A STOCHASTIC THEORY OF CHROMATOGRAPHY

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The current theories of chromatography may be divided in two main groups. The first group embraces theories which could be called macroscopic, since no explicit assumption is made about microscopic characteristics of the chromatographic process. Such are the theories of mass transport (continuous and discontinuous models), which are based on the theoretical plate concept[1,2,3].

In the second group of theories the fundamental concepts are the microscopic characteristics of the chromatographic process and its statistical nature[4,5,6].

The use of these two different approaches have lead to very different results, a fact that does not emphasize the intimate relations which must exist between the microscopic and the macroscopic description of the same phenomenon.

In this paper a microscopic theory is presented, in which the

stochastic variable is the displacement of the particles along the chromatographic system. This treatment allows an easy derivation of the main results of the chromatographic theories based on the theoretical plate concept.

I. CONCEPTS AND DEFINITIONS

The chromatographic system is constituted by a stationary phase uniformly distributed in the whole volume of an experimental arrangement, and a fluid phase which flows through it. Sites which can adsorb particles (molecules or ions) from the mobile fluid phase are distributed in the stationary phase (paper, resins, clays, alumine, etc.).

We shall use the term adsorbent for the stationary phase, solvent for the moving fluid phase and solute for the substance which is dissolved in the fluid phase and can be adsorbed by the adsorbent. Such designations are clearly not adequate for all types of chromatography but they can be easily adapted to particular systems.

We shall assume a spatially uniform distribution of sites of the adsorbent, which is a good approximation for adsorbents with a large number of sites per unit volume.

In their passage through the adsorbent the particles of the solute are alternatively and successively adsorbed and desorbed. When desorbed the particles are carried along in their motion by the solvent which flows continuously. When adsorbed the particles remain essentially motionless on the adsorbent, being thus retarded with respect to the front of the solvent.

The motion of the particles in the solvent posesses a random characteristic arising from its collisions with the molecules of the

surrounding fluid. The interaction of the molecules of the solvent
with the particles of the solute imposes on them a movement with
brownian character. The trajectory of a particle in the solvent will
be that of a typical random-walk motion which is superimposed upon
the uniform drift by the solvent. If T is the temperature of the sys-
tem, the mean energy associated with the chaotic motion of the par-
ticles is 3/2 kT per particle.

The random characteristics of the adsorption-desorption process
are the following. At the instant of desorption the particle posesses
a well-defined velocity in magnitude and direction. We shall assume,
as is generally done in adsorption theory that this vector does not
possess any preferential direction and has in consequence a statisti-
cal uniform distribution in the space. In consequence the active
sites of the adsorbent simply retain the particles from the solute and
do not impose any oriented contribution to their movement.

While the particle remains fixed to a site it will uninterrup-
tedly suffer collisions from the molecules of the solvent. After a
certain time the particle will pick up such an amount of energy that
it may overcome the adsorption barrier and is thus desorbed. The de-
sorption energy which determinates the magnitude of the velocity vec-
tor in the instant of desorption arises thus from thermal energy fluc-
tuations. Its mean value is 3/2 kT, since the process is assumed to
be isothermic.

We shall assume that for large intervals of time there exists a
constant relation between the time during which the particle remains
adsorbed and the time during which it remains desorbed. If αt is the
adsorption time, it is clear that $(1 - \alpha)t$ will be the fraction of
the time spent while desorbed. For systems with a large number of

particles the relation $\alpha/(1 - \alpha)$ is the equivalent of the partition coefficient of the particles in the two phases. However when the system contains only a small number of particles this thermodynamic concept loses its usual significance. In either case α and $(1 - \alpha)$ are respectively the probabilities for a particle to be adsorbed and desorbed.

This assumption is a simplification which implies the following consequences. In the first place we take the isotherm of adsorption as a linear isotherm. In the second place we suppose that the total time a particle spends adsorbed is not a random variable. This approximation is valid for a very large number of adsorption-desorption events occuring during the transit of the particle through the adsorbent. It is important to observe that the stochastic character of the retention time is the theoretical basis of the Giddings treatment[4,5].

II. MATHEMATICAL TREATMENT

During its path through the adsorbent a particle from the solute can be in two essentially distinct states, adsorbed or desorbed. In consequence its motion along an axis parallel to the flow of the solvent (X-axis) must be described by two sequences of equations. One sequence is valid for those intervals of time during which the particle is in motion in the solvent. The other is valid for intervals of time in which the particle remains adsorbed.

As a first approximation we shall assume that the column is infinite, that is, the dominion of the x variable is $-\infty$, $+\infty$.

The initial conditions for one particle are

$$x = 0 \quad \text{for} \quad t = 0 \tag{1}$$

In the solvent the particle is submitted to a force acting along the X-axis which can be resolved into three components. One component is the dynamical friction between the particle and the surrounding media, which is given by:

$$- c \cdot dx/dt \qquad (2)$$

where dx/dt is the velocity of the particle along the X-axis and c the dynamical friction coefficient. This constant depends on the size and shape of the particle. In the usual cases where the dimensions of the particle are comparable to those of the molecules of the solvent the friction coefficient is not the Stokes law coefficient[7].

A second component is the force F which drags the particle together with the solvent. If v is the linear velocity of flow along the X-axis, we can write:

$$F = c \cdot v \qquad (3)$$

These two components give a systematic contribution to the motion of the particles. A third component will give a fluctuating contribution which is characteristic of the brownian movement. This fluctuating part $X(t)$ is the instantaneous component along the X-axis of the force exercised by the molecules of the solvent on the particle over and above the viscosity force. Regarding $X(t)$ the following assumptions are made[8,9,10]:

a - $X(t)$ is independent of the velocity of the particle.

b - $X(t)$ varies extremely rapidly compared to the variations of dx/dt. It follows that during the interval of time Δt, dx/dt changes relatively slowly while $X(t)$ fluctuates strongly. In other words, there is no correlation between $X(t)$ and $X(t + \Delta t)$ except when Δt is very small.

c - The mean value of $X(t)$ for intervals of time sufficiently large is equal to zero.

The sum of the three components is equal to the instantaneous force which acts on the particle of mass m and we can write:

$$md^2x/dt^2 = -c.dx/dt + F + X(t) \qquad (4)$$

This equation is valid for the intervals (t_{2n}, t_{2n+1}) during which the particle is in motion. The equation of motion (4) is the Langevin stochastic equation[8,9,10] if the intervals of time (t_{2n}, t_{2n+1}) between two consecutive adsorptions are large when compared with the intervals of time between consecutive collisions of the particle with the molecules of the solvent. This requirement is largely satisfied in the usual conditions of chromatography.

The initial conditions for (4) are:

$$x = x_{2n} \quad \text{for} \quad t = t_{2n}$$
$$dx/dt = v_{2n} \quad \text{for} \quad t = t_{2n} \qquad (5)$$

where x_{2n} is the ordinate from the active site where the particle was desorbed in the beginning of the interval (t_{2n}, t_{2n+1}) and v_{2n} is equal to the velocity along the X-axis with which the particle was desorbed. According to the assumptions made in part I the mean value of the velocities v_{2n} for a large number of desorptions is equal to zero, since v_{2n} is the component along an axis of a vector uniformly distributed in all space.

The sequence of equations for a particle fixed on the adsorption sites is

$$x = x_{2n} \quad \text{for} \quad t_{2n-1} \leqslant t \leqslant t_{2n} \qquad (6)$$

For the explicit integration of equations (4) and (6) it is

convenient to introduce a new variable defined by

$$\tau = t \qquad \text{for} \qquad t_0 \leq t \leq t_1$$

$$\tau = t - \sum_1^n (t_{2\nu} - t_{2\nu-1}) \quad \text{for} \quad t_{2n} \leq t \leq t_{2n+1}$$

$$\tau = 0 \qquad \text{for} \qquad t_{2n-1} \leq t \leq t_{2n} \qquad (7)$$

It can readily be verified that when the particle is in motion

$$dx/dt = dx/d\tau$$

$$d^2x/dt^2 = d^2x/d\tau^2 \qquad (8)$$

The fluctuating force $X(t)$ in the new time coordinate becomes $\mathcal{X}(\tau)$ with the same properties of $X(t)$.

The initial conditions (5) must also be expressed in the new coordinate τ. This is easily done by introducing a new instantaneous force $\psi(\tau)$ acting on the particle at the instant t_{2n} of the desorption – and consequently at the instant $\tau = t_{2n} - \sum_1^n (t_{2\nu} - t_{2\nu-1})$ and imparting to it a velocity along the X-axis equal to v_{2n}. According to the assumptions made in part I, $\psi(\tau)$ will be a fluctuating force with mean value equal to zero for a large number of desorptions.

In this way we get instead of equations (4), (5) and (6) a single stochastic equation:

$$m \cdot d^2x/d\tau^2 = -c \cdot dx/d\tau + F + \mathcal{X}(\tau) + \psi(\tau) \qquad (9)$$

or

$$m \cdot d^2x/d\tau^2 = -c \cdot dx/d\tau + F + \phi(\tau)$$

where the fluctuating part $\phi(\tau) = \mathcal{X}(\tau) + \psi(\tau)$ has the same properties as $X(t)$.

Equation (9) is the Langevin stochastic equation with a driving force F. We introduce now the following variable:

$$x' = x - v \cdot \tau \tag{10}$$

and equation (9) becomes

$$m \cdot d^2 x'/d\tau^2 = -c \cdot dx'/d\tau + \phi(\tau) \tag{11}$$

The well-known solution of this equation[8,9,10] gives the probability distribution $P(x', \tau)$ that the particle will find itself between x' and $x' + dx'$ after a time τ:

$$P(x', \tau)dx' = \left[\frac{c^2}{2\pi \, kTm(\frac{2c\tau}{m} - 3 + 4e^{-\frac{c\tau}{m}} - e^{-\frac{2c\tau}{m}})} \right]^{1/2}$$

$$\cdot \exp \left[\frac{-c^2 \left(x' - \frac{mv}{c}(1 - e^{-\frac{c\tau}{m}})\right)}{2kTm \left(\frac{2c\tau}{m} - 3 + 4e^{-\frac{c\tau}{m}} - e^{-\frac{2c\tau}{m}}\right)} \right] dx'$$

In the usual situation the exponential $e^{-c\tau/m}$ is quite small and returning to the variable x we have:

$$P(x, \tau) = \left[\frac{c}{4\pi kT \tau} \right]^{1/2} \exp \left[\frac{-c(x - v\tau)^2}{4 \, kT \tau} \right] dx \tag{12}$$

At this point it is convenient to pass from the probability distribution in x and τ to the probability distribution in x and t. As we have assumed a probability distribution in t arises only because the particle has spent a fraction of the time t in movement. Consequently the distribution in t must be equal to the distribution in τ, since τ corresponds to the fraction of the time t during which the particle was in motion. From the previous definitions this fraction is equal to $(1 - \alpha)t$ and equation (12) becomes:

$$P(x,t)dx = \left[\frac{c}{4\pi kT\ (1-\mho)t} \right]^{1/2} \exp \left[\frac{-c\ (x-v(1-\alpha)t)^2}{4\ kT(1-\alpha)t} \right] dx \quad (13)$$

Passing from probabilities to frequencies we find:

$$\frac{dZ}{Z} = \left[\frac{c}{4\pi kT\ (1-\alpha)t} \right] \exp \left[\frac{-c\ (x-v(1-\alpha)\ t)^2}{4\ kT\ (1-\alpha)t} \right] dx \quad (14)$$

where Z is the total number of particles from the solute which take part in the process and dZ the number of such particles that will be found in the interval $(x, x + dx)$ at the time t.

It follows from the previous definitions that the probability $P_s(x,t)$ for a particle to be in the solution (desorbed) in the interval $(x, x + dx)$ after the time t is given by:

$$P_s(x,t)\ dx = (1-\alpha)\ P(x,t)dx$$

Substituting in (14) we obtain:

$$\frac{dZ_s}{Z} = \left[\frac{c(1-\alpha)}{4\pi kT\ t} \right]^{1/2} \exp \left[\frac{-c\ (x-v(1-\alpha)t)^2}{4\ kT(1-\alpha)\ t} \right] dx \quad (15)$$

where dZ_s is the number of particles that are in the solution at the time t in the interval $(x, x + dx)$.

Equations (13), (14) and (15) are the fundamental relations for the chromatographic process in an infinite column and we shall now analyse some physical consequences.

III. CONSEQUENCES

The general equation (13) is valid for systems with an extremely low number of particles or even with a single particle. However, it is known that the deduction of (13) from the stochastic equation

(4) requires that certain statistical requirements must be fulfilled without which it is not possible to specify a probability distribution. Suppose that the solvent contains a single particle of the solute. The validity of equation (13) requires that the time of contact solute-solvent with the adsorbent must be large enough to ensure that a large number of adsorption-desorption events will occur. In these conditions the prediction of the position of the particle at the instant t in the adsorbent can be made from equation (13) with the usual statistical estimatives.[1] It should be noted that in ion-exchange experiments with Mendelevium the elution position of this transcurium element has been determined with a single atom of the element[11].

We shall now consider other consequences which follow from equations (14) and (15).

For a chromatographic column (or paper) with constant cross-section S we have the following relations:

$$V_t = S.v.t \tag{16}$$

where V_t is the volume of solvent that has passed through the column until the time t.

The volume of column from the origin x = 0 to the length x is

$$V_x = S \cdot x$$

Introducing the variables V_t and V_x in (15) we found

$$\frac{dZ}{Z} = \left[\frac{S \cdot F}{4\pi kT (1 - \alpha) V_t} \right]^{1/2} \exp \left[\frac{-F(V_x - (1 - \alpha)V_t)^2}{4 \ kT (1 - \alpha)S \cdot V_t} \right] dx \tag{17}$$

Since $(dZ/dx) \cdot (m/S) = C_x$

where C_x is the total concentration of particles (adsorbed and in the

solvent) in the segment of column between x and x + dx, we find by substitution in (17):

$$C_x = M \left[\frac{F}{4\pi kT \ (1-\alpha) \ S \cdot V_t} \right]^{1/2} \exp \left[\frac{-F\left(V_x - (1-\alpha)V_t\right)^2}{4kT \ (1-\alpha) \ S \cdot V_t} \right] \qquad (18)$$

where M is the total mass of solute.

It can be seen that independently from the values of the constant parameters F, T, α and S, the function represented by (18) has a bell-shaped form with increasing flattness as V_t increases. It is important to point that the retention of the particles by the adsorbent sites have a strong influence in the dispersion of curve (18). The presence of the factor $(1 - \alpha)$ is responsable for this influence.

In order to obtain the concentration in solution C_s in the segment of column between x and x+dx after passing a volume V_t of solvent we must start from equation (15) and making the above mentioned substitutions we get;

$$C_s = M \left[\frac{F(1-\alpha)}{4\pi kTSV_t} \right]^{1/2} \exp \left[\frac{-F\left(V_x - (1-\alpha)V_t\right)^2}{4kT(1-\alpha)S \cdot V_t} \right] \qquad (19)$$

The value of x at the time t corresponding to the maximum concentration (peak of the elution band) is given by:

$$V_x = (1-\alpha) \ V_{t,x} \qquad (20)$$

or explicitly by

$$x = (1-\alpha)v \cdot t_x \qquad (21)$$

In the case of chromatography in a strip of paper we have

$$v \cdot t_x = x + y \qquad (22)$$

where x + y is the linear distance travelled by the front of the

solvent.

Substituting (22) in (21) we obtain:

$$1 - \alpha = x/x + y = \text{constant} \tag{23}$$

a relation which is equivalent to Martin and Synge's expression for R_f.

For a chromatographic column the relation (20) takes a more convenient form introducing the volume V_ℓ sweep by the peak of the elution curve until the length ℓ. $V_{t,\ell}/V_\ell$ is now the number of "column volumes" of solution which it is necessary to elute before the peak of the band attains the ordinate ℓ of the column. According to expression (20) we have:

$$V_{t,\ell}/V_\ell = 1/(1-\alpha) \tag{24}$$

Remembering that $\alpha/(1-\alpha)$ is equivalent to the partition coefficient D, we obtain the well-known relation[12]:

$$D = (V_{t,\ell}/V_\ell) - 1$$

The maximum concentration in solution $C_{s,m}$ at the instant t is obtained from (19) which, taking into account (24) gives:

$$C_{s,m} = \frac{M}{V_{t,\ell}} \cdot \left[\frac{F \cdot \ell}{4\pi kT} \right]^{1/2} \tag{25}$$

Introducing (24) and (25) in (19) we obtain:

$$C_s = \frac{M}{V_{t,\ell}} \cdot \left[\frac{F \cdot \ell}{4\pi kT} \right]^{1/2} \exp \left[\frac{-F \cdot \ell (V_{t,\ell} - V_t)^2}{4kT \, V_{t,\ell} \cdot V_\ell} \right] \tag{26}$$

Expression (26) may be used as an approximation for the calculation of the concentration of solute when the elution is made through a column of finite length ℓ.

From equation (26) it is possible to derive, as a particular case, a relation that was deduced by Glueckauf from the plate theory[3].

Assuming that the column up to the length ℓ is divided in N equal sections of height $\Delta \ell$, we clearly have:

$$\ell = N.\Delta \ell \tag{27}$$

Introducing this relation in equation (26) we get:

$$C_x = C_{s,m} \cdot \exp \left[\frac{-F.N.\Delta \ell (V_{t,\ell}-V_t)^2}{4kT \cdot V_{t,\ell} \cdot V_t} \right] \tag{28}$$

where

$$C_{s,m} = \frac{M}{V_{t,\ell}} \cdot \left[\frac{N}{2\pi} \right]^{1/2} \cdot \left[\frac{F \cdot \Delta \ell}{2kT} \right]^{1/2} \tag{29}$$

Equations (28) and (29) became identical to those derived by Glueckauf if we make

$$\Delta \ell = 2kT/F \tag{30}$$

which is always possible since in equation (27) $\Delta \ell$ is not uniquely determined.

According to Keulemans and Kwantes[13] the height of the equivalent theoretical plate is given by the sum of three terms, one of which is equivalent to expression (30), resulting from the contribution of diffusion. The other two terms arise from physical characteristics of the chromatographic process which has been eliminated in our model due to the simplifications assumed.

IV. PROBABILITY DISTRIBUTION AS A FUNCTION OF TIME

Expression (12) or its equivalent (14) and (18) gives the distribution of the particles in the chromatographic system for a fixed value of the time t. This expression is of particular interest for paper chromatography, since in this case the variable which is directly observed is the distribution of the solute along the paper strip.

However for other systems it is convenient to express the probability distribution (or the concentration distribution) of the solute as a function of the time t, for a fixed length x. Such is the situation, for instance, when the elution of the solute is observed through a column. The curve thus obtained expresses the concentration of the solute at the bottom of the column (length ℓ) as a function of the eluted volume, or, at constant flow rate, as a function of the time t.

In terms of the previously described model the problem is as follows. In an infinite column a particle is initially at the level x = 0. After the time t it attains, for the first time, the level $x = \ell$. What is the probability distribution in t for a given $x = \ell$?

An exactly analogous problem is the so-called problem of the first passage, which has been correctly solved for the first time by Schroedinger[14]. This solution, applied to our problem, gives the following expression:

$$\pi(t, \ell) = \left[\frac{\ell \cdot c^{1/2}}{4\pi kT (1- \alpha)} \right] \cdot \frac{1}{t^{3/2}} \exp \left[\frac{-c (\ell - (1- \alpha)v \cdot t)^2}{4 k T (1 - \alpha) t} \right] dt \tag{31}$$

where the symbols have the same meaning as stated above.

The mean time of elution is easily calculated from equation (31):

$$\bar{t} = \frac{\ell}{(1- \alpha) \cdot v} \tag{32}$$

As is apparent $\bar{t}$ is the time required for the maximum of the probability curve (12) in x to pass by $x = \ell$.

The value t_{max} of the time for which $\pi(t, \ell)$ is maximum expressed as a function of the mean time $\bar{t}$ is

$$t_{max} = \bar{t} + 3 \sigma^2 / 4 \ell^2 \tag{33}$$

where σ is the variance of distribution (12). For very large values of the elution time (large variance) the difference between t_{max} and $\bar{t}$ becomes significant, which obviously indicates an increasing assymetry of the elution curve.

It is important to observe that the distribution in time (31) is very different from that derived by Giddings and Eyring. This is due to the fact that in Gidding and Eyring's treatment the stochastic variable is the time of retention whereas in our model is the displacement of the particle.

ACKNOWLEDGMENTS

1. A. J. P. Martin and R. L. M. Synge, Biochem. J. (London), 35, 1358 (1941).

2. S. W. Mayer and E. R. Tompkins, J. Am. Chem. Soc., 69, 2866 (1947).

3. E. Glueckauf, Trans. Far. Soc., 51, 33 (1955).

4. J. C. Giddings and H. Eyring, J. Phys. Chem. 59, 416 (1955).

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

6. J. H. Beynon, S. Clough, D. A. Crooks and G. R. Leister, Trans. Far. Soc., 54, 705, (1958).

7. J. G. Kirkwood, J. Chem. Phys. 14, 180 (1946).

8. S. Chandrasehkar, Rev. Mod. Phys. 15, 1 (1943).

9. G. E. Uhlenbeck and L. S. Ornstein, Phys. Rev. 36, 823 (1930).

10. J. E. Moyal, J. Roy. Stat. Soc. 11, 150 (1949).

11. A. Ghiorso, B. G. Harvey, G. R. Choppin, S. G. Thompson and G. T. Seaborg, Phys. Rev. 98, 1518 (1955).

12. K. A. Kraus and G. E. Moore, J. Am. Chem. Soc., 73, 9 (1951).

13. Keulemans and Kwantes, Vapour phase chromatography, Butterworths Scientific Publications, London (1957).

14. E. Schroedinger, Physik. Zeit., 16, 289 (1915).

ERRATA

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1. In page 8 equation without number:

$$P(x', \tau)\, dx' = \ldots\ldots\ldots \cdot \exp\left[\frac{-\alpha^2\left(x' - \frac{mv}{\alpha}\left(1 - e^{-\frac{\alpha\tau}{m}}\right)\right)^2}{2kTm \ldots\ldots\ldots\ldots\ldots\ldots}\right] dx'$$

2. In equation (12), instead of $P(x, \tau) = \ldots\ldots$

   let us read $P(x, \tau)\, dx = \ldots\ldots\ldots$

3. In equation (13), instead of $P(x, t)\, dx = \left[\dfrac{c}{4\pi k\, T\, (1 - \tau)\, t}\right]^{1/2} \ldots\ldots$ let us read

   $$P(x, t)\, dx = \left[\frac{c}{4\pi k\, T\, (1 - \alpha)\, t}\right]^{1/2} \ldots\ldots$$

4. In equation (14), instead of $\dfrac{dZ}{Z} = \left[\dfrac{c}{4\pi k\, T\, (1 - \alpha)\, t}\right] \ldots\ldots$ let us read

   $$\frac{dZ}{Z} = \left[\frac{c}{4\pi k\, T\, (1 - \alpha)\, t}\right]^{1/2} \ldots\ldots$$

5. In equation (26), instead of $\ldots\ldots \exp\left[\dfrac{-F \cdot \ell\, (V_{t,\ell} - V_t)^2}{4kT\; V_{t,\ell} \cdot V_\ell}\right] \ldots$ let us read

   $$\ldots\exp\left[\frac{-F \cdot \ell\, (V_{t,\ell} - V_t)^2}{4kT\; V_{t,\ell} \cdot V_t}\right]$$

6. In equation (31) let us read:

   $$(t,\ ) = \left[\frac{\cdot c}{4\pi k\, T\, (1 - \alpha)}\right]^{1/2} \cdot \frac{\ell}{t^{3/2}}\ \exp\ldots$$

7. In equation (33), instead of $t_{max} = \bar{t} + 3\,\sigma^2 / 4\,\ell^2$, let us read

   $$t_{max} = \bar{t} - \frac{3\,\sigma^2}{4\,\ell^2}\,\bar{L}$$

8. In page 15, first line, instead of reading "...of distribution (12).", let us read "... of distribution (13).".

9. In page 14, 23rd line, instead of reading "... probability curve (12) in..." let us read "...probability curve (13) in...".