Journal of Chromatography, 92 (1974) 213–222
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CHROM. 7307

APPLICATION OF NUMERICAL LAPLACE TRANSFORMATION TO CHROMATOGRAPHIC PEAK ANALYSIS

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(Received October 26th, 1973)

SUMMARY

The numerical Laplace transform method is introduced into the theoretical research of chromatographic peak analysis and is shown to have some useful characteristics; the numerical Laplace transform converts an experimental chromatogram into sets of discrete quantities, which enables statistical moments of the chromatogram to be calculated more accurately than with previous methods. The parameters which influence column performance, such as distribution coefficient, diffusion coefficient, mass transfer coefficient, etc., can be estimated by the aid of the statistical moments, or directly by the digitized form of the Laplace transform. The error of this analogue–digital conversion is evaluated and proved to be negligible when the numerical Laplace transform is defined in the form of Simpson's rule.

INTRODUCTION

In elution chromatography the shape of a chromatogram incorporates all the characteristics of the individual system. There have been, accordingly, many reports concerning the theory of chromatographic peak analysis. Lapidus and Amundson[1] first applied the Laplace transform method to solve the mass balance equation for a linear, non-ideal and non-equilibrium chromatographic system. The solution expressed in time domain, however, is too complicated to apply in practice. Though the extended mass balances were also solved by means of the Laplace transform method, all of the solutions were given in Laplace domain, not in time domain, and they are mostly impossible to invert into time domain. By the aid of Amundson's work Van Deemter *et al.*[2] derived their equation, which implicitly involved the idea of the statistical moments of a chromatogram. The statistical moments, thereafter, have been investigated to obtain more information from a chromatogram. When a chromatogram is regarded as a statistical distribution curve, the *n*th normal moment M_n' is defined by

$$M_n' = \int_0^\infty t^n \mathrm{f}(t)\,\mathrm{d}t \Big/ \int_0^\infty \mathrm{f}(t)\,\mathrm{d}t$$

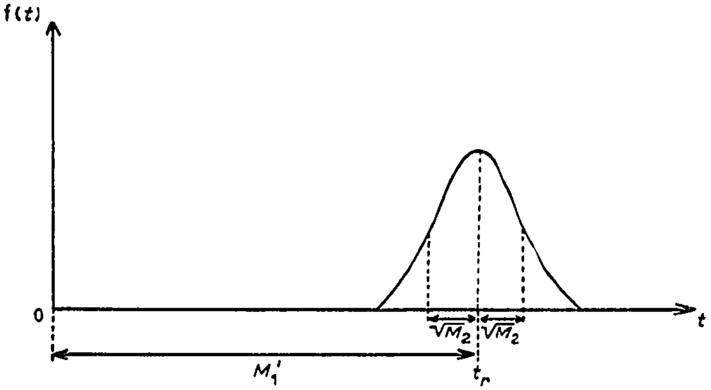

Fig. 1. The first normal moment M_1' and the second central moment M_2 on the schematic chromatogram. M_2 signifies the variance, σ^2.

and the nth central moment M_n by

$$M_n = \int_0^\infty (t - M_1')^n f(t)\,dt \Big/ \int_0^\infty f(t)\,dt$$

where f(t) denotes a function describing a chromatogram in time domain. Then the height equivalent to a theoretical plate (HETP), which is a measure of column efficiency, has a relation with the first and second moments in the form

$$\mathrm{HETP} = L\, M_2/(M_1')^2 = L\, M_2/t_r^2$$

where t_r is retention time of a given solute, L is column length, and M_1' and M_2 are the first normal and second central moments, respectively, as illustrated in Fig. 1. The higher moments have been discussed by Kučera[3], Grubner *et al.*[4], Grushka[5] and Kočiřík[6], who calculated the first five moments (moments zero to four) according to the theory of linear chromatography. On the other hand, De Clerk[7-9] investigated the first to third moments in the case of non-linear chromatography by means of the moment operator method and perturbation method. In these works the statistical moments were investigated only theoretically, and few papers have been published on the experimental treatment of the statistical moments, especially the higher moments. These preceding works suggest that the use of the Laplace transformed function facilitates the mathematical manipulation, and that the statistical moments of a chromatogram can be easily determined when a chromatogram is expressed in Laplace domain. The present work deals with an attempt to solve the problem by means of numerical Laplace transformation of a chromatogram, followed by fitting the transformed quantities to adequate power function, so that the statistical moments and the parameters which characterize each chromatographic system can be easily determined.

THEORY

Laplace transformation and statistical moments

The Laplace transform of a function f(t) is defined by

$$\tilde{f}(s) = \int_0^\infty e^{-st} f(t)\,dt \qquad (1)$$

and the nth derivative is expressed by

$$\tilde{f}^{(n)}(s) = \frac{d^n}{ds^n}\tilde{f}(s) = (-1)^n \int_0^\infty e^{-st} t^n f(t)\, dt \tag{2}$$

which gives a functional relationship between the nth normal moment M_n' and the Laplace transformed function $\tilde{f}(s)$ developed by McQuarrie[10]:

$$M_n' = (-1)^n \lim_{s\to 0} \tilde{f}^{(n)}(s)/M_0 \tag{3}$$

where M_0 is the zero moment.

Now, if we define a function $\bar{f}(s)$ by

$$\bar{f}(s) = \tilde{f}(s)\exp(M_1's) \tag{4}$$

the nth central moment M_n can be written as

$$M_n = (-1)^n \lim_{s\to 0} \bar{f}(s)/M_0 \tag{5}$$

By introducing a function h(s) defined by

$$h(s) = \ln(\tilde{f}(s)/M_0) \tag{6}$$

the first to fourth moments are expressed by

$$\begin{aligned} M_1' &= -\lim_{s\to 0} h'(s) \\ M_2 &= \lim_{s\to 0} h''(s) \\ M_3 &= -\lim_{s\to 0} h'''(s) \\ M_4 - 3M_2^2 &= \lim_{s\to 0} h^{(4)}(s) \end{aligned} \tag{7}$$

Each term on the right-hand side of these equations is called the cumulant in statistics. If we may take Taylor's expansion of h(s) at the origin, the first four terms are expressed[11] by

$$h(s) = \sum_{i=1}^{4} a_i s^i/i! \tag{8}$$

As one can see from eqn. 7, eqn. 8 has the useful property that the coefficient a_i in each term is directly related to the statistical moments in the form

$$\begin{aligned} a_1 &= -M_1' \\ a_2 &= M_2 \\ a_3 &= -M_3 \\ a_4 &= M_4 - 3M_2^2 \end{aligned} \tag{9}$$

These are the fundamental relations required to obtain the statistical moments from the Laplace transform of the function describing a chromatogram. On the other hand, statistics give the relationships between these moments and the parameters which characterize the shape of a chromatogram as

$$\begin{aligned} \mu &= M_1' \\ \sigma^2/\mu^2 &= M_2/(M_1')^2 \\ \alpha_3 &= M_3/(M_2)^{1.5} \\ \alpha_4 &= M_4/(M_2)^2 - 3 \end{aligned} \tag{10}$$

where μ, σ^2/μ^2, α_3 and α_4 are mean, relative variance, skewness and excess parameters, respectively, and the latter three parameters are dimensionless. In eqn. 10 the mean, μ, represents the retention time or retention volume and σ^2/μ^2 represents the column efficiency, because its reciprocal is the number of theoretical plates. The skewness parameter, α_3, is a measure of distortion of the chromatogram, its positive and negative values giving tailing and leading of a chromatogram, respectively. The sharpness of the peak is featured by α_4; the larger α_4, the sharper and taller the peak.

Numerical Laplace transformation

Usually an experimental chromatogram can be regarded as a continuous distribution curve and its intensity is given as analogue quantity. The numerical Laplace transform of a chromatogram is carried out after converting this analogue quantity to a discrete digitized quantity. For this purpose an experimental chromatogram is divided into m equal parts, as shown in Fig. 2, and the retention value of the ith part, t_i, and the peak height at that point, f_i are measured. The digitized data (t_i, f_i) thus obtained are then transformed into the quantity in Laplace domain with the use of Simpson's rule in the form

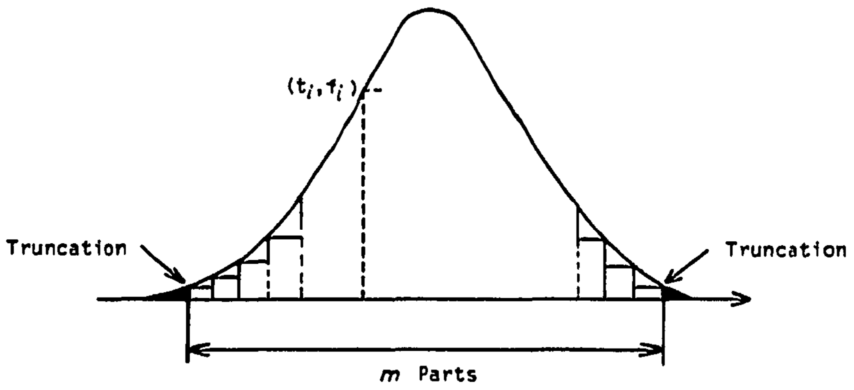

Fig. 2. Truncation and division of a chromatogram.

$$\tilde{f}_j(s_j) = \frac{\Delta t}{3}\{4 \sum_{i=1}^{m/2} \exp(-t_{2i-1}\cdot s_j)\, f_{2i-1} + 2 \sum_{j=1}^{m/2} \exp(-t_{2i}\cdot s_j)\, f_{2i} - \exp(-t_m\cdot s_j)\, f_m\};\; j = 1,\ldots,l \tag{11}$$

where m is an even number and Δt is the interval of each part. Thus the m sets of data (t_i, f_i) are converted into l sets of data $(s_j, \tilde{\mathrm{f}}_j)$. Then the data $(s_j, \tilde{\mathrm{f}}_j)$ require suitable fitting to an appropriate function. One may find it reasonable to conform this function to the Laplace transformed solution of the mass balance equation. This requirement can be satisfied by applying eqn. 8 to the discrete quantity in the form

$$\mathrm{h}_j(s) = \sum_{i=1}^{4} a_i \, s_j{}^i/i!; \quad j = 1, \ldots, l \tag{12}$$

In order to determine up to the fourth moment, according to eqns. 9 and 11, it is enough to know only four sets of the data (s_j, h_j). However, as the function $\mathrm{h}(s)$ is Taylor's expansion at the origin, it is a matter of course that the statistical moments can be determined more accurately by taking the value of s_j as near to zero as possible.

Estimation of the error of digitization

The errors which may accompany the conversion of the analogue quantity into the discrete digitized quantity were evaluated to confirm the reliability of the present method. There are two kinds of errors, *viz.* the error caused by changing the number of divisions, and the error caused by the truncation of a chromatogram. The first error is expected to decrease with increase in the number of divisions of a chromatogram, but the complications of measurement and calculation which may accompany this procedure impose a limitation on the increase in the number of divisions. The second error arises because both ends of a chromatogram are cut off at the position with a certain ratio of peak height to that of the maximum. The detailed procedure to estimate these errors is as follows: An adequate distribution function with some parameters is first chosen, and then the data (t_i, f_i) are calculated after giving proper values to these parameters, where the number of sets of data (t_i, f_i) corresponds to that of divisions. Next, from these data (t_i, f_i) the parameters are calculated by the method described below (eqns. 14, 15 and 16) and compared with their initial values. Thus the first error can be evaluated by changing the number of sets of data (t_i, f_i), and the second error by changing the threshold level under which the peak height of the ith part is truncated.

Here we used the Gram–Charlier series for the distribution function:

$$\mathrm{f}(t) = \frac{1}{\sigma} \left\{ \mathrm{g}(\tau) - \frac{\alpha_3}{3!} \mathrm{g}'''(\tau) + \frac{\alpha_4}{4!} \mathrm{g}^{(4)}(\tau) \right\} \tag{13}$$

where

$$\mathrm{g}(\tau) = \frac{1}{\sqrt{2\pi}} \exp\left(-\frac{\tau^2}{2}\right) \text{ and } \tau = (t - \mu)/\sigma$$

This function has the advantageous property that its parameters, μ, σ, α_3 and α_4, are related to the statistical moments in the forms given in eqn. 10. For the calculation of the statistical moments from the data (t_i, f_i), Simpson's rule is employed in the form

$$M_0 = \frac{\Delta t}{3} \left(4 \sum_{i=1}^{m/2} \mathrm{f}_{2i-1} + 2 \sum_{i=1}^{m/2} \mathrm{f}_{2i} - \mathrm{f}_m \right) \tag{14}$$

$$M_n' = \frac{\Delta t}{3}\left(4 \sum_{i=1}^{m/2} t_{2i-1}^n \, \mathrm{f}_{2i-1} + 2 \sum_{i=1}^{m/2} t_{2i}^n \, \mathrm{f}_{2i} - t_m^n \, \mathrm{f}_m\right)/M_0 \tag{15}$$

$$M_n = \frac{\Delta t}{3}\{4 \sum_{i=1}^{m/2} (t_{2i-1} - M_1')^n \mathrm{f}_{2i-1} + 2 \sum_{i=1}^{m/2} (t_{2i} - M_1')^n \mathrm{f}_{2i} - (t_m - M_1')^n \mathrm{f}_m\}/M_0 \tag{16}$$

These are expected to be the most useful equations for accurate results, so long as they are used for the purpose of estimating the values of the statistical moments.

The results for four parameters obtained by truncating the peak at 2% maximum height and varying the number of divisions are listed in Table I, together with the values of the parameters which were given initially to the Gram–Charlier series. Table II shows the effect of change in the threshold level on the values of these parameters. It is found from Tables I and II that the change in the number of divisions has less influence on the results than that in the threshold level, and the latter is preferably set as low as possible. Considering these observations, we chose 2% as the threshold level and fifty as the number of divisions in the experiments reported in this work. For a frame of reference, two theoretical chromatograms are illustrated in Fig. 3, one being drawn by substituting proper values of the parameters (the numerical values are shown in the legend to Fig. 3), and another by substituting the values of the param-

TABLE I

EFFECT OF CHANGING THE NUMBER OF DIVISIONS ON FOUR PARAMETERS

The initial values were: μ, 20.0; σ^2, 2.00; α_3, 1.061; α_4, 0.750.

Number of divisions	*Parameter*			
	μ	σ^2	α_3	α_4
936	20.0	2.00	0.803	0.637
468	20.0	2.00	0.803	0.635
50	20.0	2.00	0.813	0.648
24	19.9	1.99	0.796	0.568

TABLE II

EFFECT OF TRUNCATION AT VARIOUS THRESHOLD LEVELS ON FOUR PARAMETERS

The initial values were: μ, 20.0; σ^2, 2.00; α_3, 1.061; α_4, 0.750.

Threshold level (%) (number of divisions)	*Parameter*			
	μ	σ^2	α_3	α_4
1 (996)	20.0	2.05	0.836	0.751
2 (936)	20.0	2.00	0.803	0.637
5 (834)	19.9	1.85	0.721	0.390

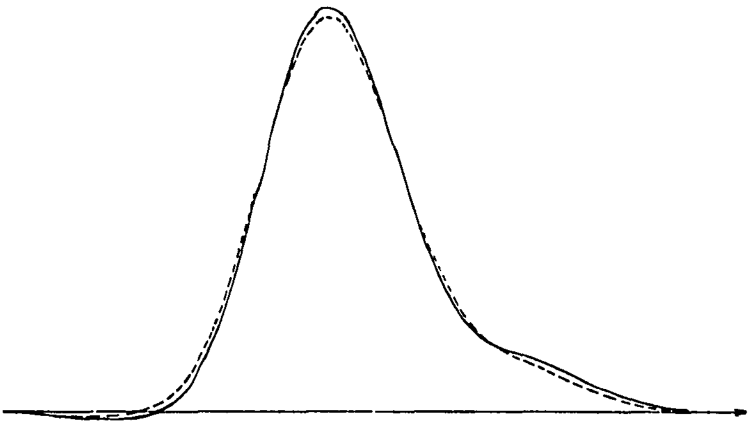

Fig. 3. Theoretical chromatograms. ———, A; — — —, B. (A) Obtained by initially substituting μ = 20.0, σ^2 = 2.00, α_3 = 1.061 and α_4 = 0.750 into a Gram–Charlier series. (B) Obtained by substituting μ = 20.0, σ^2 = 2.00, α_3 = 0.813, α_4 = 0.648 into a Gram–Charlier series. These parameters are calculated from the data (t_i, f_i) which are obtained according to chromatogram A.

eters which were calculated from the data (t_i, f_i) of the above chromatogram in the Gram–Charlier series. The two chromatograms are in good agreement with each other. This indicates that the difference between the initial and resultant values of the parameters which are shown in Tables I and II has little effect on the shapes of these two chromatograms.

Application to experimental chromatogram

The present method was applied to an experimental chromatogram and the results were compared with those of the preceding methods. The statistical moments were calculated according to eqns. 14, 15 and 16, and eqns. 6, 9, 11 and 12 were applied to an experimental chromatogram obtained under the conditions: stationary phase, 20% squalane coated on Chromosorb W (60–80 mesh); column, 3 mm × 2 m spiral glass tube; carrier gas, helium 18 ml/min; and sample, cyclohexane 2 μl. The threshold level was chosen as 2% of peak maximum and the chromatogram was divided into fifty equal parts. In the calculation of eqn. 12, we substituted zero into the initial value of s_j and 2×10^{-3} into Δs_j. The results are tabulated in Table III together with those of the following three methods. The first is the method of Grushka *et al.*[12], in which the moments are calculated from data for (t_i, f_i) according to a simple summation instead of using eqns. 14, 15 and 16. The second method is that of Grubner[13] and involves the approximation of a chromatogram to a Gram–Charlier series, followed by graphical determination of the inflection point which is related to the statistical moment. The third method, by Buys and De Clerk[14], includes an approximation to a bi-Gaussian distribution function, and is therefore expected to give poor results in this case. This method is included here in order to evaluate the error of the moments which takes place when a general chromatogram is approximated to a bi-Gaussian function.

It is seen in Table III that our results according to eqns. 6, 9, 11 and 12 are all in good agreement with those according to eqns. 14, 15 and 16, but not with those for

TABLE III

COMPARISON BETWEEN THE STATISTICAL MOMENTS CALCULATED BY VARIOUS METHODS

Methods: (1) according to eqns. 6, 9, 11 and 12; (2) according to eqns. 14, 15 and 16; (3) Grushka's method; (4) Grubner's method; (5) Buys' method.

Moment	*Method*				
	1	*2*	*3*	*4*	*5*
M_1'	17.5	17.5	17.5	17.5	17.5
M_2	0.308	0.308	0.309	0.138	0.229
M_3	0.156	0.156	0.161	0.140	0.004
M_4	0.162	0.163	0.173	0.542	—

higher moments according to the preceding methods. This may be caused by the approximations or assumptions which are involved in each of these methods. The present method is useful not only in obtaining the statistical moments but also in determining directly the parameters which characterize individual chromatographic systems. Discussion of this is given below.

Direct determination of the system parameters from the quantity in the Laplace domain

The numerical Laplace transform method is applied to the determination of the system parameters, such as distribution ratio k, mass transfer coefficient α and effective diffusion coefficient D, which characterize the efficiency of a chromatographic column. We shall now deal with linear, non-equilibrium chromatographic systems with the assumption that the pressure drop is small enough to be neglected. For this system the following mass balance has been employed[1]:

$$\frac{\partial C}{\partial t} + u \frac{\partial C}{\partial z} = D \frac{\partial^2 C}{\partial z^2} - \frac{\alpha}{\varepsilon}(K C - C_s)$$

$$\frac{\partial C_s}{\partial C} = \alpha (K C - C_s) \tag{17}$$

where $C(t, z)$ and $C_s(t, z)$ express the solute concentrations in gas and stationary phases, respectively, and K is the distribution coefficient, ε is the volume ratio of gas and stationary phases and u is the linear velocity of the carrier gas flow. Distribution ratio k is related to K and ε by

$$k = K/\varepsilon \tag{18}$$

When a solute is introduced into the column inlet as a pulse which can be regarded as delta function, the initial and boundary conditions of eqn. 17 are written as

$$C(t, 0) = M_0\, \delta(t),\ \ C(0, z) = 0,\ \ C(t, \infty) = 0$$

$$C_s(t, 0) = 0,\ \ C_s(0, z) = 0 \tag{19}$$

where M_0 is the zero moment (expressing here the amount of solute). The solution of eqn. 17 in the Laplace domain is[1]

$$C(s,z) = M_0 \exp\left[\left\{\frac{u}{2D} - \sqrt{\left(\frac{u}{2D}\right)^2 + \frac{1}{D}\psi(s)}\right\}z\right] \tag{20}$$

where

$$\psi(s) = s + \frac{k\,\alpha\,s}{s+\alpha}$$

As the function $C(t, L)$ corresponds to $\mathrm{f}(t)$, which is the function describing a chromatogram, the Laplace transformed function $\tilde{\mathrm{f}}(s)$ can be written as

$$\tilde{\mathrm{f}}(s) = M_0 \exp\left[\left\{\frac{u}{2D} - \sqrt{\left(\frac{u}{2D}\right)^2 + \frac{1}{D}\psi(s)}\right\}L\right] \tag{21}$$

which leads to

$$\psi(s) + \frac{u}{L}\ln\{\tilde{\mathrm{f}}(s)/M_0\} - \frac{D}{L^2}[\ln\{\tilde{\mathrm{f}}(s)/M_0\}]^2 = 0 \tag{22}$$

By substituting eqn. 6 into eqn. 22 for the discrete quantities (s_j, h_j), eqn. 22 can be rewritten as

$$\psi(s_j) + \frac{u}{L}\mathrm{h}_j - \frac{D}{L^2}\mathrm{h}_j^2 = 0;\ j = 1,\ldots,l \tag{23}$$

This equation suggests that the parameters k, α, D and carrier gas velocity u can be determined by solving simultaneous equations if the observed values are substituted into four sets of the data (s_j, h_j).

It is remarkable that these four unknowns can be simultaneously determined from only one chromatogram without the aid of Van Deemter's equation. For more general linear chromatographic systems, the equation corresponding to eqn. 23 may become much more complicated, but it will not be difficult to solve it if Newton–Raphson's method is applied. When the system parameters must be calculated from given values of the statistical moments, one may use eqns. 8 and 9 to convert the moments into the sets of the data (s_j, h_j) and apply eqn. 23. As four data values of the statistical moments are available in this case, one can get four sets of data (s_j, h_j), which is enough to solve eqn. 23.

CONCLUSION

The numerical Laplace transform method is useful in obtaining much information from an experimental chromatogram; the statistical moments can be determined accurately, and the system parameters which predominate the column efficiency are calculated by a single experimental chromatogram. The relation between the quantities, the digitized quantities in time domain (t_i, f_i) and in Laplace domain (s_j, h_j), the statistical moments (μ_j) and the system parameters (θ_j), which appear in this paper,

$$\begin{tikzcd}
((t_i, f_i)) \arrow[rr, shift left, "1."] \arrow[dr, "3."] & & (\mu_j) \arrow[ll, shift left, "2."] \arrow[dl, shift right, "4."'] \\
& (s_j, h_j) \arrow[ur, shift right, "5."'] \arrow[d, shift left, "7."] & \\
& (\theta_j) \arrow[u, shift left, "6."] &
\end{tikzcd}$$

Fig. 4. Relation between various quantities. (t_i, f$_i$) = Digitized quantity in time domain; (s_j, h$_j$) = numerical Laplace transformed quantity; (μ_j) = statistical moments; (θ_j) = system parameters.

are illustrated schematically in Fig. 4, where route 1 from (t_i, f$_i$) to (μ_j) corresponds to eqns. 14, 15 and 16, and its inverse route corresponds to eqn. 13. The numerical Laplace transform is represented by route 3, which corresponds to eqn. 11. Routes 4 and 5 between (μ_j) and (s_j, h$_j$) can be related to eqn. 8, and the reversible relation between (s_j, h$_j$) and (θ_j) relates to eqn. 23. As the inverse of route 3, from (s_j, h$_j$) to (t_i, f$_i$), is of no practical use and impossible to follow in most cases, it was not considered in this work.

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