(+)) to the force, or the system may be effectively static (S). These considerations lead to six fundamental categories for most separations: Sc, Sd, F(=)c, (F(=)d, F(+)c, and F(+)d. Examples are given for each category. Finally, the above classificatory system is justified by fundamental considerations of transport in separation systems.

INTRODUCTION

The great variety of approaches to the separation of chemical mixtures presents a bewildering array to the separation scientist. The wide spectrum in phases, fields, flows, columns, packing and stage geometries, procedures, apparatus size, sample size, time scales, and overall objectives tends to obscure underlying relationships. This has encouraged extremes of specialization among workers in the field.

By and large the history of separation science has been a history of diverging pathways. The consequence has been much redundancy in the independent design and optimization of systems that are based on common theory, and lost opportunities in technological spinoff from the more advanced methods to those at a less sophisticated stage of development.

The last decade or so has presented several important breaks with history. Modern liquid chromatography (LC) sprang rapidly into existence in the mid-1960s. This development was based on the firm principles of optimization established in the previous decade for gas chromatography (GC) (*1*, *2*). In 1961 Knox wrote a paper concerning only gas chromatography (GC) that became a key in the development of modern LC (*3*). It showed that speed in GC could be continuously decreased with increases in the inlet pressure, provided particle size could be appropriately diminished at the same time. The transfer of this and related concepts from GC to LC was made several years later (*4*). Other theoretical concepts developed for GC, such as the coupling theory of eddy diffusion (*5*, *6*), have provided the basis for the rapid theoretical understanding and optimization of LC (*2*).

On a broader front, several authors have developed theories and concepts intended to bring unity to the field of chemical separations. A systematic classification of driving forces and resistive forces in separations was presented in an historic paper by Strain, Sato, and Engelke (*7*). Efforts at unification and classification have appeared more frequently in the recent literature (*8–15*). Most notable in this regard is the work of Rony (*16–25*), who introduced a universal separation index termed the extent of separation (*16*, *17*, *19*, *22–25*). He also developed the general concept of partition states in separation (*18*, *20*, *21*). This appears to be a generalization of the concept of velocity states introduced by the present author (*26*). Rony's work has led to the division of separation methods into five basic classes (*25*).

CLASSIFICATORY SYSTEMS FOR SEPARATION SCIENCE

The problems in classifying separation systems remind one of the old tale from India of the six blind men who set forth to find out what an elephant was. Each categorized the creature differently according to the properties thrust into his sphere of attention. In a like manner the industrial engineer whose attention is focused by his company on production scale processes will be more inclined to classify separations on the basis of sample throughput, availability of continuous processing, and energy consumption than will the analytical chemist forced to concentrate on analysis time, resolution, and adaptability to identification. Because of such diverse emphasis and equally diverse chemical properties, numerous choices must be made. These choices lead to different methodologies. Classes of methodologies can be discerned according to the choice between external fields and nonmiscible phases, the types of fields or the types of phases, the presence or absence of flow, multiple stages, continuous throughput, high pressures, discrete zones, chemical reaction, elution, columns, porous support, large sample capacity, high energy efficiency, and so on. Each choice is important in its own right, and may become critical for certain groups of scientists and engineers seeking particular goals. In this sense every classificatory system used for separations probably has elements of validity and utility. None, or at least few, should be considered wholly wrong.

At the same time, no classificatory system is wholly comprehensive. Most workers who claim such systems have not accounted for all parts of the "elephant." Indeed, it is a simple matter to grossly underestimate the complexity of developing a comprehensive classificatory system for chemical separations. Certainly no such system will be proposed here. Nonetheless, some of the important elements required for such systems merit discussion: first, to set in proper context the classificatory system developed here, and second, to stimulate others to take up the quest for more general systems.

The theoretical study of classification is termed *taxonomy*. The science of taxonomy has by itself evolved into a far-reaching and unifying discipline. Yet this science seems not to have been invoked in any broad sense in the development of classificatory systems for separations. [It has been used recently to classify stationary phases and other aspects of chromatographic systems (*27, 28*).] It is this author's contention that the principles of taxonomy must be used for any comprehensive advances in the classification of separation methods.

Among the important developments in taxonomy is the concept of *polythetic* classifications. In this system, objects or methods are classified according to similarities and differences in many properties. In *monothetic* classifications only one property or characteristic is used. It is clear from the numerous relevant properties of separation systems noted earlier that a polythetic classification must be used for any system claiming generality.

In polythetic classifications the closeness of methods (or of variations of methods) is indicated by a combination of association or correlation coefficients of the n characteristics used for classification. Methods that are closely related can be expected to form clusters in the n-dimensional hyperspace defined by the n characteristics.

Recent developments in classification theory are discussed in an interesting paper by Sokal (*29*), where further references can be found. From this paper we take the following as the rationale for seeking to classify separations: "The paramount purpose of a classification is to describe the structure and relationship of the constituent objects to each other and to similar objects, and to simplify these relationships in such a way that general statements can be made about classes of objects." Advances toward these objectives should indeed catalyze the rapid application of basic principles throughout all relevant separation methodologies, and they should also provide a more rational basis for choosing among methods for the solution of practical problems.

CLASSIFICATION BASED ON PROFILES OF DRIVING FORCES AND FLOW

The classificatory system to be proposed here is neither monothetic nor is it in any sense complete as a polythetic system. The justification for the lack of completeness is that the system goes to the roots of the fundamental transport processes that underlie separations. It is proposed in part because its basic nature suggests that many other properties of a broad polythetic system will conveniently correlate (cluster) with the elements of this system. It is proposed mainly, however, to help "describe the structure and relationship of constituent objects" (different separation methods) and to aid in the formulation of "general statements [that] can be made about classes of objects [methods]." It is hoped, as a consequence, that the system will help consolidate diverse theoretical and conceptual approaches, crystallize the meaning of various categories in other (also incomplete) classificatory systems, call attention to common phenomena among different methods thus simplifying the learning task for the student of separations, and, finally, it will lead to suggestions for other methods of separations.

The present approach is based on the nature of the fundamental transport phenomena leading to separation. We start with the basic observation that separation is a spatial disengagement among components of a mixture. A selective displacement through space must therefore underlie all separations. On this basis, it is useful to classify displacement processes into two categories:

A. Bulk (flow) displacement. Components are almost invariably displaced when their environment (usually the surrounding fluid) is displaced. Generally the component follows the gross movement of surrounding mass unless there are rapid accelerations. The displacement can be achieved by (1) flow and (2) direct mechanical relocation. For simplicity we label both processes as flow displacements. These displacements are, of course, not selective.

B. Relative displacement. Relative displacement occurs when some effective force drives the component through its surrounding medium. (We refer to force in the generalized sense of irreversible thermodynamics. Such a force exists for any influence leading to relative displacement.) Our present purposes are served by temporarily ignoring diffusive forces in which displacement occurs solely on the basis of concentration (entropy) gradients. (While these forces sometimes drive relative displacements, they usually constitute secondary forces more important for their remixing effects.) This leaves for our consideration the underlying forces imposed by external fields or gradients and the affinity of various chemical phases.

Two basic categories of underlying forces driving relative displacement can be distinguished:

A. Continuous forces. These forces exert a steady "pull" on solute components in the separative region. External fields and gradients comprise this category.

B. Discontinuous forces. These are primarily the forces that originate at the interfacial discontinuity between two phases. This includes the forces at the surface of membranes.

We note that relative displacement can be selective while flow displacements cannot. Relative displacement processes must therefore exist in all separation systems. We consequently find that most separations fall into one of the two simple classes defined by the nature of the forces causing relative displacement, labeled as follows:

c = continuous force

d = discontinuous force

Rarely, as in electrodialysis or electrolysis, do both fundamental components occur in the same system, in which case they yield

cd = continuous-discontinuous force

Next, flow may or may not be employed to augment or structure the separation. We thus have the categories

S = static (nonflow) systems

F = flow system

Flow is used here in a relative sense, meaning bulk (flow) displacement relative to the force or field profile, or the displacement of one phase relative to another. However, flow is a vector quantity and can assume one of two basic orientations with respect to the force or to the field gradient, another vector. The flow and force directions may be parallel (e.g., filtration) or perpendicular (chromatography) to one another. These two cases can be represented by the symbols

F(=) = flow and force parallel

F(+) = flow and force perpendicular

We do not include in the flow category those systems having only various parasitic flows (convective currents, electroosmotic flow) and passive flows (continuous or "curtain" electrophoresis) that do not play an essential role in the process of separation. Omitted also are stirring motions used to aid transport and thus the approach to equilibrium without affecting the final structure of the separation.

It is found that most separation methods fall into one of the six basic categories shown in Table 1. A few techniques fall into a cd grouping, as noted earlier.

The common (and some uncommon) methods of separation are dis-

TABLE 1

Six Basic Categories for Separation Methods. S = static (nonflow); F = flow; c = continuous force; d = discontinuous force; F(=) = parallel flow; F(+) = perpendicular flow (see text)

Continuous (c) forces	Discontinuous (d) forces
Sc	Sd
F(=)c	F(=)d
F(+)c	F(+)d

tributed among the six categories as shown in Table 2. The list is not comprehensive, in part because separations have been so inadequately classified that it is not always clear which techniques constitute distinct methods and which should really be called submethods. Nonetheless, the list provides substance to the present classificatory system.

Further discussion is required to clarify the distinction between parallel flow (F(=)) and perpendicular flow (F(+)) systems. Chromatography illustrates this distinction well. The relative forces in chromatography are the strong interactive forces found at the interface between phases, and their direction is normal to the interface. Different microscopic elements of interface, however, assume different (random) orientations from place to place in most chromatographic columns. The essential fact in this case is that flow does not carry solute across the interface as is necessary for F(=) systems. Rather, it carries solute from one interfacial region to another, a characteristic that serves to define F(+)d systems. An analogous definition can be given for F(+)c systems.

Table 2 is seen to define common families for methods that we ordinarily relate to one another: electrophoresis and sedimentation; chromatography and countercurrent distribution; filtration and reverse osmosis. Thus the categories are generally consistent with experience. However, it also relates methods not commonly associated, such as ultrafiltration and

TABLE 2

Distribution of Separation Methods among the Six Basic Categories

Flow condition	Continuous (c) forces	Discontinuous (d) forces
Static, S	Electrophoresis, isoelectric focusing, dielectrophoresis, and electrostatic precipitation; sedimentation and isopycnic centrifugation	Single-stage extraction, adsorption, crystallization and sublimation; dialysis
Parallel flow, F(=)	Countercurrent electrophoresis; elutriation	Filtration, ultrafiltration, reverse osmosis and pressure dialysis; zone melting
Perpendicular flow, F(+)	Field-flow fractionation; thermogravitational methods; electrophoresis-convection	Chromatography; distillation; countercurrent distribution, adsorption, and crystallization; foam fractionation; mineral flotation

zone melting. Nonetheless, when these two methods are examined fundamentally, they are seen to have the common feature of a selective interface advancing into (or relative to) a fluid mixture. Polarization occurs in both cases, yielding a near-exponential profile of the rejected solute, which can be partially dispersed by stirring or eddy currents. In terms of basic concepts the methods are very close indeed. In a subsequent paper it will be shown that they share a common mathematical description also.

The present classificatory system does not necessarily abrogate other classifications, as noted. In fact, in conjunction with the section to follow, it helps clarify some other systems. It combines with still other systems to form the beginnings of a more general polythetic classification.

Of particular note among accepted bases of classification is the division into *rate* and *equilibrium methods* (*10, 11, 14, 15*). This, too, is a fundamental division based on the condition of transport. It is discussed in more detail later under the names *transport* (or *transient*) and *steady state* separations.

It should be noted that our system does not directly accommodate chemical reactions or selective electronic excitations (as of isotopes) that aid separation in many systems. For the most part we can regard these processes as preseparation steps that simply convert one component into another form more susceptible to selective displacement. Following this conversion the separation is then accomplished by conventional means.

In that we have referred to the term "driving forces" to describe the origin of separative displacements, some clarification is needed with respect to the same term used by Strain et al. in their original classificatory system (*7*). First, we note that our basic classificatory system does not distinguish between specialized driving forces as a basic category but only between the different spatial characteristics of the forces. Second, we observe that the original driving forces lacked some consistency in definition, and even failed to carry common units. In the next section we use basic transport equations in an attempt to maintain self-consistency so that basic and comparative theoretical studies become possible.

BASIS OF SEPARATION AND CLASSIFICATION IN TRANSPORT

The displacements essential for separations are described by equations of transport. In the process of displacement, concentration distributions evolve with diverse shapes, widths, degrees of overlap, velocities, throughputs, and so on. These characteristics largely determine the efficacy of separation.

We show by means of transport equations that characteristics crucial to the evolution of concentration distributions depend on the magnitude and spatial profile of the force or of the fields giving rise to the force. When flow properties, friction coefficients, and certain geometrical and structural parameters are also specified, the concentration distributions and thus the degree of separation becomes uniquely fixed for given initial conditions. It is found that the substitution of one solvent for another will have no effect on separation except as these few fundamental characteristics are altered in magnitude. Likewise two different external fields will generate separation based only on these characteristics, and not on the particular type of field. Furthermore, even when the magnitude of the fundamental properties varies from system to system, common characteristics in the shape and arrangements of these properties generate common families of separations. These families are the ones described in the previous sections. Their principal characteristics are based on the following considerations of transport.

Basic Transport Equations

In order to verify and elaborate on the arguments, we write two basic transport equations. The first expresses the flux density (moles crossing unit area in unit time) of solute anywhere along axis x as a function of concentration c, mean displacement or drift velocity W, and total effective diffusion coefficient D_T:

$$J = cW - D_T\, \partial c/\partial x \tag{1}$$

The second equation, which derives from the first by means of the equation of continuity, expresses the rate of gain of concentration with respect to time t:

$$\frac{\partial c}{\partial t} = -W\frac{\partial c}{\partial x} + D_T\frac{\partial^2 c}{\partial x^2} \tag{2}$$

The latter equation is based on several simplifying assumptions (constant W, constant D_T, etc.), but our conclusions are little affected by these as will be explained later. Basically this equation describes a concentration pulse moving forward along axis x at mean velocity W and spreading outward with a total diffusivity D_T. If the pulse begins as an infinitely narrow spike at $t = 0$, the solution to the partial differential equation represented by Eq. (2) is a Gaussian peak whose center travels at velocity W and whose variance becomes

$$\sigma^2 = 2D_T t \tag{3}$$

To start with, we note that W is the sum of two terms. First is U, the average x component of the relative displacement velocity of solute induced by external fields, gradients, and chemical forces. Second is v, the average x component of solute velocity induced by flow. Thus

$$W = U + v \tag{4}$$

We must recognize next that if the velocity of solute displacement due to these influences should fluctuate randomly due to nonuniformities in flow (as in a packed column or bed) or due to the rapid mass transfer of components between phases or regions having different velocities (as between the mobil and stationary phases of chromatography), the local solute velocity would assume the form

$$W_{\text{local}} = W + W_{\text{err}} \tag{5}$$

where W is the mean value noted previously and W_{err} is the erratic or local random component of displacement. If we assume that the fluctuations in W_{err} are rapid, the central limit theorem (*30*) assures us that the summed effect of the random displacements is that of a diffusion-like process characterized by an effective diffusion coefficient D_{err}. The precise magnitude of D_{err} need not concern us here; it can be calculated from nonequilibrium theory or approximated by random walk models (*26, 6*).

The coefficient D_{err} adds to mean molecular diffusion coefficient D to yield the total diffusivity D_T:

$$D_T = D_{\text{err}} + D = \theta D \tag{6}$$

In which $\theta = 1$ when erratic transport components are absent and $\theta > 1$ for $D_{\text{err}} > 0$.

Quantity D_T, if independent of c and x, influences the evolution of concentration pulses as shown by the last term in Eq. (2).

Static Systems

We now consider separation systems in which flow plays no integral part. These are without essential flow, labeled static (S) in the classification of Table 1. When the flow-induced component v of Eq. (4) is subtracted, Eq. (2) becomes

$$\frac{\partial c}{\partial t} = -U\frac{\partial c}{\partial x} + \theta D\frac{\partial^2 c}{\partial x^2} \tag{7}$$

This expression describes the evolution of solute concentration pulses in uniform systems without flow.

The motion of solute represented by Eq. (7) is simply a motion toward equilibrium. The parameters U and D, described by the science of irreversible (nonequilibrium) thermodynamics, are related to several generalized driving forces. For transport in isothermal (and isobaric) systems, the chemical potential, μ, governs equilibrium, and its gradient $-d\mu/dx$ is the driving force for the displacement toward equilibrium. For ideal solutions μ is composed of the terms

$$\mu = \mu^{\text{ext}} + \mu^{\circ} + RT \ln c \tag{8}$$

where μ^{ext} is the contribution of external fields and gradients, μ° stems from intermolecular forces (such as the distribution forces acting between two phases), and $RT \ln c$ is the contribution of entropy.

Without detailing the arguments, parameter D can be shown to represent the response to the entropy (concentration-leveling) term of chemical potential. It is given by the Einstein equation

$$D = RT/f \tag{9}$$

where f is the friction coefficient per mole—the drag force exerted on a mole of solute moving at unit velocity through its medium.

Parameter U represents the transport response of solute to the concentration-independent (largely energy) terms of chemical potential, consisting of μ^{ext} and μ°. It can be written as

$$U = (1/f)\, \partial\mu^*/\partial x \tag{10}$$

where $\mu^* = \mu^{\text{ext}} + \mu^{\circ}$. This equation is valid within all individual phases of a system but breaks down at interfaces where $(\partial\mu_0/\partial x)$ approaches infinity.

When Eqs. (9) and (10) are substituted back into Eq. (7) we get

$$\frac{\partial c}{\partial t} = \frac{1}{f}\left(\frac{\partial\mu^*}{\partial x}\right)\frac{\partial c}{\partial x} + \frac{\theta RT}{f}\frac{\partial^2 c}{\partial x^2} \tag{11}$$

an equation once again valid within uniform, bulk phases. Solute flow across interfaces is determined by equilibrium or kinetic factors, and these are related to interfacial increments in μ°.

It is convenient to introduce dimensionless coordinate χ in the form $\chi = x/L$, where L is the length of the separation path or column, or some other dimension characterizing the system. When x is replaced by χ, Eq. (11) becomes

$$\frac{\partial c}{\partial t} = \frac{1}{L^2 f}\left(\frac{\partial\mu^*}{\partial \chi}\right)\frac{\partial c}{\partial \chi} + \frac{\theta RT}{L^2 f}\frac{\partial^2 c}{\partial \chi^2} \tag{12}$$

We now write

$$\mu^* = \mu^{\text{ext}} + \mu^\circ = \Delta\mu^*\varepsilon \tag{13}$$

which expresses the overall chemical potential profile $\mu^* = \mu^{\text{ext}} + \mu^\circ$ in terms of the dimensionless fraction ε of its maximum value μ^*_{max}. The minimum value of μ^* can be taken arbitrarily as zero so that $\mu^*_{\text{max}} = \Delta\mu^*$, the total increment in μ^* used to implement separation.

By these definitions ε becomes a dimensionless chemical potential profile varying from 0 to 1 across separation path L. Only a limited number of families of ε profiles are necessary to describe separation systems. Two types of dimensionless profiles describe most systems. These are the uniform continuous profile characteristic of constant applied fields and the unit step function characteristic of two-phase systems. These are illustrated in Fig. 1.

If one forms the derivative, $\mu^{*\prime}$, of μ^* with respect to dimensionless coordinate χ, Eq. (13) becomes

$$\mu^{*\prime} = \frac{\partial\mu^{\text{ext}}}{\partial\chi} + \frac{\partial\mu^\circ}{\partial\chi} = \Delta\mu^*\varepsilon' \tag{14}$$

where $\varepsilon' = d\varepsilon/d\chi$. When this equation is substituted into Eq. (12) we have

$$\frac{\partial c}{\partial t} = \frac{\Delta\mu^*\varepsilon'}{L^2 f}\frac{\partial c}{\partial\chi} + \frac{\theta RT}{L^2 f}\frac{\partial^2 c}{\partial\chi^2} \tag{15}$$

We now define a dimensionless time τ as

$$\tau = t\Delta\mu^*/L^2 f \tag{16}$$

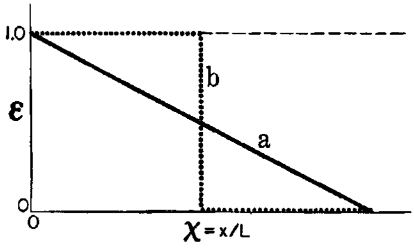

FIG. 1. Two principal types of dimensionless chemical potential profiles: (*a*) uniform continuous, and (*b*) unit step function. Other step positions are possible depending on how coordinate χ is defined, and the profiles might be reversed in direction ($\chi \rightarrow -\chi$).

With this time unit substituted into Eq. (15) we obtain

$$\frac{\partial c}{\partial \tau} = \varepsilon' \frac{\partial c}{\partial \chi} + \delta \frac{\partial^2 c}{\partial \chi^2} \tag{17}$$

where $\delta = \theta RT/\Delta\mu^*$. Equation (17) is an equation in which the evolution of concentration profiles across dimensionless coordinate χ with the passage of dimensionless time τ depends only on the ε' profile and on parameter δ.

The value of ε' at any point controls the general, nondiffusive motion of solute at that point. The ε' profile across coordinate χ therefore determines how solute is "herded" into and through different regions and thus how concentration profiles evolve and acquire structure. Parameter δ, on the other hand, expresses only the relative strength of diffusion compared to the chemical potential increment $\Delta\mu^*$ structuring the separation. Being only a single parameter, its magnitude cannot affect the mathematical form of concentration profiles but only their details within a mathematical framework fixed by the ε (or ε') profile and by the initial conditions of the system. In physical terms, δ represents the diffusion response to a concentration structure whose form is established by more basic considerations including the ε profile.

The equations for our model transport system thus suggest that basic differences in concentration structures evolve from basic differences in the shape of chemical potential profiles. That these differences have a profound effect on separation capabilities can be illustrated by comparing two systems having an equal chemical potential increment $\Delta\mu^*$, but in which the μ^* profile is continuous in one case and a step function in another. The two forms are represented by the *a* and *b* profiles of Fig. 1, respectively.

To lend concreteness to the example, we assume that a mixture of components is started as a δ-function spike at the left-hand edge. In case *a* the slope ε' of the ε profile is a negative constant representing the dimensionless velocity: $\varepsilon' = -d\chi(\text{peak})/d\tau$. In this case Eq. (17) (with appropriate boundary conditions) yields a solution in Gaussian form, as noted also for Eq. (2) earlier in the paper. In the present case the solution is

$$c = [\text{const}/(4\pi\delta\tau)^{1/2}] \exp[-(\chi + \varepsilon'\tau)^2/4\delta\tau] \tag{18}$$

The Gaussian profiles can separate into numerous resolved peaks providing ε' and/or τ/t are sufficiently different for each component, and providing δ is not too large. The number of peaks separable (the peak capacity) can be shown to equal approximately $(\Delta\mu^*/8RT)^{1/2}$ for such a system (*31*). By proper adjustment of parameters, this can be arbitrarily large. A case in point of this system is electrophoresis where dozens of solutes are simultaneously separable.

Profile *b*, by contrast to profile *a*, has two flat regions for which ε = constant and thus $\varepsilon' = 0$. In these regions Eq. (17) acquires the purely diffusive form

$$(\partial c/\partial \tau) = \delta \partial^2 c/\partial \tau^2 \tag{19}$$

Detailed arguments show that the peak maximum originally at $\chi = 0$ will not move along the positive χ axis (unless solute can be lost or absorbed at $\chi \leq 0$) but that solute from the peak will gradually diffuse to the right, eventually flattening the peak and spreading its contents across the entire region to the ε discontinuity (phase boundary). That is to say, no more than one distinct concentration maximum and thus one solute zone can ordinarily form to the left of the discontinuity. Similar arguments apply to the space (phase) to the right of the discontinuity, which is also limited to one zone. At best, and then only with considerable selectivity, no more than two distinct components can be separated from one another. That is, the maximum peak capacity is two. This is a characteristic limitation of all simple extraction processes.

The extreme advantage of profile *a* in nonflow systems stems from the fact that ε' is everywhere finite. Thus, contributing to the rise and fall of concentration is the term $\varepsilon' \partial c/\partial \chi$, i.e.,

$$(\partial c/\partial \tau) = \varepsilon' \partial c/\partial \chi \tag{20}$$

in which ε' is negative. By means of this term solute is constantly evacuated ($\partial c/\partial \tau$ negative) from the rear of every zone ($\partial c/\partial \chi$ positive) and is deposited ($\partial c/\partial \tau$ positive) at its leading edge ($\partial c/\partial \chi$ negative). Thus, in time, solute can be rather completely evacuated from entire regions, making room for other solute pulses and the development of a multicomponent separated solute spectrum. The absence of the evacuation (zone translation) term, $\varepsilon' \partial c/\partial x$, for the flat regions of profile *b* makes such multicomponent separations impossible. The profound difference in separative behavior derives directly from differences in ε profiles. The principle feature of discrimination is the presence or absence of a continuous chemical potential gradient.

The above considerations determine the potential and limitations of various forces used in separations. They specify the possible mode(s) of operation of different separation methods. It is for this reason that static (S) systems are divided into two basic classes corresponding to continuous (c) and discontinuous (d) chemical potential profiles: Sc and Sd, respectively. For completeness we note again that a very few systems (electrodialysis, electrolysis) combine c and d profiles to yield a cd class. Also, separations employing only diffusion have a zero increment in μ^*, a common limit approached both by c and d classes, but with results more characteristic of d separation.

We now turn briefly to certain universal features of separation processes that remain invariant upon substitution of one field for another or one solvent for another.

We have seen that by stipulating a certain ε (and thus ε') profile, we describe an entire family of separation methods. Equation (17) shows that, within this family, the evolution of concentration distributions in dimensionless coordinates χ and τ depends only on parameter $\delta = \theta RT/\Delta\mu^*$. For a given system geometry and structure, θ will be constant (usually unity). Thus, irrespective of the solvent employed or the nature of the field, the evolution of a zone is influenced only by the ratio of thermal energy RT to the total increment $\Delta\mu^*$ in chemical potential. (If diffusion is negligible, this ratio can be approximated by zero.) For specified values of this ratio, therefore, zone evolution in all solvents and all fields occurs identically in χ and τ. Thus, for any given τ value, all concentration distributions in coordinate χ look the same.

As a direct consequence of the latter result, and with the aid of Eq. (16), one can conclude that if a separation process occurs in two different solvents, denoted as solvents 1 and 2, the relative times required to reach a fixed state of evolution in the distribution of a particular solute are given by

$$\frac{t_2}{t_1} = \frac{L_2^2 f_2}{L_1^2 f_1} \frac{\Delta\mu_1^*}{\Delta\mu_2^*} \tag{21}$$

This equation is valid either for fixed $RT/\Delta\mu^*$ ratios or for negligible diffusion. Within these limitations (and the general limitations of our transport model), it is valid for both Sc and Sd separations. It shows that for either class of separations, zone evolution time is scaled to the respective friction coefficients in the two media, and usually therefore scaled to solvent viscosity η (as a consequence of Stoke's law and similar relationships for nonspherical particles). It also shows that time for a fixed $\Delta\mu^*$ is scaled to the length L squared of the separation or transport path. The latter dependency is utilized in part in speeding equilibration in solvent extraction by stirring, a process which temporarily reduces the transport distance between volume elements in the respective phases.

While Eq. (21) expresses zone evolution time under prescribed conditions, separation time might be altered by a change in selectivity in going from one solvent to another. This might be reflected by slight changes in $\Delta\mu^*$ that are too small to noticeably perturb the evolution of a single zone but large enough to change the relative position of two close-lying zones.

The analysis above is in a strict technical sense based on certain conditions of uniformity along the transport path: constant temperature, constant friction coefficient and diffusivity, and constant transport velocities. It is also based on the condition that dispersion processes can be described by diffusion terms. More careful considerations show that typical departures from these conditions will alter the details of zone evolution, but not their form. The basic classes related to c and d separations remain divided and intact. The increase in centrifugal force and thus transport velocity with the distance from the axis, for example, does not significantly change the form or capability of sedimentation methods relative to other Sc techniques, and therefore leaves sedimentation firmly associated with other continuous profile (c) systems. The strong temperature gradients of thermal diffusion separations yield transport that is in every sense in the c category also. The fact that two phases in a discontinuous (d) extraction system have different friction coefficients does not change the limited separative capacity of such systems and only changes speed-of-separation arguments by requiring that some average friction coefficient be used to describe the two phases. While these and other related departures could be developed in detail, it would at present only interfere with our general purpose of developing and characterizing general classes of separations.

Transport and Steady-State Separations

The basic transport equations describe concentration distributions from the onset of transport to the final approach to steady-state or equilibrium conditions. However, the capacity to separate often changes dramatically during the full course of transport. This is implicitly recognized in the widely employed classification of separation techniques as either *rate* or *equilibrium* methods (*10, 11, 14, 15*). [The terms *transport* (or *transient*) (tr) and *steady-state* (ss), respectively, are preferred here, as the former are more descriptive than "rate" and the latter is more general than "equilibrium."]

The arguments developed previously concerning the limitations to a peak capacity of two in static discontinuous (Sd) profile separations apply during all stages of transport in such systems and in the asymptotic limit of equilibrium as well. By contrast, the capabilities of static continuous (Sc) profile separations change dramatically during transport. During intermediate stages of transport an arbitrarily large number of components can be separated to an arbitrary level of purity, providing $\Delta\mu^*$ can be increased sufficiently. Equilibrium in most such systems, however, is approached at an inert wall or at an electrode where all solutes reaccumulate in a common region. Separative power is lost in the final approach to equilibrium. Thus equilibrium sedimentation methods, for example, are useful for molecular weight determinations, but they are of little value in separating components into distinct regions as are the transport sedimentation methods.

An exception occurs when a secondary gradient serves to create a different equilibrium (or steady-state) position for each component. These positions generally exist at the bottom of U-shaped chemical potential wells. The secondary gradients responsible for such wells are pH gradients in electrophoresis (giving the technique of isoelectric focusing) and gradients in density in sedimentation (giving density-gradient or isopycnic sedimentation). Two other secondary gradients have been proposed but not developed. Theory shows that the peak capacity for such systems is roughly equivalent to that for transport systems of equal primary field strength (*32*).

FLOW SYSTEMS OF SEPARATION

The role of flow in separation systems is best elucidated by reference to the general transport equations. If Eq. (4) is substituted into Eq. (2), we have

$$\frac{\partial c}{\partial t} = -(U + v)\frac{\partial c}{\partial x} + D_T\frac{\partial^2 c}{\partial x^2} \tag{22}$$

This equation shows that the velocity of relative solute displacement U and the flow velocity v are interchangeable insofar as the evolution of a single zone along principal axis x is concerned. However, U and v are subject to quite different limitations and manipulations, and so rarely play equivalent roles in practice. For example, U alone is selective between solutes, and thus, unlike v, can induce separation. Flow velocity v, on the other hand, can readily assume values orders of magnitude larger than U, and these values can be made to persist over far longer separation paths. Thus

U and *v* generally play complementary rather than equivalent roles in chemical separations.

It was shown earlier that a critical role played by velocity *U* in nonflow chemical separations (e.g., electrophoresis) is to force the evacuation of solute from broad regions, freeing space for occupancy by other solutes. This was explained in terms of dimensionless coordinates in the discussion following Eq. (20). It is clear from the equivalence of *v* and *U* in Eq. (22) that *v* also can evacuate solute and create free space for other solutes. In a few rare cases *v* and *U* play equivalent roles in this regard. For example, the selective removal (evacuation) of a solute through a semipermeable membrane can occur by means of an applied electrical field (electrodialysis) or by flow (pressure dialysis). The selectivity in this case is provided by the chemical potential barrier at the membrane surface.

In steady-state systems the displacement represented by *U* frequently balances an opposing diffusive flux. In this case the *U*-induced displacement does not serve to evacuate new space, but instead serves to maintain existing evacuated space against diffusion. Again, *v* can assume the same role. Thus in field-flow fractionation (FFF), steady-state layers can be formed using electrical, sedimentation, or thermal fields, or equivalently by using a cross flow. (The latter perhaps deserves a separate category, such as F(+)F, in Table 2.) The mathematics in the two cases is essentially equivalent. This and other steady-state processes in separations will be discussed in a subsequent paper.

As noted earlier, a separation method is regarded as a flow technique only if the flow plays an integral role in structuring the separation. Two categories of such separative flow were distinguished: F(=) for flow parallel to the force(s) of relative displacement and F(+) for flow perpendicular to the force(s). The role of flow in these two cases will now be identified.

Flow Parallel to Force, F(=)

As noted in Table 2, this flow category includes the various filtration methods along with zone melting, elutriation, etc. In these methods, flow carries solute into a selective chemical potential gradient (F(=)c) or barrier (F(=)d). If the barrier is sufficiently permeable to some solutes, flow evacuates those solutes from one side, thus separating them from nonpermeating solutes. In some cases a steady-state condition is approached in which flow holds solute against diffusion in a narrow zone (as adjacent to a membrane filter) where active separation occurs, or maintains narrow zones in different steady-state positions (elutriation).

We note that zone melting and the various filtration methods fall into the same category (F(=)d) of Table 2. The suggested similarity is indeed very fundamental, as noted earlier. In each case there is a relative motion (flow) of liquid into a selective chemical potential barrier. Species strongly rejected by the barrier diffuse back into the liquid against the flow, forming a polarized layer. A loss of selectivity accompanies the formation of the layer, but this can be mitigated by stirring currents. Thus layer dynamics and the general physical relationship of flow and chemical potential barrier are essentially identical in the two groups of methods. The principal difference lies in the detailed physical and chemical nature of the barriers. Thus the two systems are applicable to different classes of solutes because of their unlike interaction with solutes.

Flow Perpendicular to Force, F(+)

Flow in this category is an integral factor in such separation methods as chromatography, distillation, countercurrent distribution, field-flow fractionation, and other methods listed in Table 2. Because flow is essentially perpendicular to the primary force(s) of relative displacement acting in such systems, a second displacement axis is created. Separation and enrichment along the primary axis occur in much the same manner as in static (nonflow) systems. Usually a steady-state or equilibrium condition is approached along this axis. However, in F(+) systems one often utilizes weak forces (e.g., thermal diffusion) or inefficient forces (those giving solute distribution in two-phase systems) that are by themselves quite ineffective for complicated separations without the aid of flow. Nonetheless, the primary forces provide selective enrichment in certain flow regions so that the flow displacement itself becomes selective.

Displacement along the flow axis z can then be described by Eq. (2), where we replace displacement velocity W by Rv

$$\frac{\partial c}{\partial t} = -Rv\frac{\partial c}{\partial z} + D_T\frac{\partial^2 c}{\partial z^2} \tag{23}$$

where v is now the mean fluid velocity along axis z and R is the *retention ratio*, indicating the departure of solute from velocity v due to the partitioning between velocity states (regions having different flow velocities). Quantity R varies from solute to solute because the partitioning is a selective process.

The term $-Rv\ \partial c/\partial z$ serves the same function along axis z as we have discussed for $\varepsilon'\ \partial c/\partial \chi$ along dimensionless axis χ and for the term $W = U + v$ along axis x: it serves to displace solute zones at velocity Rv to new positions along the flow axis and at the same time forces the evacuation of solute from positions previously occupied so that other solutes may form separated zones there. Mathematically the process is equivalent to that occurring in static continuous-force (Sc) systems like electrophoresis, where the basis of multicomponent separations was previously explained. The difference lies only in the different origin of displacement and selectivity, and in the greater strength of flow displacements compared to field-induced (relative) displacements. This increased strength, which permits a wide choice of flow velocities in columns up to a mile in length, is largely responsible for the enormous power and versatility of chromatography as a separation device.

In F(+) systems then, the role of flow is simply to create a new displacement axis of arbitrary length along which separation can occur. Selectivity originates through enrichment along the primary force axis. With selectivity, the nature of flow displacement is such that it leads to the formation of narrow zones in separate locations along the flow axis. With a sufficient extension in length of the flow axis, separations are ultimately achievable for components which show very little selectivity in enrichment along the primary force axis. Thus flow serves to magnify small differences in solute properties and, consequently, small primary enrichment processes into effective separations.

For completeness it should be noted that several F(+) methodologies do not lead to multicomponent separations. In the thermogravitational column, for example, the flow path simply serves to magnify the relative enrichment of two fractions provided by the basic thermal diffusion process.

The foregoing discussion shows that flow assumes a distinctly different role in F(+) separations than in F(=) methods. The differences are so profound that they readily justify these two categories as basic components of a system of classification.

CONCLUSIONS

Separation processes by their very nature are transport processes. The nature of separation is therefore controlled by the underlying transport phenomena. Different categories of transport quite naturally, therefore, impose different characteristics, limitations, and capabilities upon the separation methods associated with them. Recognition of this fact not only promotes an understanding of the basic similarities and differences between separation methods, but it leads to a system of classification of the most fundamental kind. This system is shown in Table 1.

Hopefully, additional work will serve to tie the present approach to classification into a broader classificatory system having a more universal applicability.

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