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On the Measurement and Evaluation of Separation

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Abstract

The entropy of multicomponent mixtures is examined and two reference states of unique entropy values are defined, the completely mixed and the separated states. The position of any system relative to these fixed points is accounted for in terms of four entropy terms, one for chemical specie separation and three for physical or spatial separations. An apt comparison of separations must acknowledge the possibility of these four distinct processes. An alternative approach to the evaluation of a separation is based on the reduction of the information in a matrix of pairwise criterion of separation to a single point in vector space. This vector distance as a measure of separation is illustrated for differential migration processes.

The problem of evaluating, quantitatively, a separation either for comparison with another separation or with some pre-established goal has not been solved. Most of the effort in this direction has centered on finding a suitable "criterion of merit" (*1*) to serve as a definition of separation. For the techniques of separation classified as differential migrations, especially chromatography, the use of resolution (*2*), separation number (*3*), extent of separation (*4*), peak to valley ratios (*5*), impurity index (*6*), separation function (*7*), and entropy of separation (*8*) have been proposed and each criterion has its proponents. Each of these criteria, with the exception of entropy, is applied to the separation between two components of the mixture and is not a single measure of the total separation for a many-component mixture; each is a criterion of pair separations. With the capability of modern techniques to separate a mixture with 50 or 100 components, an overall measure of the degree of separation would be welcome.

In this paper I will discuss the difficulties in the use of entropy as a unique measure of separation and will discuss an alternative approach to the problem through the use of a resolution matrix. Two methods of measurement and evaluation of separation will be presented.

ENTROPY AS A MEASURE OF SEPARATION

De Clerk and Cloete (*8*) have proposed the use of entropy as a general criterion of separation. This suggestion reflects the thought that separation is a process of ordering. De Clerk and Cloete have shown how the entropy can be evaluated by an appropriate summing of impurity indicies of various regions. What they have not considered is the diversity of physical distributions which can exist when different methods of separation are employed. This leads to difficulties in the definition of a region for the calculation of impurity indicies. They did not consider the importance of spatial separations which coexist with chemical specie separation in some separation techniques. This can lead to the comparison of separation defined by different standards.

Consider the block diagrams in Fig. 1. Pathway A represents an idealized differential migration similar to a chromatographic process. The physical expansion of the total system of components while chemical separation occurs is an increase in the entropy of the system. The entropy increase as a result from the greater volume occupied by the component migration exactly compensates the entropy decrease due to the chemical ordering which occurs, and the process from State I to State III is an isoentropic process under the idealization invoked (see Ref. *9* for a detailed discussion of the isoentropic process). Here is a separation where chemical disorder is traded for physical disorder, and the separation is a disorder exchange rather than an ordering process.

To the argument that the entropy measurement should be restricted to separation of chemical species, i.e., purification, it must be answered that the expansion and other physical separations which can occur lead to different results in the separation of the same sample by various techniques. Compare State AIII and State BIII in Fig. 1. State BIII is the ideal separation achieved by a process such as distillation.

Separation is a setting apart. If there is a setting apart or disuniting of

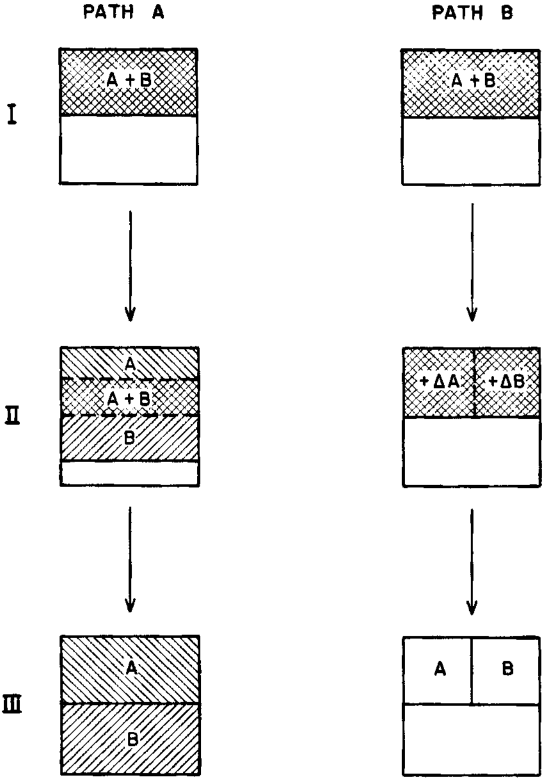
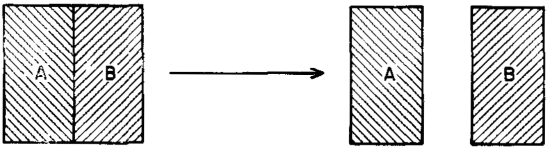
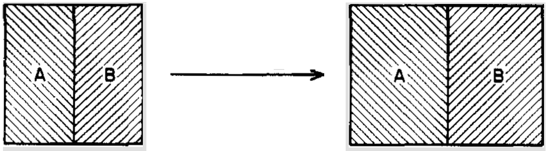


FIGURE 1.

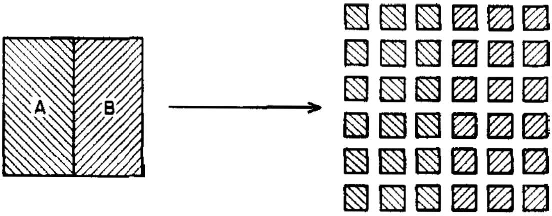
different chemical species, purification occurs, an ordering on the basis of chemical composition. This kind of separation is accompanied by a decrease in the entropy of the system and is the normal goal in separation processes. Other disuniting processes can occur which do not distinguish the parts on the basis of their chemical compositions. These occur at the molecular, micro-, or macrolevel and are accompanied by an increase in entropy of the system. Generally these result from the opening of the system to the surroundings so that an inert carrier is added to the system while spatial separation occurs. These physical processes are illustrated in Fig. 2. The process labeled *migration* is a setting apart of whole regions, a macroscopic process. The process labeled *expansion* is a molecular level process where the average distance between molecules is increased. The



MIGRATION



EXPANSION



DISPERSION

FIGURE 2.

dispersion process is a microscale process where chemically identifiable regions are broken into many separate subregions.

Migration is particularly important in the differential migration techniques and is the reason for the preference of many chromatographers for resolution and separation number as separation criteria. These measures of separation report both overseparation and underseparation. The existence of overseparation in a procedure is costly in time and materials and has resulted in the development of programmed temperature and gradient techniques for the destruction of excessive separation in particular methods. With the separating power which is available today with differential migration techniques, it is likely that some investigators are as often faced with the desire to eliminate excess resolution in order to gain speed as with the need to increase resolution.

The second kind of physical separation is expansion. Returning for the moment to Fig. 1 and considering Path B, we see the kind of separation that can ideally be accomplished by a process such as fractional distillation. Assuming the idealization that the partial molar volume is always equal to the molar volume of the components, we find that the chemical specie separation occurs without increasing the total volume occupied by the components. Complete specie separation as depicted in State III of Paths A and B is not the same. Isoentropic separation by chromatography is not comparable to the results of separation by distillation, an entropy minimizing process. The removal of the inert diluent or condensation of the results of a chromatographic separation to make them equivalent to the results of a distillation process would require an additional ordering process.

Let us select State IIIB as representing a reference state, the separated state. Figure 1 represents two possible pathways from the complete mixture, State I, to the separated state. Ignoring for the moment the expansion of State A, compare the distributions of components in the two partially separated states as represented by IIA and IIB of Fig. 1. There are, undoubtedly, an infinite number of distributions for the same degree of separation, and the concept of region for entropy calculations is difficult to define.

An example of physical separation which is excluded by a restriction to constant partial molar volumes is expansion. The separation of a gas from its solution in a liquid would be an example where there is entropy increase during separation due to expansion as well as entropy decrease due to chemical separation.

The third kind of physical separation which accompanies some specie separations is dispersion. An excellent example of this would be the precipitation reactions. The formation of a fine suspension of $BaSO_4$ in preparation for a gravimetric sulfate determination is a good example of a dispersed state. Even though chemical separation is immediately accomplished, the suspension or dispersion of crystals formed require digestion and filtration before the defined separated state of Fig. 1 (IIIB) is achieved. Peptization and aerosol formation are common processes by which a dispersed state is formed.

Thus, when we wish to describe a separation, a description of only the purity achieved gives an incomplete measure of the state of the system and of the separation. The three major kinds of physical separation can occur both individually or in various combinations. Perhaps the evaluation of the entropy change resulting from each of the four processes, demixing or chemical specie separation, migration, expansion, and dispersion, separately, and in various combinations, would be an useful approach. If so, we need to consider the properties of an entropy scale as a measure of that separation.

Entropy has several features analogous with temperature which recommend it for establishing a scale of degrees. There is an absolute zero of temperature. Is there an absolute zero of entropy? The Third Law suggests that there is but care must be taken. While most pure components may be assumed to have a Third Law entropy of zero, a system of components may have a spatial arrangement which must be given a statistical weight. An AB arrangement may be distinguished from a BA arrangement when related to the process or equipment of separation. Also, when migration, expansion, or dispersion occurs it is the result of an opening of the system, the addition of an inert diluent or carrier which can change the number of allowed permutations of spatial arrangement. Generally, there will be an irreducible entropy, dependent only on the number of components in the system and the dimensionality of the system. For a system, a state of absolute minimum entropy can be defined at absolute zero and can provide a bottom to a scale in the same manner that absolute zero does for the temperature scales, but the statistical weight must be accounted for since changes in the statistical weight of the system during separation are not properly measured if the reference state is arbitrarily called zero.

This minimum statistical weight arrangement can persist for the separated state at temperatures above absolute zero and provides a more convenient unique and fixed reference state at a practical temperature. The pure separated components, with the total volume equal to the sum of the component volumes, i.e., no spatial separation, at the specified temperature and pressure and in a spatial array of minimum statistical weight provides a suitable fixed point on the entropy scale as the ice point does for a temperature scale. The entropy of this state can be decreased only by variation in the temperature or pressure of the system. These relationships are illustrated in Fig. 3. The perfect solution or mixture is another reference state available to fix the entropy scale at the specified temperature and pressure. This is a higher entropy state due to the mixing. This ideal state is not a minimum in the same sense that the reference separated state is because the entropy of real systems can be lower as a consequence of orientation forces and decreases in the partial molar volumes of the real components. This is a minor and measurable perturbation which should not detract from the utility of this ideal state as a fixed point on the entropy of separation scale. However, some investigators

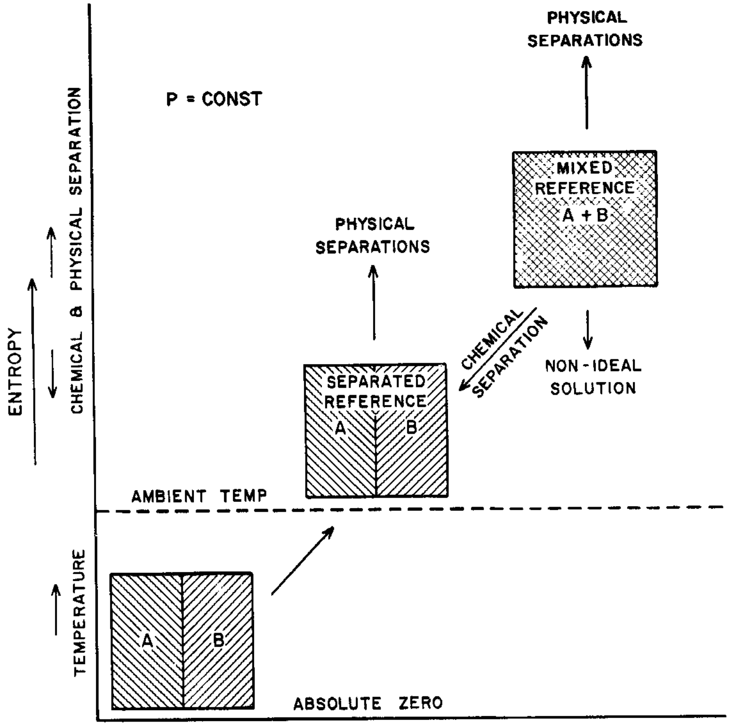


FIGURE 3.

may prefer the choice of the real to the idealized reference state. This should not alter the arguments presented.

We now have a set of two states of uniquely defined entropies, the mixed state reference and the separated state reference. Starting at the mixed state, demixing is measured by the decrease in entropy as the system moves toward the defined separation. The decrease in entropy relative to the entropy difference of the two fixed states measures the degree of separation. Two difficulties remain. The first of these is the fact that the scale applies to the chemical aspects of separation and does not handle or report the physical processes that may accompany separation. The spatial separation must be reported separately to give a complete description of the separation achieved at each point in the process. There are an infinite number of pathways between the two reference states. Recall the comparison between comparable impurity indicies achieved by distillation and differential migration as illustrated in Fig. 1.

A second, and perhaps more serious difficulty, arises because a partially separated system may have a completely different statistical weight from the weight of the reference states, a statistical weight which is a function of the method of separation. Returning to Fig. 1, and considering the States IIA and IIB, we see, even without the expansion aspect of IIA, that the materials being separated have different distributions: State IIA has two regions of pure material and one region of mixture while State IIB has two regions of enriched components. It is often the practice to treat State IIA as two regions (e.g., by dropping a line at the valley on a chromatogram) for the purpose of comparing separations achieved by different techniques. This is a case of comparing the fraction of material which is pure with the fractional purity of the material. It is wise to treat the system of Path A as a closed system of three components rather than an open system to which the carrier fluid is added.

To summarize, two reference states can be defined which will serve for any separation, the completely mixed state and the separated state. Each has a unique entropy value. If any increase of entropy occurs due to one of three spatial separations, this can be noted independently by three other entropy terms and the chemical separation can be accepted as a monotonic decrease from the mixed state entropy to the separated state entropy. The specie separation entropy does not define the distribution or statistical weight of the system, and this must be reported separately. These four entropy terms plus the distribution information define a partially separated system relative to the reference states, and this information will serve as a basis for comparison of separations. If the physical, chemical, and probability aspects of a separation are acknowledged, the extensive nature of entropy allows us to escape the lengthy paired component comparisons of different separations of multicomponent mixtures.

This approach to the comparison of separations by locating systems in a four-dimensional entropy field does not lend itself to easy quantitation when dealing with mixtures of many components. It does serve as a conceptual tool to remind us of differences that exist in the separations achieved by different techniques. Another approach, most useful for comparison of differential migrations and based on a reduction of information in a paired component description, is discussed next.

THE RESOLUTION MATRIX

The development in this section will be restricted to separations accomplished by differential migration as defined by Path A in Fig. 1. That

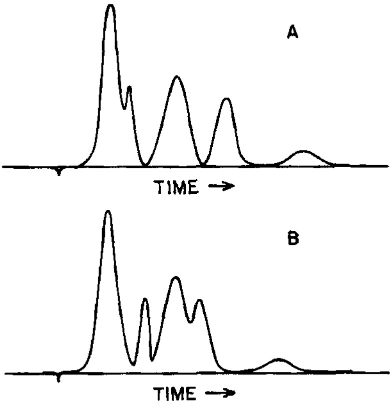


FIGURE 4.

the discussion can be extended to other separation techniques, and even to an entropy-based scale, will be evident.

We are searching for a method of comparison of separations such as represented by the two chromatograms of Fig. 4, and we ask the question, "Which is the better separation?"

The most widely accepted measure of separation in differential migration is the resolution. This is usually defined as the ratio of the separation of centers of two solute zones to the average base width of the two, where the solute zones are considered to have Gaussian distributions. Resolution is a paired component measure. Boyd (*10*) has pointed out that resolution is restricted to two components and that it has a directional characteristic; A resolved from B is not the same as B resolved from A. Pair selection is not restricted to nearest neighbors. The following discussion will use Boyd's concept of resolution and will not be concerned with the particular formula used for its evaluation with a directional character.

The resolution has an additional feature reflecting concepts discussed earlier. It not only measures overlap or impurity factors for the pairs of solute zones but, after baseline or total resolution has been achieved, it continues to increase in magnitude as overseparation occurs. It measures the physical separation of expansion by migration discussed in earlier sections. This is a feature missing from such criteria of merit as valley height and index of separation. This overseparation expansion of the total system is the most important form of physical separation that occurs in differential migration techniques, and it has led to the development of special gradient methods designed to minimize this expansion.

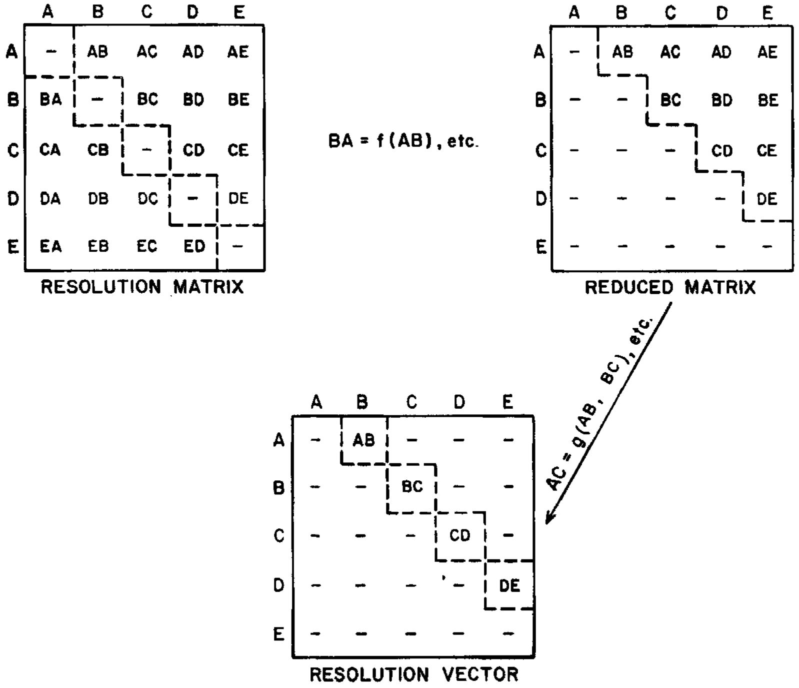


FIGURE 5.

In the separation of a mixture of N components there are $N(N-1)$ distinct ordered pairs. These are displayed in Fig. 5 as a skew matrix, which I call the resolution matrix. The element AB is read as "the resolution of A from B." If there is reasonable peak symmetry and there is knowledge of the relative quantities of the components, the element BA can be calculated from the element AB. Half of the matrix can be eliminated with little information loss and we have the reduced matrix of $(N/2)(N-1)$ elements. With the same information, amount, and zone shape, the element AC can be argued from the nearest neighbor elements AB and BC. This further reduces the number of elements necessary to describe the separation to $N-1$ nearest neighbor elements. This is the usual description of a separation in terms of resolution. This minimum set of ordered numbers I will call the resolution vector to distinguish it from the complete set in the resolution matrix (see Fig. 5 for illustration of these relations). Note that the analysis to follow is valid for both the total resolution matrix and the reduced number of elements in the resolution vector.

	A	B	C	D	E
A	0	.4	1.4	2.5	4.0
B	.4	0	1.0	2.1	3.6
C	1.4	1.0	0	1.1	2.6
D	2.5	2.1	1.1	0	1.5
E	4.0	3.6	2.6	1.5	0

ACTUAL

	A	B	C	D	E
A	0	1	2	3	4
B	1	0	1	2	3
C	2	1	0	1	2
D	3	2	1	0	1
E	4	3	2	1	0

STANDARD

	A	B	C	D	E
A	0	-.6	-.6	-.5	0
B	-.6	0	0	.1	.6
C	-.6	0	0	.1	.6
D	-.5	.1	.1	0	.5
E	0	.6	.6	.5	0

DEVIATION

VECTORS

ACTUAL - STANDARD = DEVIATION

(.4, 1.0, 1.1, 1.5) - (1.0, 1.0, 1.0, 1.0) = (-.6, 0, .1, .5)

POSITIVE DEVIATION (.1, .5) NEGATIVE DEVIATION = (-.6)

$d = (\Sigma d^2)^{1/2} \cong 0.8$

$d_+ \cong 0.6 \qquad d_- \cong 0.5$

FIGURE 6.

The reduction of the matrix to the vector, from $N(N-1)$ elements to $N-1$ elements, is not necessary for the following analysis. The discussion is simplified by the small number of terms in the resolution vector, and this corresponds to the usual practice of investigators analyzing a chromatogram.

The $N-1$ ordered numbers are to be compared with either a standard of perfection or a preset goal. This is represented by the standard matrix in Fig. 6. A resolution of unity is often taken as the desired separation in chromatography, larger numbers representing overseparation and smaller numbers representing underseparation. A vector, representing the real separation, can be compared with the standard vector. The difference between the two, obtained by simple subtraction of element from corresponding element, yields a deviation vector (Fig. 6) which indicates how far the reality is from the desired state of the standard vector.

The deviation vector has elements of both positive and negative sign, the negative sign representing underseparation and the positive sign representing overseparation. If the mixture contains a large number of components, this is still a complex representation and further reduction of the data is desired.

The ordered set of numbers represents a point in an $N - 1$ dimensional space. The standard vector represents the origin of deviation vector space. The resolution vector represents the point in that deviation vector space that our system has reached. The measure of the separation is the distance between these two points is the length of the deviation vector. This separation distance can be calculated as the root of the squares of the elements of the deviation vector, $d = (\Sigma(\Delta AB)^2)^{1/2}$. A single number measures how close a given separation is to a perfect separation as defined by the standard vector.

The analysis above weights overseparation and underseparation equally. Various schemes are easily devised for neglecting or weighting overseparation in the measurement of deviation from the standard. What would be desirable is a simple way of noting direction in the deviation vector space.

A sense of direction in $N - 1$ dimensional space is a difficult abstraction and is not readily reduced to a single number in the same way that the sense of distance has been reduced. A counting of negative elements and of positive elements gives one an idea of the balance between over- and underseparation that exists in the system. A somewhat clearer representation can be gained by dividing the deviation vector into two vectors, one composed of the negative elements, the negative deviation vector, and one composed of the positive elements, the positive deviation vector. From these two the distance of overseparation and the distance of underseparation can be calculated separately as a d_+ and a d_-. A numerical example is given in Fig. 6. The total deviation distance is composed of these two which may be recombined to give the value d. It should be noted that comparison of these vector lengths must be restricted to comparison in space of the same dimension (i.e., samples with the same number of components). It should be noted that if the difference in the positive and negative distances is negative, there is not sufficient resolution in the procedure to achieve the standard separation, whereas if the difference is positive, we are faced with a problem of distribution of resolving power among the pairs.

In summary, it is proposed that the $N(N - 1)$ bits of information that represent the state of resolution of an N-component mixture be displayed as a matrix which (either by itself or in a reduced vector form) is a point in an $N(N - 1)$ (or $N - 1$) deviation space. There is another point in this space described by the standard matrix which represents perfect resolution. Each dimension through the standard point has a negative unresolved direction and a positive resolved direction. The distances along each of these dimensions to the point represents the position of the actual system, and this can be represented as the combination of two distances d_+ and d_-. This provides both a quantitative and a conceptual basis for measurement and comparison of degrees of separation in differential migration processes.

Any system of components being separated which can be characterized by a set of separation criterion numbers for paired components can be represented as a point in deviation vector space, and the model need not be restricted to differential migration processes.

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