Separation Science and Technology
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713708471

Contributions to the Stochastic Theory of Chromatographic Kinetics

George H. Weiss[a][b]
[a] IMPERIAL COLLEGE LONDON, ENGLAND [b] Physical Sciences Laboratory, Division of Computer Research, Department of Health, Education, and Welfare, National Institutes of Health, Bethesda, Maryland

To cite this Article Weiss, George H.(1970) 'Contributions to the Stochastic Theory of Chromatographic Kinetics', Separation Science and Technology, 5: 1, 51 — 62
To link to this Article: DOI: 10.1080/00372367008057946
URL: http://dx.doi.org/10.1080/00372367008057946

SEPARATION SCIENCE, 5(1), pp. 51–62, February, 1970

Contributions to the Stochastic Theory of Chromatographic Kinetics

GEORGE H. WEISS*
IMPERIAL COLLEGE
LONDON, S.W.7, ENGLAND

Summary

The stochastic theory of chromatographic kinetics is extended in two directions: (a) To include diffusion effects, and (b) to treat the n-site adsorption problem. In the first case we show that the solution to a first passage problem yields the moments of residence time in the mobile phase in a rather simple form. For the second problem we show that the central limit theorem allows us to deduce rather general results about the distribution of residence time.

1. INTRODUCTION

The study of the stochastic theory of chromatographic kinetics was initiated by Giddings and Eyring (*1*), and important contributions to that theory were subsequently made by Giddings (*2–4*) and by McQuarrie (*5*). These authors, among other questions discussed, suggested two problems which have not yet been resolved in a practical way. The first of these is the effect of nonzero diffusion in the mobile phase, and the second relates to the effects of multisite adsorption on the kinetics. McQuarrie and Beynon (*6*) et al. in their treatment of diffusion effects both assume that the time spent by a molecule in the mobile phase is a random variable with a Gaussian distribution. Although this does appear to be a reasonable approximation, it is possible to calculate the residence time distribution in a more funda-

---

* Permanent address: Physical Sciences Laboratory, Division of Computer Research, National Institutes of Health, Department of Health, Education, and Welfare, Bethesda, Maryland 20014.

mental way by analyzing the first passage time distribution for a molecule in a column of finite size. This program will be carried out in the present paper. The second problem, that of multisite adsorption, can be solved formally for a finite number of types of sites, but the solutions do not readily lend themselves to use. Furthermore, the problem has only been discussed for a first-order kinetic model of interchange between the mobile and stationary phases. Since such transitions depend in a complicated way on molecular conformation and the geometry of the stationary matrix, it is open to question whether such a model is accurate. In Sect. 3 we will discuss more general models. We will show that when there are a large number of mobile phase-stationary phase transitions, limit laws apply which depend only on the moments of the residence time in either phase, and not on the detailed expressions for the distributions. Hence some of the results derived by earlier authors for the kinetics are of more generality than they assumed.

2. DIFFUSION EFFECTS

Let us consider first the effects of a nonzero diffusion constant D on the statistics of residence time in the mobile phase. Let the chromatographic column be of length L with the input ordinate $x = L$ and the elution taking place at $x = 0$. We will calculate the effects of diffusion in the mobile phase by assuming the absence of a stationary phase. Let the amount of material in the layer $(x, x + dx)$ at time t be $c(x, t)\,dx$, and let V be the mean drift velocity in the mobile phase. Then $c(x, t)$ satisfies

$$\frac{\partial c}{\partial t} = D\frac{\partial^2 c}{\partial x^2} + V\frac{\partial c}{\partial x} \tag{2.1}$$

subject to an initial condition $c(x, 0) = c_0\delta(x - L)$, where $\delta(x)$ is the Dirac delta function. This equation is to be solved subject to boundary conditions which say that there is no flow out of the column at $x = L$, and that molecules which reach $x = 0$ are withdrawn. These conditions respectively imply that

$$\begin{aligned} D\frac{\partial c}{\partial x} + Vc &= 0 \qquad x = L \\ c(0, t) &= 0 \end{aligned} \tag{2.2}$$

What is required is not $c(x, t)$ itself, but rather the probability that a molecule introduced at $t = 0$ remains in the column for a time t or longer. This probability is just

$$G(t) = \frac{1}{c_0} \int_0^L c(x, t)\, dx \tag{2.3}$$

If $g(t)\, dt$ is the probability that a given residence time is between t and $t + dt$ then $g(t)\, dt = G(t) - G(t + dt)$ or

$$g(t) = -\frac{1}{c_0} \frac{d}{dt} \int_0^L c(x, t)\, dx \tag{2.4}$$

A solution to Eq. (2.1) is most easily obtained by introducing a new dependent variable $\rho(x, t)$ by

$$\frac{c(x, t)}{c_0} = \rho(x, t) \exp\left(-\frac{Vx}{2D} - \frac{V^2 t}{4D}\right) \tag{2.5}$$

which transforms Eq. (2.1) to

$$\frac{\partial \rho}{\partial t} = D \frac{\partial^2 \rho}{\partial x^2} \tag{2.6}$$

with boundary conditions

$$D \frac{\partial \rho}{\partial x} + \frac{V}{2} \rho = 0, \qquad x = L \tag{2.7}$$
$$\rho(0, t) = 0$$

This set of equations is equivalent to a heat conduction problem, and the solution can be taken immediately from standard references (7). The solution for $c(x, t)$ can be expressed as

$$\frac{c(x, t)}{c_0} = \exp\left[\frac{V}{2D}(L - x)\right] \sum_{n=1}^{\infty} \frac{\sin \omega_n L \sin \omega_n x}{N_n} \exp\left[-\left(\frac{V^2}{4D} + D\omega_n^2\right) t\right] \tag{2.8}$$

where the ω_n are the roots of

$$\frac{\tan \omega_n L}{\omega_n L} = -\frac{2D}{VL} \tag{2.9}$$

and the N_n are normalizing factors given by

$$N_n = \frac{L}{2}\left(1 - \frac{\sin 2\omega_n L}{2\omega_n L}\right) \tag{2.10}$$

A short table of roots of Eq. (2.9) is given in Reference *7*. The probability density for residence time, $g(t)$, can be obtained from Eqs. (2.4) and (2.8), and is

$$g(t) = D \exp\left(\frac{VL}{2D}\right) \sum_{n=1}^{\infty} \frac{\omega_n \sin \omega_n L}{N_n} \exp\left[-\left(\frac{V^2}{4D} + \omega_n{}^2 D\right) t\right] \quad (2.11)$$

Although the complete probability density $g(t)$ requires numerical evaluation, it is possible to obtain expressions for the moments of residence time rather easily by recognizing that the problem we have just solved is a first passage time problem (*8*). In particular for the problem posed in Eqs. (2.1) and (2.2), one can show that the moments, $\mu_n(x)$, defined by

$$\mu_n(x) = \int_0^\infty t^n g(t)\, dt \quad (2.12)$$

satisfy a simple ordinary differential equation. In the above equation the variable x (not necessarily $= L$) is assumed to be the point of injection at $t = 0$. We are interested in $\mu_n(L)$ for present purposes but require the general $\mu_n(x)$ to calculate higher moments. The $\mu_n(x)$ can be shown (*8*) to satisfy the equations

$$D \frac{d^2\mu_n}{dx^2} - V \frac{d\mu_n}{dx} = -n\mu_{n-1}, \qquad n \geq 1 \quad (2.13)$$

where $\mu_0 = 1$ by definition. These equations are to be solved subject to the boundary conditions

$$\mu_n(0) = 0, \qquad \left.\frac{d\mu_n}{dx}\right|_{x=L} = 0 \quad (2.14)$$

The first moment $\mu_1(L)$ and the variance $\sigma^2(L) = \mu_2(L) - \mu_1^2(L)$ are found to be

$$\begin{aligned} \mu_1(L) &= \frac{L}{V}\left[1 - \frac{D}{VL}\left(1 - e^{-VL/D}\right)\right] \\ \sigma^2(L) &= \frac{D^2}{V^4}\left[\frac{2VL}{D} - 5 + 4\left(1 + \frac{VL}{D}\right)e^{-VL/D} + e^{-2VL/D}\right] \end{aligned} \quad (2.15)$$

Thus, in the present model diffusion always serves to decrease the average residence time, although the effect will usually be small, as measured by the dimensionless parameter $D/(VL)$. In this approximation the variance of residence time can be approximated by

$$\sigma^2(L) \sim 2DL/V^3 \tag{2.16}$$

so that $\sigma^2(L)$ is proportional to L as in the theory of Beynon (*6*) et al. Higher moments can be generated by the relations

$$\mu_n(L) = \frac{n}{V}\int_0^L \mu_{n-1}(x)(1 - e^{-Vx/D})\,dx \tag{2.17}$$

where $\mu_n(x)$ is

$$\mu_n(x) = \frac{1}{D}\left\{S_{n-1}(L) + \frac{D}{V}e^{-VL/D}R_{n-1}(L)\right\}(e^{Vx/D} - 1) - \frac{e^{Vx/D}}{D}S_{n-1}(x)$$

$$R_{n-1}(x) = n\int_0^x \mu_{n-1}(u)\,du, \qquad S_{n-1}(x) = \int_0^x R_{n-1}(u)e^{-Vu/D}\,du \tag{2.18}$$

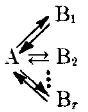
It has been shown that for L sufficiently large, the first passage density tends to a Gaussian form (*9*) and this is a convenient approximation for the present analysis, although the use of Eq. (2.11) enables one to calculate the density more exactly. The width of the peak is measured by $\sigma(L)/\mu_1(L)$ which is approximately

$$\frac{\sigma(L)}{\mu_1(L)} = \sqrt{\frac{2D}{VL}} \tag{2.19}$$

in the limit of small $D/(VL)$.

3. MULTISITE THEORY

Considerable effort has been devoted to obtaining exact solutions for multisite adsorption models, but the resulting solutions have often proved difficult to evaluate except numerically. Giddings and Eyring (*1*) and Giddings (*2*) discussed the two site model when both adsorption and resorption occur according to first-order kinetics. McQuarrie (*5*) has analyzed the n site problem, obtaining an exact solution in terms of a contour integral. He was able to extract an asymptotic expansion (for $t \to \infty$) for the two site case. It does not seem to have been noticed before that fairly simple results can be obtained subject to the assumption that the number of adsorptions is large during the course of a column traversal. If this assumption is permitted, one can also consider more general residence time distributions than arise from the commonly analyzed case represented by



$$\begin{array}{l} \nearrow\!\!\!\swarrow\ B_1 \\ A \rightleftarrows B_2 \\ \searrow\!\!\!\nwarrow\ \vdots \\ \qquad B_r \end{array} \tag{3.1}$$

where A represents the mobile phase and B_r represents adsorption by a site of type r. Since adsorption is a complex phenomenon resulting from the interaction between a complicated geometric structure and an equally complicated molecular conformation, it would be surprising if a description by first-order kinetics is correct. As we will show later, the probability density for traversal time is insensitive to detailed features of the residence time distributions provided that the number of adsorption events is large. We will derive limiting results on this assumption, but our methods do not suffice to obtain information about cases in which trapping is infrequent, a case of potential interest in the discussion of tailing.

The idea behind the following calculation is to assume that all sites have statistically identical parameters, rather than being identical in every respect. Thus, we define a generalized first-order reaction which can be depicted in the usual way as

$$\mathrm{A} \underset{k'}{\overset{k}{\rightleftarrows}} \mathrm{B} \tag{3.2}$$

but now we assume that the rate constants are random variables rather than being fixed. This model, as will shortly be shown, contains as a special case the situation shown in Eq. (3.1), but allows the study of a much wider class of problems. To see what Eq. (3.2) implies, let us suppose that a particle enters the stationary phase at some time. Then the probability that it remains in the stationary phase for a time between t and $t + dt$ is $k' \exp(-k't)\, dt$. Let $h_s(k')\, dk'$ be the probability that the reaction rate at a given site is between k' and $k' + dk'$. Then the probability that a molecule remains trapped at an arbitrary site for a time between t and $t + dt$ is $p_s(t)\, dt$, where

$$p_s(t) = \int_0^\infty k h_s(k) e^{-kt}\, dk \tag{3.3}$$

As a special case, if there are n types of sites, the proportion of type r being f_r, then

$$h_s(k) = \sum_r f_r \delta(k - k_r) \tag{3.4}$$

leads to results equivalent to those generated by the kinetic scheme of Eq. (3.1). If $n = 1$ we are led back to the single-site situation. Similar remarks apply to the forward reaction rate k, and a function $h_m(k)\, dk$ will denote the probability that a trapping rate at a specific site is between k and $k + dk$.

The total time to traverse the column will be denoted by T and can be written

$$T = \tau + t_1 + t_2 + \cdots + t_{n(\tau)} \tag{3.5}$$

where τ is the time in the mobile phase, t_j is the time spent in the stationary phase on the j'th occasion, and $n(\tau)$ is the number of adsorptions during a time τ. It is possible to derive expressions for the moments of T starting from this general expression. Furthermore, one can show that under certain circumstances the limiting distribution of T is Gaussian, so that only the first two moments of T are required in those instances. In order to calculate the moments of T we need to either find or define moments of the auxiliary random variables τ, t_j, and $n(\tau)$. We first note that the moments of τ are just the $\mu_r(L)$, whose calculation was discussed in Sect. 2. The r'th moment of sojourn time will be denoted by $\overline{t^r}$ and is defined by

$$\overline{t^r} = \int_0^\infty t^r p_s(t)\,dt = r!\int_0^\infty \frac{h_s(k)}{k^r}\,dk \tag{3.6}$$

where the second integral representation is a consequence of Eq. (3.3). In the Giddings-Eyring model where a single rate constant k' characterizes sojourn time

$$\overline{t^r} = \frac{r!}{(k')^r} \tag{3.7}$$

In the present more general model we need not be this specific and can allow any proper sequence of moments. Another sequence of moments needed is that corresponding to the number of trapping events in time τ. If we let the probability that there are n trapping events in time τ be $\omega_n(\tau)$, and denote the r'th moment of the number of trapping events by $\overline{n^r(\tau)}$, then by definition

$$\overline{n^r(\tau)} = \sum_{n=1}^{\infty} n^r \omega_n(\tau) \tag{3.8}$$

In the Giddings-Eyring first-order kinetics model the function $\omega_n(\tau)$ is

$$\omega_n(\tau) = \frac{(kt)^n}{n!}\, e^{-k\tau} \tag{3.9}$$

so that the first two moments are

$$\begin{aligned} \bar{n}(\tau) &= k\tau, \qquad \overline{n^2(\tau)} = k\tau + (k\tau)^2 \\ \sigma_n^2(\tau) &= \overline{n^2(\tau)} - [\bar{n}(\tau)]^2 = k\tau \end{aligned} \tag{3.10}$$

Since τ is itself random, we shall also need the moments averaged over τ. These will be denoted by ν_r and are defined by

$$\nu_r = \int_0^\infty \overline{n^r(\tau)}g(\tau)\,d\tau \tag{3.11}$$

In the Giddings-Eyring model $\tau = L/V$ exactly so that

$$\nu_1 = \frac{kL}{V}, \qquad \sigma_\nu^2 = \nu_2 - \nu_1^2 = \nu_1 \tag{3.12}$$

Again, the present calculations allow for more general forms for $\overline{n^r}(\tau)$ and therefore for ν_r.

We are now in a position to evaluate the moments of T. For simplicity, this will be done in two steps. In the first τ will be held fixed, and we will calculate value of the r'th moment of T which contain τ. These will be denoted by $\overline{T^r}(\tau)$. In the final step we will average over τ to obtain the moments $\overline{T^r}$. These moments are obviously related to $\overline{T^r}(\tau)$ by

$$\overline{T^r} = \int_0^\infty \overline{T^r(\tau)}g(\tau)\,d\tau \tag{3.13}$$

For the first moment we find that

$$\bar{T}(\tau) = \tau + n(\tau)\bar{t} \tag{3.14}$$

since the expected value of $t_1 + t_2 + \dots + t_{n(\tau)}$ is $n(\tau)$ multiplied by the expected value or any t_j of $n(\tau)\bar{t}$. The averaged value $\bar{T}$ is now found to be

$$\bar{T} = \mu_1(L) + \nu_1\bar{t} \tag{3.15}$$

For the Giddings-Eyring model, $\mu_1(L) = L/V$, and

$$\bar{T}_{G-E} = \frac{L}{V}\left(1 + \frac{k}{k'}\right) \tag{3.16}$$

Calculation of the second moment, or variance, is slightly more difficult. By squaring Eq. (3.5) and performing the averaging process with fixed τ, we find that

$$\overline{T^2}(\tau) = \tau^2 + 2\tau n(\tau)\bar{t} + n(\tau)\overline{t^2} + n(\tau)[n(\tau) - 1]\bar{t}^2 \tag{3.17}$$

The last two terms in this expression are the average of $(t_1 + t_2 + \dots + t_{n(\tau)})^2$; the first of these terms representing the average of terms of the form t_j^2, and the last representing the average of terms with different indices $t_i t_j$. If we now perform the average over τ we find that

$$\overline{T^2} = \mu_2(L) + \nu_1\overline{t^2} + (\nu_2 - \nu_1)\bar{t}^2 + 2\bar{t}\,\overline{\tau n(\tau)} \tag{3.18}$$

in which we see that a new type of average, $\overline{\tau n(\tau)}$, is required. This difficulty does not arise in the analysis of the Giddings-Eyring model, since in that case

$$\overline{\tau n(\tau)} = \tau\overline{n(\tau)} \tag{3.19}$$

and the τ can be separated from the product. In the present case the separation cannot be made since τ and $n(\tau)$ are obviously correlated. The longer the traversal time τ, the larger $n(\tau)$ tends to be. In order to calculate the required average we will need some results from renewal theory that will enable us to calculate a good approximation, rather than an exact expression, for $\overline{\tau n(\tau)}$.

Using the definition of $\omega_n(\tau)$ introduced above, we can write for the desired average

$$\overline{\tau n(\tau)} = \int_0^\infty \tau g(\tau) \sum_n n\omega_n(\tau)\,d\tau = \int_0^\infty \bar{n}(\tau)\tau g(\tau)\,d\tau \tag{3.20}$$

This expression is still an exact one. We will now make use of two approximations which are valid in almost all situations of interest. The first is that the effects of diffusion are small so that the peak broadening measured in time units is small in comparison with the traversal time. Specifically we require that $\sigma(L)/\mu_1(L) \ll 1$ or, from Eq. (2.15), that

$$\frac{2D}{VL} \sim \frac{2DT}{L^2} \ll 1 \tag{3.21}$$

where T is approximately equal to the traversal time. The second approximation is that the expected number of sorptions in the course of traversing the column is large, i.e., $\nu_1 \gg 1$. When these approximations hold, $\bar{n}(\tau)$ will also be large, and we can use the asymptotic form for $\bar{n}(\tau)$ to get an approximate expression for the integral in Eq. (3.20). It can be shown by the use of techniques from renewal theory (*10*) that

$$\overline{n(\tau)} \sim \frac{\nu_1\tau}{\mu_1(L)} + \epsilon(\tau) \tag{3.22}$$

where $\epsilon(\tau)$ is negligible in comparison to the first term for values of τ during which $g(\tau)$ allows substantial contributions. Hence the term $\overline{\tau n(\tau)}$ can be approximated by

$$\overline{\tau n(\tau)} \sim \nu_1 \frac{\mu_2(L)}{\mu_1(L)} \tag{3.23}$$

This result is exact for the Gidding-Eyring model. It is possible to derive an exact expression for $\overline{\tau n(\tau)}$ in terms of the parameters appearing in the exact solution in Eq. (2.8), but the result given in Eq. (3.23) will lead to negligible error for parameters of chemical interest.

With the result just given we can finally write down the expression for $\overline{T^2}$ as

$$\overline{T^2} = \mu_2(L) + \nu_1\overline{t^2} + (\nu_2 - \nu_1)\bar{t}^2 + 2\nu_1\bar{t}\,\frac{\mu_2(L)}{\mu_1(L)} \tag{3.24}$$

It is of interest also to give an expression for the variance $\sigma_T^2 = \overline{T^2} - \overline{T}^2$ by combining Eqs. (3.15) and (3.24). In this way we find that

$$\sigma_T^2 = \sigma_\nu^2\bar{t}^2 + \nu_1\sigma_t^2 + \left(1 + \frac{2\nu_1\bar{t}}{\mu_1(L)}\right)\sigma^2(L) \tag{3.25}$$

where $\sigma^2(L)$ is the variance given in Eq. (2.15), and σ_ν^2 and σ_t^2 are just

$$\sigma_\nu^2 = \nu_2 - \nu_1^2, \qquad \sigma_t^2 = \overline{t^2} - \bar{t}^2 \tag{3.26}$$

We see from Eq. (3.25) that there are three types of contributions to the variance of traversal time. The first is σ_ν^2, the variance due to fluctuations in the number of adsorptions, the second is σ_t^2, the variance due to fluctuations in adsorption times for single events, and the third is $\sigma^2(L)$, the variance due to diffusion effects. In the n-site analogue of the Giddings-Eyring model the probability densities for rate constants are

$$\begin{aligned} h_m(k) &= \sum_{r=1}^{n} f_r\delta(k - k_r) \\ h_s(k') &= \sum_{r=1}^{n} f_r\delta(k' - k_r') \end{aligned} \tag{3.27}$$

where k_r and k'_r are the forward and backward rate constants to a site of type r, and f_r is the fraction of r sites. When diffusion effects are absent (in any case they will be small), the averages that are required for the evaluation of T and σ_T^2 are

$$\begin{aligned} \overline{t^j} &= j!\Sigma f_r/(k'_r)^j \\ \nu_1 &= \bar{k}L/V, \qquad \sigma_\nu^2 = \bar{k}L/V \end{aligned} \tag{3.28}$$

where $\bar{k}$ is defined to be

$$\bar{k} = \sum_{j=1}^{n} f_j k_j \tag{3.29}$$

For this model we can write T and σ_T^2 explicitly as

$$\bar{T} = \frac{L}{V}\left(1 + \bar{k}\sum_r \frac{f_r}{k'_r}\right) \tag{3.30}$$

$$\sigma_T^2 = \frac{2\bar{k}L}{V}\sum_r \frac{f_r}{(k'_r)^2} \tag{3.31}$$

It is clear that higher moments of the traversal time can be obtained by the same methods that we have used, albeit with considerably more algebra.

Although we have been able to calculate the moments of the transit time distribution, it appears to be much more difficult to calculate the distribution itself. We can, however, obtain an approximate distribution if τ is assumed to have a Gaussian distribution. Let the traversal time T be decomposed as

$$T = \tau + T_1 \tag{3.32}$$

where

$$T_1 = t_1 + t_2 + \cdots + t_{n(\tau)} \tag{3.33}$$

As pointed out above, the Gaussian distribution of T_1 follows from the central limit theorem. Thus T can be written as the sum of two dependent Gaussian random variables, hence T itself has a Gaussian distribution. Our calculations show that the mean and variance of T are given in Eqs. (3.15) and (3.25).

REFERENCES

1. J. C. Giddings and H. Eyring, *J. Amer. Chem. Soc.*, **59**, 416 (1956).

2. J. C. Giddings, *J. Chem. Phys.*, **26**, 169 (1957).

3. J. C. Giddings, *J. Chem. Phys.*, **31**, 1462 (1959).
4. J. C. Giddings, *J. Chromatogr.*, **3**, 443 (1960).
5. D. A. McQuarrie, *J. Chem. Phys.*, **38**, 437 (1963).
6. J. H. Beynon, S. Clough, D. A. Crooks, and G. R. Lester, *Trans. Faraday Soc.*, **54**, 705 (1958).
7. H. S. Carslaw and J. C. Jaeger, *Conduction of Heat in Solids*, Clarendon Press, Oxford, 1959.
8. G. H. Weiss, in *Advan. Chem. Phys.*, Vol. 13, Wiley, New York, 1967, p. 1.
9. M. K. Tweedie, *Ann. Math. Stat.*, **28**, 362 (1957).
10. D. R. Cox, *Renewal Theory*, Wiley, New York, 1963.

Received by editor October 2, 1969