Journal of Analy

: Di usion; Dynamic light scattering; Micelles; Monomers

Solute molecules associate via a variety of mechanisms driven by molecular and ionic interactions. Examples of these mechanisms are polymerization, aggregation, and the formation of micelles [1-5]. e di usion of such solutes has been the subject of many studies and has proven to be a useful measure of the strength and nature of these interactions.

Mutual di usion coe cients and interaction parameters can be measured for associating solutes via a range of methods including dynamic light scattering (DLS), which is a well-established method, and Taylor dispersion analysis (TDA), which is relatively new. e latter can be achieved via concentration titration methods [6-9] or from a single measurement [10]. Mutual di usion refers to the uxes of solute and solvent molecules produced by changes or gradients in the concentration of the solution. Furthermore, the concentration dependence of mutual di usion coe cients is widely used to characterize the behavior of molecules in solution and, in particular, to identify conditions where molecular interactions are most favorable in terms of stability. is is because typically, the strengths of these interactions become more pronounced with increasing solute concentration as the solution tends to non-ideality [10], thereby leading to a dependence of the di usion coe cient on solute concentration. is is of great importance in the development of biopharmaceutical drugs [11-13] where it can be used to determine the second virial coe cient (B_2), which is a measure of the strength of protein-protein interactions for example.

e di usion interaction parameter, k_D, is a metric that describes the variation of a binary di usion coe cient with solute concentration in a given medium and is de ned by:

$$D^m = D_0(1 + k_D C) \quad (1)$$

where D^m is the measured mutual di usion coe cient at a

From Eq. (3),

$$c_i' = iK_i c_1^{i-1} c_1' \quad (i \geq 1) \tag{9}$$

which gives

$$\sum_{i=1}^{n} i^2 K_i c_1^{i-1} D_i c_1' = D^m \sum_{i=1}^{n} i^2 K_i c_1^{i-1} c_1' \tag{10}$$

where K_1=1.

Dividing by c_1 and re-arranging with the aid of Eq. (3) gives

$$D^m = \frac{\sum_{i=1}^{n} i^2 c_i D_i}{\sum_{i=1}^{n} i^2 c_i} = \frac{\sum_{i=1}^{n} i^2 K_i c_1^i D_i}{\sum_{i=1}^{n} i^2 K_i c_1^i} \tag{11}$$

Henceforth, this will be referred to as the intrinsic mutual diffusion coefficient.

[illegible]

For DLS, each D_i is weighted by the product of the mass concentration C_i and mass m_i. Hence the weight factor is m_i^2. This is proportional to $i^2 c_i^2$. Therefore, for a DLS measurement, Eq. (11) can becomes weighted as follows:

$$D_{DLS}^m = \frac{\sum_{i=1}^{n} i^4 c_i^3 D_i}{\sum_{i=1}^{n} i^4 c_i^3} = \frac{\sum_{i=1}^{n} i^4 (K_i c_1^i)^3 D_i}{\sum_{i=1}^{n} i^4 (K_i c_1^i)^3} \tag{12}$$

For TDA, where the dispersion of a plug of solute within a capillary is monitored as a function of time, it is the dispersion coefficient d that is determined using the form of Eq. (11) i.e.,

$$d = \frac{\sum_{i=1}^{n} i^2 c_i d_i}{\sum_{i=1}^{n} i^2 c_i} = \frac{\sum_{i=1}^{n} i^2 K_i c_1^i d_i}{\sum_{i=1}^{n} i^2 K_i c_1^i} \tag{13}$$

The mutual diffusion coefficient D^m is obtained from the dispersion coefficient via the reciprocal relation [18]:

$$d = \frac{r^2 v^2}{48 D^m} \tag{14}$$

where

$$d_{TDA} = \frac{\sum_{i=1}^{n} i^3 c_i^2 d_i}{\sum_{i=1}^{n} i^3 c_i^2} = \frac{\sum_{i=1}^{n} i^3 (K_i c_1^i)^2 d_i}{\sum_{i=1}^{n} i^3 (K_i c_1^i)^2} \tag{15}$$

r is the capillary radius and v is the average flow speed. For a mass-concentration sensitive instrument, the dispersion coefficients d_i are weighted by m_i ($\propto ic_i$), hence for TDA, the weighted dispersion coefficient becomes. This gives:

[illegible]

Note that $K_2c_1=c_2$ from Eq. (3).

It is also instructive to investigate the behavior of the interaction parameter. e interaction parameter, which is de ned in Eq. (1), may be estimated from the rst derivative of the di usion coe cient with respect to concentration and is given by:

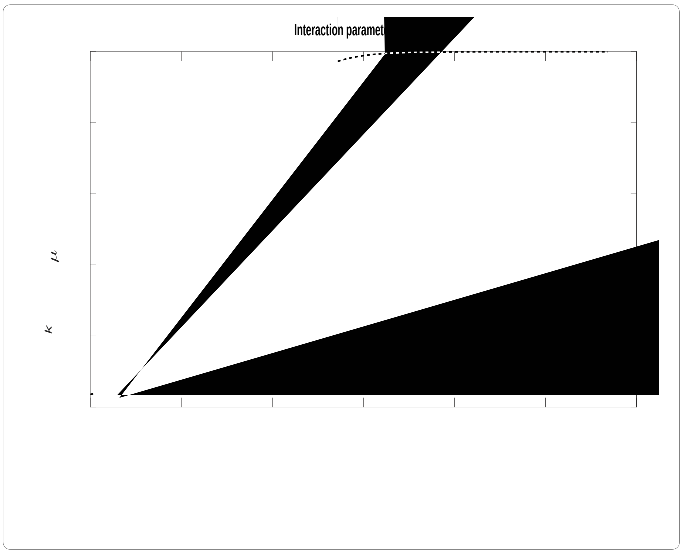
$$k_D \quad \frac{1}{{}_0}\frac{dD^m}{}$$

all three interaction parameters tend to zero. ese observations are better appreciated by expanding the expressions for the interaction parameters in these limits. At low concentrations, they reduce to:

$$k_D \quad C \to 0 \quad 4K_2 \frac{(D_2 \quad 4€ D_1)ð}{D_1}$$

$$k_D^{DLS} \quad C \to 0 \quad 48K_2{}^3 c_1^2 \frac{(D_2 \quad D_1)}{D_1}$$

$$k_D^{TDA} \quad C \to 0 \quad 16K_2{}^2 c_1 \frac{(D_2 \quad D_1)}{D_2}$$



Leaist D, Hui L (1990) Intradiffusion coeffcients and integral mutual diffusion coeffcients of dilute associating solutes are identical: caffeine in water. Journal

Latunde-Dada S, Bott R, Barker D, Leszczyszyn OI (2016) Methodologies for the rapid determination of the diffusion interaction parameter using Taylor