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Rapid determination of hydrodynamic radii beyond the limits of Taylor dispersion

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ABSTRACT

Taylor dispersion analysis (TDA) is an absolute method for determining the diffusion coefficients, and hence the hydrodynamic radii, of particles by measuring the dispersion in a carrier medium flowing within a capillary. It is applicable under conditions which allow the particles to radially diffuse appreciably across the cross-section of the flow before the measurement and therefore implies long measurement times are required for large particles with small diffusion coefficients. In this paper, a method has been developed by which the diffusion coefficients of large particles can be rapidly estimated from the shapes of the concentration profiles obtained at much earlier measurement times. The method relies on the fact that the shapes of the early-time concentration profiles are dependent on the diffusion coefficient, flow rate and the capillary radius through the dimensionless residence time which, theoretically, is a measure of the amount of radial diffusion undergone by the particles. The amount of radial diffusion for nanospheres of varying sizes was estimated by quantifying the relative change in the shapes of concentration profiles obtained at two points in the flow and a correlation was obtained with the variation of the dimensionless residence time to confirm the theory. This correlation was then tested by applying it to another set of measurements of solutes and solute mixtures of different sizes including a protein. The estimated diffusion coefficients were found to be in good agreement with the expected values. This demonstrates the potential for the method to extend dispersion analysis to regimes well outside the TDA limits to enable the rapid characterization of large particles.

1. Introduction

Taylor dispersion analysis (TDA) is an absolute method for determining the diffusion coefficients, and hence the hydrodynamic radii of particles. The method, sometimes referred to as Taylor-Aris dispersion, was first described by Taylor in his classic paper [1]. In 1956, Aris developed the method further by accounting for the longitudinal diffusion of the particles [2].

This technique was first applied to the determination of gaseous [3] and then liquid diffusion coefficients [4–6]. With the use of fused silica capillaries, TDA regained interest and has been used to analyze amino acids, peptides, proteins, small molecules, macromolecules, nanoparticles and biosensors [7–27].

Taylor dispersion within a capillary arises as a combination of the spreading due to axial convection which is regulated by molecular diffusion across the capillary radius. Hence, for TDA to be applicable, the measurement time must be long enough for radial diffusion and hence complete Taylor dispersion to occur and the characteristic Gaussian concentration profiles to develop [28]. This condition is usually expressed with a dimensionless quantity, the dimensionless residence time $\tau = Dt/r_c^2$, which is the ratio of the residence time t to the characteristic time required for a molecule of diffusion coefficient D to diffuse across the capillary radius r_c. τ is therefore a measure of the degree of radial diffusion and is typically required to be greater than 1.4 [13]. This implies that for large particles (with small values of D) long measurement times are required for TDA to be applicable. Note also that τ is a similarity parameter, i.e. molecules with differing diffusion coefficients but measured at points with the same values of τ have similar concentration profiles.

Recently, a dispersion solution which is applicable at all measurement times [29] has been used to extract the diffusion coefficients from early-time concentration profiles [24]. This approach,

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however, requires the location of the transition point between convection and Taylor dispersion which can be prone to error or in some cases be obscured by the response of smaller particles which may be present and which undergo complete Taylor dispersion. Furthermore, mismatches between the concentrations of the solute buffer and run buffer may significantly alter the shape of the trace and result in a poor fit.

An empirical method for the estimation of the diffusion coefficients of large particles based on the shape of their concentration profiles has been developed in the past [30–32]. The method is applicable to particles which undergo partial Taylor dispersion and correlates the relative heights of the Taylor dispersion peaks and the convection fronts with the diffusion coefficient and flow rate.

In this paper, an alternative method for estimating the diffusion coefficients of large particles at times much earlier than required for TDA is proposed. The method relies on the quantification of the degree of radial diffusion (or partial Taylor dispersion) that occurs between two spatially separated points along the flow. Two measures of the degree of radial diffusion are defined and correlated. The first measure is the variation of the dimensionless residence time $\Delta\tau$ between two measurement points, which is a function of the diffusion coefficient, whilst the second measure is a directly measureable quantity f which is a function of the ratios of the maximum amplitudes of the convection fronts observed at the two measurement points. Using samples of known diffusion coefficients, the correlation between f and $\Delta\tau$ is determined so that when D (and hence $\Delta\tau$) is unknown, it may be estimated by determining f which is directly measurable from the observed concentration profiles.

The paper is organized as follows. First, the dimensionless residence time τ is introduced as a measure of the degree of radial diffusion. Next, the early-time radial diffusion of particles and the shapes of the corresponding concentration profiles are discussed. A method for estimating the degree of radial diffusion f from these concentration profiles is then described. The correlation between f and $\Delta\tau$ is determined and subsequently used to make predictions for the diffusion coefficients of a wide range of particles.

2. Theory

2.1. The dimensionless residence time τ

Taylor dispersion is achieved when there is a balance between axial convection which tends to disperse the particles along the streamlines and the radial diffusion that arises from the resulting concentration gradients which limits the dispersion. At early times, convective transport is dominant before eventually the degree of radial diffusion becomes sufficient for the solute particles to limit the dispersion and give rise to the spatially symmetric concentration profiles attributable to Taylor dispersion. A measure of the degree of the radial diffusion is the dimensionless residence time τ which is defined as the ratio of the residence time t_m to the characteristic time required for a molecule to diffuse across the capillary radius and is given by

$$\tau = \frac{Dt_m}{r_c^2} \tag{1}$$

where D is the diffusion coefficient and r_c is the capillary radius. The larger the value of τ, the greater the degree of radial diffusion that has occurred. As mentioned in the previous section, a value of τ greater than 1.4 is used as the condition for complete Taylor dispersion and the applicability of TDA.

2.2. Early-time dispersion and the Taylor-dispersed fraction f

For the Poiseuille flow of a fluid in a circular capillary of radius a, the velocity u at a distance r from the central line is

$$u = u_0\left(1 - \frac{r^2}{a^2}\right) \tag{2}$$

where u_0 is the maximum velocity at the axis. If a symmetrical distribution of solute particles is introduced into the flow, the dispersion equation for the concentration distribution is given by [1]

$$\frac{\partial C}{\partial t} + u\frac{\partial C}{\partial x} = D\left(\frac{\partial^2 C}{\partial r^2} + \frac{1}{r}\frac{\partial C}{\partial r} + \frac{\partial^2 C}{\partial x^2}\right) \tag{3}$$

where C is the mean concentration of the solute particles over the cross-section of the tube, t is the time and x is the distance from the point of injection. If we denote the solute concentration at a radial distance r as C_r, the mean concentration C is defined by

$$C = \frac{2}{a^2}\int_0^a C_r r dr \tag{4}$$

Under pure convection, the diffusion term on the right hand side of the dispersion equation can be neglected. Therefore, a solute of initial concentration C_0 injected for a time t_{inj} under constant pressure into the capillary will occupy an initial length $X = u_0 t_{inj}$. If the solute injection is assumed to be stopped at time $t = 0$, the solution obtained for the initial average spatial concentration distribution C_c is given by:

Time $t = 0$ (Injection):

$$\begin{aligned} C_c &= 0 : (x < 0) \\ C_c &= C_0\left(1 - \frac{x}{X}\right) : (0 < x < X) \\ C_c &= 0 : (x > X) \end{aligned} \tag{5}$$

For flow-times $t > 0$ after the injection, there are two time domains with different concentration profiles. These are:

Time $t < X/u_0$ (Post-injection):

$$\begin{aligned} C_c &= 0 : (x < 0) \\ C_c &= \frac{C_0}{u_0 t}\left(x - \frac{x^2}{2X}\right) : (0 < x < u_0 t) \\ C_c &= C_0\left(1 + \frac{u_0 t - 2x}{2X}\right) : (u_0 t < x < X) \\ C_c &= \frac{C_0}{u_0 t}\left(\frac{X}{2} - (x - u_0 t)\left(1 - \frac{x - u_0 t}{2X}\right)\right) : (X < x < X + u_0 t) \\ C_c &= 0 : (x > X + u_0 t) \end{aligned} \tag{6}$$

Time $t > X/u_0$ (Post-injection):

$$\begin{aligned} C_c &= 0 : (x < 0) \\ C_c &= \frac{C_0}{u_0 t}\left(x - \frac{x^2}{2X}\right) : (0 < x < X) \\ C_c &= C_0\frac{X}{2u_0 t} : (X < x < u_0 t) \\ C_c &= \frac{C_0}{u_0 t}\left(\frac{X}{2} - (x - u_0 t)\left(1 - \frac{x - u_0 t}{2X}\right)\right) : (u_0 t < x < X + u_0 t) \\ C_c &= 0 : (x > X + u_0 t) \end{aligned} \tag{7}$$

Full derivations of these concentration profiles are given in the Appendix. Similar expressions for the concentration profiles that