Simple Moment Analysis for a Kinetic Study of the Chromatographic Behavior of Spherical Particles and Silica Monoliths

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A simple procedure of moment analysis was proposed for a kinetic study of the rate processes in the columns packed with full-porous spherical particles and silica monoliths. Previous chromatographic data measured in reversed-phase HPLC systems using Mightysil and Chromolith columns were analyzed by a simple moment analysis. The surface of the packing materials is chemically modified with octadecyl alkyl ligands. A mixture of methanol and water (80/20, v/v) and alkylbenzene homologous series ($C_6H_5C_nH_{2n+1}$, $n = 0 - 7$) were used as the mobile-phase solvent and sample probes, respectively. More detailed information about the experimental conditions is provided in Supporting Information. The values of the intra-stationary phase diffusivity (D_e) and the surface diffusion coefficient (D_s), derived by the simple moment analysis, were almost the same as those by the conventional moment analysis. The simple moment analysis is effective for quantitative studies of mass transfer in chromatographic systems. The previous chromatographic data were also analyzed by assuming external porosity (ϵ_e) as typical values, *i.e.*, 0.40 for spherical particles and 0.70 for silica monoliths. The resulting values of D_e and D_s were of the same order of magnitude as those derived by using ϵ_e experimentally measured. Even if ϵ_e is assumed to be typical values, the simple moment analysis is effective for preliminary studies of the mass-transfer kinetics in the columns.

Keywords Moment analysis, first absolute moment, second central moment, rate theory, mass transfer kinetics, intra-stationary phase diffusivity, surface diffusion coefficient, spherical particles, silica monolith, column external porosity

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Introduction

High-performance liquid chromatography (HPLC) has been extensively used as one of the most powerful separation techniques. Various types of separation media have been used to achieve a faster separation with a high efficiency, such as silica monoliths and core-shell spherical particles.^{1,2} Compared with conventional full-porous spherical particles, the separation media have extremely different structural characteristics concerning the shapes and porosities. The chromatographic behavior of separation media has usually been analyzed from kinetic points of view by using ordinary rate equations,^{3,4} such as the van Deemter equation. However, it seems that the rate equations are not necessarily sufficient for a detailed and quantitative kinetic study of their chromatographic behavior because of the following three problems.

At first, the rate equations were not developed by considering the intrinsic structural characteristics of the separation media. Second, most of the rate equations neglect the existence of some mass-transfer processes in a column, *i.e.*, external mass transfer and surface diffusion,^{5,6} which have an important influence on the column efficiency. Finally, the rate equations contain some fitting parameters, of which the physical definition is not necessarily clear. It is impossible to quantitatively derive kinetic

information about chromatographic separations, such as diffusivities and mass transfer coefficients, by analyzing the flow rate dependence of HETP (H).

In spite of the drawbacks of the ordinary rate equations, they have been extensively used because their description is usually quite simple. For example, the van Deemter equation is written as follows.

$$H = A + \frac{B}{u} + Cu \quad (1)$$

where u is the flow velocity of the mobile phase. As is well known, A , B , and C are the coefficients of the A-, B-, and C-term, respectively. It is possible to divide the contributions of the A-, B-, and C-term to band broadening and to derive the values of A , B , and C . However, it is impossible to quantitatively determine the values of the diffusivities and mass transfer coefficients from those of the coefficients and to analyze chromatographic behavior in detail, even if the correlation between H and u is experimentally measured as accurately as possible.

Moment theory based on the general rate model of chromatography is one of the strategies for representing chromatographic behavior. It has been used for deducing information about the retention equilibrium and the mass-transfer and reaction kinetics in the column from the first absolute (μ_{1A}) and second central (μ_{2C}) moment of elution peaks.⁷⁻¹⁰ In the moment theory, chromatographic processes in

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$$H_{\text{total}} - D^*u_0^{\frac{2}{3}} = \frac{B^*}{u_0} + A^* + C^*u_0 \quad (7)$$

Equation (7) represents the correlation of $(H_{\text{total}} - D^*u_0^{2/3})$ with u_0 , and has the same formula with the van Deemter equation, *i.e.*, Eq. (1). However, Eqs. (5) – (7) are essentially different from Eq. (1) in terms of the following two points. At first, the contribution of external mass transfer (D^* -term) to H_{total} is considered in Eq. (7). Second, the definition and physical meanings of the parameter C^* in Eq. (7) are clearly explained. As shown in Eqs. (5) – (7), D_e can quantitatively be calculated from the value of C^* . The mechanism of mass transfer in the stationary phases can be analyzed in more detail by considering the contributions of pore diffusion and surface diffusion to D_e . These are obvious differences between the van Deemter equation and Eqs. (5) – (7).

Silica monolith (full-porous cylindrical fiber)

Similar to the case of full-porous spherical particles, simplification of the moment analysis procedure of the chromatographic behavior in a column packed with silica monoliths is explained in detail in Supporting Information. The original moment equations for silica monolithic columns, *i.e.*, Eqs. (2) and (3) ($\theta = 2$, $\omega = 8$), were developed by assuming as a first approximation that the unit structure of the continuous porous packing material in monolithic columns consisted of a cylindrical silica skeleton of the stationary phase including meso- and micropores, which were surrounded by a through macropore spaces filled with the mobile-phase solvent.^{10–12,14}

Similar to Eq. (5), Eq. (8) is derived in the same manner for silica monoliths.

$$H_{\text{total}} = \frac{2\varepsilon_e\gamma_1 D_m}{u_0} + 2\varepsilon_e\gamma_3 R_{ss} + \frac{2R_{ss}^2\lambda^2}{8(1-\varepsilon_e)D_e}u_0 + \frac{2R_{ss}\lambda^2}{2(1-\varepsilon_e)\phi}u_0^{\frac{1}{2}} + \frac{2v^2}{(1-\varepsilon_e)(1-\varepsilon_i)k_{rk}}u_0 \quad (8)$$

where R_{ss} is the radius of the cylindrical stationary phase silica skeleton and γ_3 is the geometrical coefficient. Equation (8) is simply written as follows.

$$H_{\text{total}} = \frac{B^*}{u_0} + A^* + C^*u_0 + D^*u_0^{\frac{1}{2}} + E^*u_0 \quad (9)$$

Equation (9) is rearranged as follows.

$$H_{\text{total}} - D^*u_0^{\frac{1}{2}} = \frac{B^*}{u_0} + A^* + C^*u_0 \quad (10)$$

The contribution of E^* -term to H_{total} is similarly assumed to be negligibly small in the case of RPLC systems.⁸ Equation (10) represents the correlation of $(H_{\text{total}} - D^*u_0^{1/2})$ with u_0 and has the same formula with the van Deemter equation, *i.e.*, Eq. (1).

Experimental

In a previous paper,²¹ the chromatographic behavior of two different types of separation media, *i.e.*, full-porous spherical particle and silica monolith, was studied from kinetic points of view. The flow-rate dependence of H_{total} was analyzed on the basis of the moment theory. In this study, the same experimental data were analyzed by applying a simple moment analysis

Fig. 1 Flow-rate dependence of H and the contributions of A^* -, B^* -, C^* -, and D^* -term to H . Open circles represent the original experimental data of (a) propylbenzene and (b) hexylbenzene, which were measured by using the Mightysil column. The data were analyzed by a simple moment analysis procedure.

procedure. The basic information about HPLC experiments is briefly described in Supporting Information. Further details about the experiments and data analysis can be found in a previous paper.²¹

Results and Discussion

Full-porous spherical particles (Mightysil)

Figures 1a and 1b illustrate the correlation between H and u_0 for propylbenzene (PBz) and hexylbenzene (HBz) in the RPLC system using the Mightysil column, respectively. The solid line is the correlation line of open circles, which represent experimental data. Figure 1 also illustrates the flow rate dependence of the contributions of the A^* -, B^* -, C^* -, and D^* -term to H_{total} . The chromatographic behavior of the Mightysil column was also analyzed by the conventional moment analysis. The profiles of the straight and curved lines obtained by the conventional moment analysis are superposed with those in Fig. 1 (not shown). Both the simple and conventional moment analyses provided the same results. At first, as explained from Eq. (S17) to Eq. (S20) in Supporting Information, the contribution of the D^* -term to H_{total} was calculated as Eq. (5) on the basis of the k_f value, which was estimated by using the Wilson-Geankoplis equation. Then, the flow-rate dependence of the right-hand side in Eq. (7) was analyzed to obtain the coefficients, A^* , B^* , and C^* . The values of the coefficients

Table 1 Resulting values derived by the simple moment analysis

Column	Solute	k	K_a	$D_e/\text{m}^2 \text{ s}^{-1}$	$D_p/\text{m}^2 \text{ s}^{-1}$	$D_s/\text{m}^2 \text{ s}^{-1}$
Mightysil	Propylbenzene	2.9 (2.9)	5.4 (5.4)	1.9×10^{-10} (1.9×10^{-10})	3.2×10^{-11} (3.2×10^{-11})	4.9×10^{-11} (5.2×10^{-11})
	Hexylbenzene	9.9 (9.9)	18 (18)	2.3×10^{-10} (2.3×10^{-10})	2.6×10^{-11} (2.6×10^{-11})	1.8×10^{-11} (1.9×10^{-11})
Chromolith	Propylbenzene	1.2 (1.2)	6.5 (6.5)	1.8×10^{-10} (1.7×10^{-10})	5.1×10^{-11} (5.1×10^{-11})	3.9×10^{-11} (3.6×10^{-11})
	Hexylbenzene	4.2 (4.2)	22 (22)	2.8×10^{-10} (2.7×10^{-10})	4.1×10^{-11} (4.1×10^{-11})	2.1×10^{-11} (2.0×10^{-11})

The values in parentheses are the retention and kinetic parameters derived by the conventional moment analysis.

were estimated by the least-squares method so that Eq. (7) represented the experimental curve profile between H_{total} and u_0 as well as possible. In addition, the value of C^* was analyzed to study the mass-transfer kinetics in the stationary-phase particles, as explained in the following.

As indicated in Eqs. (5) – (7), the values of D_e can be calculated from the slope of the straight lines for the C^* -term in Fig. 1. Table 1 lists the values of D_e determined by the simple moment analysis as 1.9×10^{-10} and $2.3 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$ for PBz and HBz, respectively. The same values of D_e were also obtained by the conventional moment analysis. The mechanism of mass transfer in the stationary phase can be analyzed in more detail by considering the contributions of pore diffusion and surface diffusion to D_e . As listed in Table 1, almost the same values of D_s were obtained by both the simple and conventional moment analyses. Table 1 also lists the values of pore diffusivity (D_p), which were estimated by Eqs. (S36) – (S38). The value of the tortuosity factor of internal pores (k_t^2) was calculated as 8.4 for the Mightysil column from the elution peak profiles of uracil.²¹ The comparison of D_e and D_p indicates that the contribution of surface diffusion to the molecular migration of PBz and HBz in Mightysil particles is *ca.* 5 – 8 times larger than that of pore diffusion. It is indicated that surface diffusion has a predominant role for intraparticle mass transfer. A determination procedure of D_p and D_s is explained in detail in Supporting Information.

The accuracy of the resulting values of diffusivities and mass transfer coefficients determined in this study is affected by the uncertainties in the estimate of some kinetic parameters, *i.e.*, D_m , k_f , and D_p , because literature correlations were used for estimating their values. At first, as indicated in Eq. (S37), the value of D_m was estimated by the Wilke–Chang equation.²² It is reported that the average error for estimating D_m by various correlations is slightly less than 10%.²³ The estimation error of D_m affects the accuracy of the results in this study because the values of k_f and D_p were calculated on the basis of the estimated value of D_m .

As explained by Eqs. (S17) – (S19) in Supporting Information, the k_f value was estimated by the Wilson–Geankoplis equation. The error of k_f made by the propagation of the uncertainty of D_m should be smaller than about 6% because D_m is estimated with an error of 10% or less and because k_f is proportional to $D_m^{2/3}$. Figures 1 and 2 indicate that the value of D^* -term increases with an increase in u_0 and that its contribution to H_{total} is about 30% at maximum in the high flow rate range. It seems that the influence of the uncertainty of k_f on the error of the moment analysis is about 2% at maximum.

As described by Eq. (S36) in Supporting Information, the uncertainty of D_p is proportional to that of D_m . However, the contribution of surface diffusion to intraparticle mass transfer

in Mightysil particles is *ca.* 5 – 8 times larger than that of pore diffusion. This means that surface diffusion has a predominant role in the intraparticle diffusion as much as *ca.* 83 – 89%. The influence of the error made in the estimation of D_p on the determination of D_s is calculated to be *ca.* 1.1 – 1.7%. Similarly, as described later, the contribution of surface diffusion to intrastationary phase diffusion is larger than that of pore diffusion by a factor of *ca.* 2.5 – 6.0 for Chromolith column. The error of D_s made by propagation of the uncertainty of D_m should be about 1.4 – 2.9% because about 71 – 86% of solute molecules migrate in silica-monolith by surface diffusion. The inaccuracy of D_p does not seriously affect the accuracy of D_s . In addition, the information about other parameters, *e.g.*, K_h and k_t^2 , are necessary when the values of k_f and D_p are estimated. The error in the estimations described above is responsible for the accuracy of the moment analysis. It seems that the overall error of the moment analysis is on the order of several percent.

As indicated in Eqs. (5) – (7), only ε_e is necessary as information about the porosities for the simple moment analysis when the E^* -term is neglected. Various methods have been proposed for measuring ε_e of HPLC columns packed with porous materials, *e.g.*, Donan exclusion method,²⁴ inverse size exclusion chromatography,²⁵ and total pore blocking.²⁶ Simple moment analysis of the chromatographic behavior of HPLC columns packed with spherical particles can accurately be conducted by using ε_e experimentally measured by the methods. On the other hand, it is reported that ε_e is typically around 0.40 – 0.41 in analytical columns packed with spherical particulate packing materials.⁹ Giddings also indicates that a fairly well-packed chromatographic column will typically have $\varepsilon_e = 0.4 \pm 0.03$.³ Similar values of ε_e were experimentally measured in the range from *ca.* 0.35 to 0.43.^{27–32} It would be convenient that the simple moment analysis of chromatographic behavior of HPLC columns packed with spherical particles can be conducted by using the empirical ε_e values.

Figure S1a illustrates the correlation between D_e and ε_e . The value of ε_e was hypothetically changed in the range from 0.35 to 0.45, which was wider than the previous observations.^{3,9} The D_e values were calculated at the different ε_e values by the simple moment analysis from the $H - u_0$ plots for PBz and HBz in Figs. 1a and 1b. When ε_e is assumed to be 0.40, the values of D_e are 1.6% and 2.6% larger than those of D_e at $\varepsilon_e = 0.39$ for PBz and HBz, respectively. Although the ε_e value experimentally measured was 0.39 in this case, the D_e values were derived with an error of a few percent when ε_e was assumed to be 0.40. Figure S1a indicates that the relative error of D_e at ε_e between 0.35 and 0.45 against D_e at $\varepsilon_e = 0.40$ is 7.1 – 9.2% and 12 – 16% for PBz and HBz, respectively. It would be impossible to describe the correlation between D_e and ε_e by using a simple equation. As indicated in Eq. (S14), all of the contributions of

H_{ax}^* , H_d^* , H_f^* , and H_{rk}^* to H_{total} depend on the value of ϵ_e because they contain ϵ_e . In addition, as described in Eqs. (S8) and (S12), ϵ_e is also included in both the functions for λ and ν . As explained in Eqs. (S21) and (S22), the value of D_e was calculated from that of C^* . Although the dependence of D_e on ϵ_e is relatively complicated as explained above, the moment analysis is useful to clarify the correlation between D_e and ϵ_e as illustrated in Figs. S1a and S2a.

Figure S1b similarly illustrates the correlation between D_s and ϵ_e . The value of D_s was calculated by Eqs. (S34) and (S36) – (S38) from that of D_e , which was obtained by a simple moment analysis at different ϵ_e values. When ϵ_e is assumed to be 0.40, the values of D_s are 4.1% and 5.0% larger than those of D_s at $\epsilon_e = 0.39$ (experimentally measured) for PBz and HBz, respectively. It seems that the D_s values were derived with an error of several percent when ϵ_e was assumed to be 0.40. Figure S1b indicates that the relative error of D_s at ϵ_e between 0.35 and 0.45 against D_s at $\epsilon_e = 0.40$ is *ca.* 17 – 23% and 21 – 31% for PBz and HBz, respectively. It is concluded from the results described above that preliminary information about the mass transfer in the stationary phase particles can be obtained with a moderate accuracy by assuming $\epsilon_e = 0.40$. When accurate results of moment analysis are required, it is required to experimentally measure the value of ϵ_e .

Full-porous cylindrical fiber (Chromolith)

Similar to Fig. 1, Fig. 2 illustrates the correlation between H and u_0 for PBz and HBz in the RPLC system using the Chromolith column. Figure 2 also illustrates experimental data (open circles) and the contributions of the A^{*}-, B^{*}-, C^{*}-, and D^{*}-term to H_{total} , which was analyzed by a simple moment analysis. The profiles of the straight and curved lines in Fig. 2 are superposed with those obtained by the conventional moment analysis (not shown). Both the simple and conventional moment analyses provided the same results for the chromatographic behavior of the Chromolith column.

As indicated in Eqs. (8) – (10), the values of D_e can be calculated from the slope of the straight lines for the C^{*}-term in Fig. 2. As listed in Table 1, the value of D_e was calculated as 1.8×10^{-10} and $2.8 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$ for PBz and HBz, respectively, by the simple moment analysis. On the other hand, D_e was respectively calculated as 1.7×10^{-10} and $2.7 \times 10^{-10} \text{ m}^2 \text{ s}^{-1}$ for PBz and HBz by the conventional moment analysis. Almost the same values of D_e were obtained by both the simple and conventional moment analyses.

Similar to the Mightysil column, it was tried to quantitatively analyze the mechanism of mass transfer in the stationary phase of the Chromolith column. The value of D_s was calculated in the same manner. The hindrance parameter of internal pores (K_h) was estimated by Eq. (S38) around 0.80 for the three solutes in the RPLC systems using the Chromolith column. It was reported for the Chromolith column that the value of k_t^2 ranged from 5.5 to 6.7.³³ In this study, an average value, *i.e.*, 6.1, was used as k_t^2 , which was a typical value for porous silica gel.⁸ As listed in Table 1, almost the same values of D_s were obtained by both the simple and conventional moment analyses. Table 1 also lists the values of D_p , which were estimated by Eqs. (S36) – (S38). The values of D_e are several times larger than those of D_p , suggesting that surface diffusion plays an important role for the molecular migration in the stationary phase of the Chromolith column. The contribution of surface diffusion to intra-stationary phase diffusion of PBz and HBz is larger than that of pore diffusion by a factor of *ca.* 2.5 – 6.0.

As indicated in Eqs. (8) – (10), only ϵ_e is necessary for the simple moment analysis when the E^{*}-term is neglected. It has

Fig. 2 Flow-rate dependence of H and the contributions of A^{*}-, B^{*}-, C^{*}-, and D^{*}-term to H . The open circles represent the original experimental data of (a) propylbenzene and (b) hexylbenzene, which were measured by using a Chromolith column. The data were analyzed by a simple moment analysis procedure.

been reported that ϵ_e is usually ranging from 0.65 to 0.75 in Chromolith columns.^{27,29,34,35} The values of ϵ_e were experimentally measured in the same range.^{31,35,36} It has been tried to analyze the chromatographic behavior of the Chromolith column by using the empirical ϵ_e values. Figure S2a illustrates the correlation between D_e and ϵ_e . The value of ϵ_e was hypothetically changed in the range of 0.65 to 0.75. The D_e values were calculated at the different ϵ_e values by the simple moment analysis from the $H - u_0$ plots for PBz and HBz in Figs. 2a and 2b. When ϵ_e is assumed to be 0.70, the values of D_e are 2.2% and 4.3% larger than those of D_e at $\epsilon_e = 0.69$ for PBz and HBz, respectively. Although the experimental value of ϵ_e was 0.69, the D_e values were derived with an error of several percent when ϵ_e was assumed to be 0.70. Figure S2a indicates that the relative error of D_e at ϵ_e between 0.65 and 0.75 against D_e at $\epsilon_e = 0.70$ is 9.7 – 15% and 17 – 29% for PBz and HBz, respectively.

Figure S2b illustrates the correlation between D_s and ϵ_e . The value of D_s was calculated from that of D_e , which was obtained by the simple moment analysis at the different ϵ_e values. When ϵ_e is assumed to be 0.70, the values of D_s are 1.3% and 2.4% larger than those of D_s at $\epsilon_e = 0.69$ (experimentally measured) for PBz and HBz, respectively. It seems that the D_s values were derived with an error of a few percent when ϵ_e was assumed to be 0.70. Figure S2b indicates that the relative error of D_s at ϵ_e between 0.65 and 0.75 against D_s at $\epsilon_e = 0.70$ is *ca.* 5.8 – 7.0% and 10 – 14% for PBz and HBz, respectively. It is only required to measure ϵ_e experimentally when more accurate results of

moment analysis are necessary.

Conclusions

It was tried to simplify the moment analysis procedure for a kinetic study on chromatographic behavior of spherical particles and silica monoliths. The simple procedure for a moment analysis of μ_{2C} was proposed without using K_a and ϵ_i . However, similar to the conventional moment analysis, the contributions of axial molecular diffusion, Eddy diffusion, external mass transfer, intra-stationary phase diffusion, and reaction kinetics on the stationary phase surface to the variance of an elution peak could be quantitatively analyzed. Some chromatographic data measured by using the Mightysil column (full-porous spherical particles) and the Chromolith column (silica monoliths) were analyzed by applying the simple moment analysis procedure. Both the simple and conventional moment analysis procedures provided almost the same values of D_e and D_s . The simple moment analysis is effective for quantitatively studying the mechanism of mass transfer in the stationary phases in detail with considering the contributions of pore diffusion and surface diffusion to D_e . It was also tried to analyze the same chromatographic data by assuming $\epsilon_e = 0.40$ for spherical particles and 0.70 for silica monoliths. Although the values of D_e and D_s change depending on the ϵ_e values, they were of the same order of magnitude with each other. Even if ϵ_e is hypothetically assumed to be typical values, the simple moment analysis is effective for a preliminary study of the mass-transfer kinetics in the columns. When more accurate results of moment analysis are required, the value of ϵ_e should experimentally be measured. In this study, the simple procedure of moment analysis was proposed for the analysis of chromatographic data measured by using HPLC columns packed with spherical particles and cylindrical rod fibers, such as silica monoliths. There is no necessary condition for a simple moment analysis, e.g., the types of solutes and stationary phases and the size and porosity of the packing materials, because it was theoretically developed on the basis of the general rate model of chromatography.

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Supporting Information

The simplification of moment analysis procedure is explained in detail. Supporting Information provides a detailed explanation about chromatographic experimental conditions and kinetic analysis of intraparticle mass transfer. Experimental results of the correlations between D_e and ϵ_e and that between D_s and ϵ_e are illustrated. This material is available free of charge on the Web at <http://www.jsac.or.jp/analsci/>.

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