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Theoretical Considerations Regarding Tandem Column Arrangements with Application to Gas–Liquid and Gel Permeation Chromatography

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Summary

It is proven that, given a constant flow rate throughout the system, the $(2n)!$ possible arrangements (including 180° rotation of any column along the long axis) of n chromatography columns arranged in tandem yield identical elution curves (and therefore identical values of mean residence time and variance). The columns must be of the same cross-sectional area but each can be of arbitrary length. The proof is independent of the nature of the packing material in each column and holds for any given input distribution in time and/or constitution.

Also discussed are earlier results for a much more restrictive model, proving the equivalence of n columns in tandem with one long column containing a homogeneous mixture of the n types of packing material in the proper proportion.

Knowledge of the effects on separation efficiency of various series arrangements of a set of columns has value in gas–liquid chromatography and gel permeation chromatography. Workers in either of these fields might also wish to know the conditions under which n short columns packed with different materials and arranged in series would be equivalent to one long column containing a homogeneous mixture of the n types of packing materials in the proper proportions. In this paper a formal analysis of the first situation is presented in the proof of two theorems. The previously published results of a more restrictive model for the second situation are also discussed.

THEOREM 1

Given a constant flow rate throughout the system (or equivalently, zero pressure drop) the $n!$ arrangements (excluding 180° rotation of any column) of n chromatography columns arranged in tandem (series) yield identical elution curves for any given input distribution(s) in time and/or constitution.

Proof

Consider n chromatography columns of lengths l_1, l_2, l_3, . . . , l_n, respectively, each with cross-sectional area a. These columns are characterized by the nature of the packing material and the manner of packing such that each column has, in general, a unique separating capability for any given solute. In the case of columns used in gel permeation chromatography, these separating capabilities could be specified by some measure of the molecular weight range of polymer that could be separated by a particular column. We require that the n columns be arranged in tandem (series) with infinitely short connecting links. We wish to describe the events occurring in any given column by means of a random variable. A random variable is a function defined on a sample space such that there is a unique rule that associates a number with each sample point (*1*). In the case of a discrete sample space the random variable T can be tabulated by enumerating in some order the points of the space and associating with each the corresponding value of T. In the case of a random variable describing a process in time, each instant t corresponds to a point in the sample space (*2*). The formal definition required here for a random variable is a function T such that for each time t the event $\{T < t\}$ consists of finitely many intervals. The proof will be developed in terms of random variables for formal simplicity. However, a probability distribution is associated with each random variable and the probability distribution is directly associated with the elution curve. Excluding extra-column contributions, the probability distribution is identically the experimental elution curve. Let T_i be the random variable representing the total time spent in the ith column. Events occurring during the chromatographic process in different columns are independent of one another. That is to say, once a molecule has entered a column it cannot reenter the column from which it has just escaped, and, furthermore, the molecule carries with it no past history of events in which it has participated. Let T be the random variable representing the total time spent in all the columns:

$$T = \sum_{i=1}^{n} T_i \tag{1}$$

As previously defined, each of the random variables T_i can be interpreted as a vector (a set of ordered n-tuples) in the n-dimensional vector space of real numbers, $V_n(R)$ (3) with one exceptional characteristic. All the properties of elements contained in $V_n(R)$ except the existance of an inverse can be applied to our random variable T_i(4,5). In particular, for any random variables T_α, T_β,

$$T_\alpha + T_\beta = T_\beta + T_\alpha \qquad \text{(commutative law)} \tag{2}$$

where the operation of addition means the addition of corresponding elements of the vectors.

Since independent random variables follow the commutative law under the operation of addition, Eq. (1) yields the identical value of T regardless of the permutation of the T_i. Since we required that the carrier velocity be constant throughout the system, the permutation of the T_i is identical with the permutation of the columns in tandem. The proof is nearly complete. We must simply show the exact relationship between T_i and the corresponding columns. This is done through the probability distribution for each T_i. The aggregate of all sample points in which the random variable X assumes the fixed value X_j forms the event that $X = X_j$. The probability is denoted by $P\{X = X_j\}$. The function $P\{X = X_j\} = f(X_j)$, $j =$ 1, 2, . . . , is called the probability distribution of the random variable X. Clearly $f(X_j) \geqslant 0$, $\Sigma_{j=1}^{n} f(X_j) = 1$. Saying that T_i and T_j are independent random variables with distributions f and g means that the joint probability distribution of (T_i, T_j) is given by the product $f(t_i)g\,(t_j)$ (6). The random variable T is thus represented by the product, taken in any order, of the probability distributions associated with each of the n columns. This product is the total column contribution to the experimentally observed elution curve. Furthermore, if $\rho_\nu^{(i)}$ is the νth cumulate of T_i, then $\rho_\nu = \Sigma_{i=1}^{n} \rho_\nu^{(i)}$. Cumulants are related to central moments by a general formula (7). The first four are $\rho_1 = m$, $\rho_2 = m_2$, $\rho_3 = m_3$, and $\rho_4 = m_4 - 3m_2^2$, where m_j is the jth central moment and m is the mean. For example, the mean time at which a particular sample appears is the sum of the mean times spent in the individual columns plus external contributions (i.e., time lag from finite injection time, time spent in the detection system).

THEOREM 2

Given a constant flow rate, the $(2n)!$ arrangements of n chromatography columns arranged in tandem yield identical elution curves.

The proof of theorem 2 follows directly by using theorem 1 and lemma 1, which is proved next.

LEMMA 1

The 180° rotation of any column about the long axis produces a column arrangement identical in separating ability with the original arrangement.

Proof

Let T be the random variable associated with an arbitrary chromatography column. Let T be represented as the ordered n-tuple (i.e., $t_m > t_{m-1}$, $0 < m \leqslant n$):

$$T = (t_1 \to T_1,\ t_2 \to T_2,\ \ldots,\ t_n \to T_n) \tag{3}$$

where $t_n \to T_n$ means that a time t_n is associated with the particular value T_n of the random variable T.

Define T_{rot} as the random variable associated with the column after rotation.

$$T_{\text{rot}} = (t_1 \to T_n,\ t_2 \to T_{n-1},\ \ldots,\ t_n \to T_1) \tag{4}$$

Recall that the probability distribution $P\{T = t_j\} = f(t_j)$, $j = 1, 2, 3,$ is the probability of the aggregate of all sample points in which $T = t_j$ regardless of the order in which they appear in the sample space. Therefore, the probability distributions associated with T and T_{rot} are identical. Therefore the column contributions to the elution curves and all cumulants are identical in the two cases.

DISCUSSION

Research using gel permeation chromatography is most frequently done with columns in tandem. Hopefully workers in this field will find the results of the present article beneficial. These results will perhaps also be of benefit to workers pursuing the experimental extension of gel permeation chromatography to on-line automatic analysis and control of molecular weight distribution in large-scale batch and continuous polymerization reactors.

An analytical analysis of identically packed columns of arbitrary length in tandem has been presented by McQuarrie (*8*) for a model in which molecules are assumed to be present in either mobile or stationary states within a given column. Under these restrictions he has shown that the elution curve of a column of length l $(= \Sigma_{i=1}^{n} l_i)$ is equivalent to the elution curve obtained from n columns of lengths $l_1, l_2, \ldots, l_n$ arranged in tandem. It may be possible to obtain such a proof for a less restrictive model.

Experimentally, Porter et al. (9) have shown that retention times of a variety of columns with mixed packing are the sums of retention times of two columns if a negligible pressure drop occurs over the columns. The sum of lengths of the two columns equaled in each case the length of the longer column and the cross-sectional area of all columns were identical. Other experimental references supporting these conclusions were cited in Ref. 9.

Kwok et al. (*10*) have utilized some of the results proven in theorem 1 in several applications. In particular, assuming columns 1, 2, . . . , n in series using a noncompressive liquid phase (liquid chromatography), these workers correctly stated that

$$t_R = \sum_{i=1}^{n} (t_R)_i \tag{5a}$$

and

$$\sigma^2 = \sum_{i=1}^{n} (\sigma^2)_i \tag{5b}$$

where t_R represents retention time and σ^2 represents variance.

The general validity of Eq. (5b) was not established in their paper. However, results of several numerical calculations were presented for which Eq. (5a) was satisfied. Under their physical assumptions for tandem columns in liquid chromatography, we have shown that Eq. (5a), (5b), and similar expressions for higher cumulants must hold exactly.

Using Eq. (5a) and (5b), Kwok et al. proved an interesting result. They showed that the number of theoretical plates, N, of the sum of n independent columns in tandem does not equal the sum of theoretical plates of the individual columns, i.e., $N \neq \Sigma N_i$.

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