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A theoretical plate model accounting for slow kinetics in chromatographic elution

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ABSTRACT

The chromatographic elution has been studied from different perspectives. However, in spite of the simplicity and evident deficiencies of the plate model proposed by Martin and Synge, it has served as a basis for the characterization of columns up-to-date. This approach envisions the chromatographic column as an arbitrary number of theoretical plates, each of them consisting of identical repeating portions of mobile phase and stationary phase. Solutes partition between both phases, reaching the equilibrium. Mobile phase transference between the theoretical plates is assumed to be infinitesimally stepwise (or continuous), giving rise to the mixing of the solutions in adjacent plates. This yields an additional peak broadening, which is added to the dispersion associated to the equilibrium conditions. It is commonly assumed that when the solute concentration is sufficiently small, chromatographic elution is carried out under linear conditions, which is the case in almost all analytical applications. When the solute concentration increases above a value where the stationary phase approximates saturation (i.e. becomes overloaded), non-linear elution is obtained. In addition to overloading, another source of non-linearity can be a slow mass transfer. An extended Martin and Synge model is here proposed to include slow mass-transfer kinetics (with respect to flow rate) between the mobile phase and stationary phase. We show that there is a linear relationship between the variance and the ratio of the kinetic constants for the mass transfer in the flow direction (τ) and the mass transfer between the mobile phase and stationary phase (ν), which has been called the kinetic ratio ($\kappa = \tau/\nu$). The proposed model was validated with data obtained according to an approach that simulates the solute migration through the theoretical plates. An experimental approach to measure the deviation from the equilibrium conditions using the experimental peak variances and retention times at several flow rates is also proposed.

1. Introduction

Finding an accurate model to describe the chromatographic elution is practically an unsolvable problem, as has been commented by Giddings and Eyring [1], due to the complexity and the unknown factors involved in the process, beginning with the nature of the multi-site surface up to the particularities of the stationary phase packing. In spite of this, a huge effort has been done to develop models to understand the peak shape and the main factors that affect it [2–7].

The models that describe the equilibrium conditions in liquid chromatography can be classified as linear and non-linear [6,8]. In the linear models, the amount of solute associated to the stationary phase is assumed to be proportional to its concentration in the mobile phase. This implies that the equilibrium between the mobile phase and stationary phase is instantaneous. Also, the sample components do not compete for the stationary phase, nor interact among them; their elution is, therefore, independent from each other. This means that each peak in a mixture has independent characteristics and is identical to that obtained upon elution of an isolated standard.

Linear chromatography has been studied from three different perspectives: (i) the plate models proposed by Martin and Synge [9], and Craig [10], (ii) the differential rate model that describes the mass balance and mass-transfer kinetics, proposed by Lapidus and Amundson [11], and van Deemter et al. [12], and extensively applied by other authors [13–17], and (iii) the statistical models developed by Giddings and Eyring [1], and followed by Dondi et al. [18,19].

The plate models envision the chromatographic column as an arbitrary number of theoretical plates, each of them consisting of identical repeating portions of stationary phase and mobile phase. It is assumed that the solute partitions between both phases, reaching the equilibrium. In the model proposed by Craig [10], there is no mixing mechanism and the mobile phase is transferred downstream completely from one plate to the following, in a discrete way (stepwise). The final band broadening is produced exclusively by the quantitativeness of the distribution equilibrium of the solute

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between the two phases along the column theoretical plates, which gives rise to solute dispersion along the theoretical plates. The Craig model gives rise to a distribution, which can be approximated to a Gaussian profile with the following variance [4]:

$$\sigma^2 = \frac{t_R(t_R - t_0)}{N} \tag{1}$$

where t_R is the retention time (time at the peak maximum), t_0 the dead time (the time at which a non-retained solute elutes) and N the number of theoretical plates (or efficiency). According to this model, a non-retained solute (i.e. in the absence of interactions) would elute with the dead volume, with a null peak width.

In the model proposed by Martin and Synge [9], mobile phase transference between plates is assumed to be infinitesimally stepwise (or continuous), giving rise to the mixing of the solutions in adjacent plates. This yields an additional peak broadening, which is added to the dispersion associated to the equilibrium conditions. The final peak profile is an Erlang distribution [20], which can also be approximated to a Gaussian with a variance:

$$\sigma^2 = \frac{t_R^2}{N} \tag{2}$$

In the absence of interactions between solute and stationary phase (i.e. for a non-retained solute), this model predicts a minimal peak broadening:

$$\sigma_0^2 = \frac{t_0^2}{N} \tag{3}$$

In spite of the simplicity and evident deficiencies of the Martin and Synge plate model, it has served as a basis for the characterization of columns up-to-date. These deficiencies have been partially overcome by newer models [4,7,17]. We make a new proposal, which is explained below.

It is commonly assumed that when the solute concentration is sufficiently small, chromatographic elution is carried out under linear conditions, which is the case in almost all analytical applications. When the solute concentration increases above a value where the stationary phase approximates saturation (i.e. becomes overloaded), non-linear elution conditions are obtained. This means that the concentration in the stationary phase increases slower than in the mobile phase. Accordingly, solutes at different concentrations tend to move along the column at different velocities: the peaks become asymmetrical and the retention times depend on the solute concentration in the mobile phase. This behaviour is described by non-linear isotherms that follow different models, as the Langmuir or Freundlich-type isotherms [8].

In addition to overloading, another source of non-linearity can be a slow mass transfer. In this case, the changes in the solute concentration in the stationary phase will depend, not only on the solute concentration in the mobile phase, but also on the stationary phase. In this work, the Martin and Synge model is extended to include slow mass-transfer kinetics between the mobile phase and stationary phase.

2. Theory

The plate count theory assumes that the chromatographic column is divided in N theoretical plates. According to this, we have developed a global approach that considers the partition process along the whole column. A system of N differential equations (one equation for each theoretical plate) is obtained, which is solved using the Laplace transform. The approach is applied below to equilibrium and slow mass-transfer conditions in chromatography.

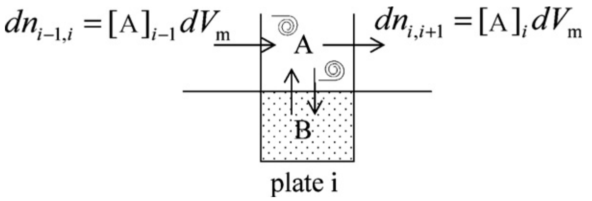

Fig. 1. Change in the moles of solute in the mobile phase associated to a theoretical plate. A and B indicate the solute in the mobile phase and stationary phase, respectively; $dn_{i-1,i}$ and $dn_{i,i+1}$ denote the moles that enter and leave the i theoretical plate in dt.

2.1. Linear equilibrium elution

2.1.1. Peak function

Fig. 1 depicts the mass transfer for a given solute associated to an i theoretical plate, in an infinitesimal time interval dt. The change in the moles of solute in a theoretical plate will be:

$$dn_i = [\mathrm{A}]_{i-1} dV_m - [\mathrm{A}]_i dV_m \tag{4}$$

where $[\mathrm{A}]_i$ and $[\mathrm{A}]_{i-1}$ are the solute concentrations in the mobile phase associated to the i and $i-1$ theoretical plates, respectively, and dV_m is the mobile phase volume that is transferred from one plate to the next in the time interval dt. Assuming that the distribution equilibrium between mobile phase and stationary phase is reached instantaneously, the partition constant is expressed as:

$$K = \frac{[\mathrm{B}]_i}{[\mathrm{A}]_i} = \frac{b_i}{a_i}\frac{V_m}{V_s} \tag{5}$$

$[\mathrm{B}]_i$ is the solute concentration in the stationary phase, and V_m and V_s are the volumes of mobile phase and stationary phase associated to a theoretical plate, respectively, which do not change along the column; a_i and b_i are the moles of solute in the mobile phase and stationary phase in the i theoretical plate, respectively. The total moles in the i theoretical plate will be:

$$n_i = a_i + b_i \tag{6}$$

From Eq. (5):

$$n_i = a_i + K a_i \frac{V_s}{V_m} = a_i\left(1 + K\frac{V_s}{V_m}\right) \tag{7}$$

The moles of solute in the mobile phase can be thus expressed as a fraction of the total moles:

$$a_i = p n_i \tag{8}$$

with

$$p = \frac{1}{\left(1 + K\frac{V_s}{V_m}\right)} = \frac{1}{1+k} = \frac{t_0}{t_R} \tag{9}$$

k being the retention factor:

$$k = \frac{t_R - t_0}{t_0} \tag{10}$$

Therefore, the solute concentration in the mobile phase associated to the i theoretical plate will be:

$$[\mathrm{A}]_i = \frac{p n_i}{V_m} \tag{11}$$

On the other hand, dV_m and dt are related through:

$$dV_m = u\,dt = \frac{N V_m}{t_0} dt \tag{12}$$

where u is the flow rate and NV_m represents the total column volume accessible to the mobile phase. Going back to Eq. (4), and taking into account Eqs. (11) and (12):

$$dn_i = \frac{N}{t_0} p n_{i-1} dt - \frac{N}{t_0} p n_i dt \tag{13}$$