Nonmonotonic density dependence of the diffusion of DNA fragments in low-salt suspensions

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The high linear charge density of 20-base-pair oligomers of DNA is shown to lead to a striking nonmonotonic dependence of the long-time self-diffusion on the concentration of DNA in low-salt conditions. This generic nonmonotonic behavior results from the strong coupling between the electrostatic and solvent-mediated hydrodynamic interactions, from the renormalization of these electrostatic interactions at large separations, and specifically from the dominance of the far-field hydrodynamic interactions caused by the strong repulsion between the DNA fragments.

With the increasing importance of biophysics, there is a greater overlap between the subjects of the physics of biological molecules and colloidal physics, which deals with small particles in suspension. Many of the techniques that have been developed in colloidal physics are directly applicable to biological molecules, such as proteins, and cells. DNA in particular is a very interesting biomolecule which exhibits a wide range of behaviors due to its interactions with proteins and enzymes, but also due to its physical characteristics. A particular feature of DNA that is of interest to colloidal scientists is its high linear charge density [1,2]. The interaction energy between DNA molecules and the structure of suspensions of DNA fragments have been shown to be strongly affected by this charge density. Consequently, other effects associated with a strong charge, such as electrolyte screening, electrolyte friction, charge condensation, charge inversion, and like-charge attraction in the presence of multivalent salt ions, have also been predicted and investigated [3–6]. Several investigations have considered the effect on the structure due to the renormalization of charge [2,7]. Little work, however, has been performed on the interesting consequences of a high charge on the dynamics of these molecules.

Highly charged colloids present an entirely different paradigm of particle interactions to the classical hard-sphere model. Well-known features of a low-salt suspension of charged colloids are the low osmotic compressibility of the suspension and the fact that the mean distance between the particles scales with the inverse of the cube root of the colloid concentration over a wide range of concentrations [8]. This scaling, corresponding to the formation of a correlation hole around the particles, leads to the domination of far-field over near-field hydrodynamic interactions (HIs) and therefore to an altered dynamic behavior which is unlike that of hard-sphere colloids.

Wilk *et al.* [1] have measured the long-time translational self-diffusion coefficient $D^L=(D^L_\parallel+2D^L_\perp)/3$ of isotropic dispersions of 20-base-pair oligomers of DNA by fluorescence correlation spectroscopy for various salt concentrations. DNA is a suitable molecule for studying effects resulting from electrostatic and hydrodynamic coupling due to its

large linear charge density of approximately $-2e/3.4$ Å. The 20-mer DNA are almost perfectly monodisperse, rigid cylindrical rods with length $L=6.8$ nm and diameter $d=2$ nm (aspect ratio of 3.4), a bare valency of $Z=-42$ in neutral or basic pH solutions, and a translational free diffusion coefficient of $D^0=1.07\times10^{-6}$ cm^2 s^{-1}. The long-time coefficient D^L was found to have an unexpected nonmonotonic concentration dependence in low-salt conditions.

In this article we describe a versatile theoretical scheme that we have developed for the calculation of D^L in colloidal systems [3,9,10]. This scheme includes the long-range far-field part of the HIs between the particles, which dominates in low-salt suspensions. We will show that in combination with colloid charge renormalization, this scheme successfully describes the nonmonotonic dependence of $D^L(\phi)$ on the macro-ion volume fraction ϕ. This effect is of general importance and may be observed in any dispersion of colloids or biomolecules where long-range repulsive interactions are prevalent. The nonmonotonicity in ϕ is unusual since it requires a delicate interplay of HIs and electrosteric repulsions over a sufficiently broad concentration range. In contrast, a nonmonotonic ϕ dependence is not uncommon for transport properties such as the primary electroviscous coefficient $p(\phi)$, associated with the suspension viscosity η [11], and the collective diffusion coefficient D^c [8]. Moreover, the electrophoretic mobility μ [12] as well as $1/\eta$ and $D^L(\phi=0)$ exhibits a minimum as a function of the electrolyte concentration. The minimum in $D^L(0)$ is found for globular macro-ions [9,13] and also for semiflexible charged polymers as shown recently in experiments and simulations [14]. In all cases considered, HIs play a decisive role; e.g., the maximum of $D^c(\phi)$ arises from a balance of the slowing HIs and the speed-up of density relaxations caused by the electrosteric repulsion. The maximum in $p(\phi)$ at intermediate salinity arises from a competition between the velocity gradient inside the macro-ion double layer that grows with ϕ and the shrinking double-layer distortion [11]. Ignoring HIs can lead to nonphysical results such as the failure to predict the maximum in the electrophoretic mobility of a short polyelectrolyte chain as a function of the monomer number [15,16].

Due to the increasing power of computers, substantial progress has been made in the simulation of transport properties in non-dilute-charged colloidal dispersions. Formerly, simulations that include the electrokinetic effect of electro-

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lyte ions have been difficult due to the large asymmetry between these components, in both size and charge. These simulations have focused largely on the challenging problem of electrophoresis [12,17,18], frequently used for particle characterization, but for which a complete theory in dense systems, in which there is strong overlap of the electrical double layers, is still lacking. Our theoretical scheme is therefore also presented as a significant step in developing a versatile statistical-mechanical tool to describe the electrokinetic transport in nondilute suspensions.

Our scheme is based on an exact memory equation for the self-intermediate scattering function of colloids undergoing overdamped Brownian motion. The irreducible memory function in this equation is approximated using the idealized mode-coupling theory for Brownian fluids, with the important extension of including the HIs between all ionic species. Instead of solving the mode-coupling equations fully self-consistently, which would be a very challenging numerical task in the presence of HIs, we use a simplified solution scheme which retains analytical simplicity and yields only small differences in the numerical results [19].

According to our scheme, the long-time coefficient D^L of a nondilute suspension is given by the Stokes-Einstein-like relation [3]

$$\frac{D^L}{D^0} = \left[1 + \frac{\Delta\zeta^{CF}}{\zeta^0} + \frac{\Delta\zeta^{EF}}{\zeta^0} \right]^{-1}, \qquad (1)$$

which includes, in addition to the colloid-solvent friction $\zeta^0 = 6\pi\eta^0 a$, where η^0 is the solvent viscosity and a the colloid radius, a colloid friction (CF) and an electrolyte friction (EF). The colloid friction arises from the micro-ion-averaged electrosteric and HIs between the colloids, and is present even when the micro-ion degrees of freedom are ignored. It is given in our scheme by [3]

$$\frac{\Delta\zeta^{CF}}{\zeta^0} = \frac{n}{6\pi^2} \int_0^\infty dk\, k^2 \frac{\left[h(k) - \dfrac{1}{D^0} h^d(k) \right]^2}{2 + n\left[h(k) + \dfrac{1}{D^0} h^d(k) \right]}, \qquad (2)$$

where n is the colloid number density, $h(k)$ is the total correlation function of the colloids, $h^d(k)$ is the distinct hydrodynamic function of the colloids, and D^0 is the free-diffusion constant. This expression for $\Delta\zeta^{CF}$ only requires the colloid static structure factor $S(k) = 1 + nh(k)$. Equation (2) is the zeroth-order term in the expansion of the total long-time friction coefficient, $\Delta\zeta = \Delta\zeta^{CF} + \Delta\zeta^{EF}$, in terms of the colloid–micro-ion mobility ratio D^0/D_i^0. Equation (1) states that the extra friction due to the fast kinetics of the mobile salt ions, $\Delta\zeta^{EF}$, is given by the difference of the total friction coefficient and $\Delta\zeta^{CF}$ [3]. The EF is due to the noninstantaneous relaxation of the micro-ionic atmosphere. We have derived a simple expression for the long-time EF contribution, valid for the case when the free-diffusion coefficients of the various salt-ion species, D_i^0, are much greater than the colloid free-diffusion coefficient. This expression is

$$\frac{\Delta\zeta^{EF}}{\zeta^0} = \frac{2}{3\pi^2} \sum_{i=1}^m n_i \frac{D^0}{D^0 + D_i^0} \int_0^\infty dk\, k^2$$

$$\times \left\{ \frac{\left[1 + nh(k) \right] \dfrac{1}{D^0} h_{ci}^d(k) - h_{ci}(k)\left[1 + n\dfrac{1}{D^0} h^d(k) \right]}{2 + n\left[h(k) + \dfrac{1}{D^0} h^d(k) \right]} \right\}^2,$$

where the sum goes over all micro-ion species of number density n_i and where $h_{ci}(k)$ and $h_{ci}^d(k)$ are the partial total correlation and partial distinct hydrodynamic functions between the micro-ions and colloids. The EF contribution to D^L is significant in very dilute systems, but is negligible when the mobility difference between the colloidal spheres and the micro-ions is large and when ϕ is increased. The second finding is attributed to the enhanced homogenization of the electrolyte background with increasing ϕ [3].

Since the dynamic effect of the micro-ions is small, we can simplify the problem by considering the colloids as interacting with an effective pair potential. In the resulting one-component model of weakly charged colloids, the effective interaction between colloids of radius a and bare valency Z_{bare} follows the repulsive part of the Derjaguin-Landau-Verwey-Overbeek (DLVO) potential [20]:

$$\beta u(r) = L_B Z_{bare}^2 \left(\frac{e^{\kappa a}}{1 + \kappa a} \right)^2 \frac{e^{-\kappa r}}{r}, \quad r > 2a,$$

where $L_B = e^2/(\epsilon k_B T)$ is the Bjerrum length in a solvent of dielectric constant ϵ and κ is the inverse Debye screening length determined by the concentration of added salt ions and monovalent counter-ions. In a 1:1 electrolyte solution, $\kappa^2 = 4\pi L_B(2n_s + n|Z_{bare}|)$. For strongly charged colloids where $L_B|Z_{bare}|/a > 1$, this potential is still suitable, but only with the charge and screening parameter replaced by an effective charge Z_{eff} and screening parameter κ_{eff} due to the condensation of counter-ions near the colloid surfaces. There exist several schemes for the calculation of these effective quantities, and these have recently been of considerable interest. Those mostly used are the cell-model approximation of Alexander *et al.* [21] and the renormalized jellium approximation (RJA) [22].

The RJA for the effective macro-ion charge in a closed suspension with a fixed salt concentration, as opposed to a system in contact with a reservoir, involves numerically solving the Poisson equation for the mean electric potential $\psi(r)$ of a single colloidal sphere, surrounded by a Boltzmann-distributed micro-ion cloud and a uniform negatively charged background of charge density nZ_{eff}, which describes the jellium representing the other macro-ions. The resulting equation for the reduced potential, $y(r) = \beta e\psi(r)$, is

$$\nabla^2 y(r) = 4\pi L_B \{2n_s \sinh[y(r)] + nZ_{eff}(e^{y(r)} - 1)\}, \qquad (3)$$

with the boundary conditions $y(\infty) = 0$, $y'(\infty) = 0$, and $y'(a) = -L_B Z_{bare}/a^2$. The numerical solution of Eq. (3) is asymptotically matched to the solution of the linearized equation $\nabla^2 y_{lin}(r) = \kappa_{eff}^2 y_{lin}(r)$, where κ_{eff} is the effective screening parameter, $\kappa_{eff}^2 = 4\pi L_B(2n_s + n|Z_{eff}|)$. The effective charge comes from the linearized solution at the inner boundary,
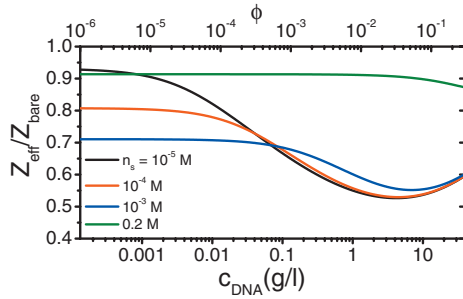
FIG. 1. (Color) Effective charge of 20-mer DNA ($Z_{\text{bare}}=-42$), determined via the RJA, as a function of DNA and salt concentrations.

$y'_{\text{lin}}(a)=-L_B Z_{\text{eff}}/a^2$. Since the effective charge also appears in Eq. (3), this solution procedure must be iterated until self-consistency in Z_{eff} has been established [22].

With the so-determined interaction potential, $S(k)$ is calculated using standard integral equation theories. For this study, we use the rescaled mean spherical approximation (RMSA) [23], known to be a reasonably accurate theory of the structure of charged colloids.

Equation (2) has been developed for spherically symmetric particles and is therefore not directly applicable to rodlike particles in high-salt suspensions. On the other hand, in low-salt suspensions, as measured by Wilk *et al.*, the microstructure is mostly determined by the long-range electrostatic monopole term which is spherically symmetric. Therefore, we treat the DNA fragments as spheres with an effective radius a_{eff}. This radius appears in the solution of the effective charge and thus in the calculated structure factor. The largest effect of a_{eff}, however, is to determine the scaling used to map the volume-fraction-dependent calculations onto the weight-concentration-dependent measurements by $c(\text{g/L})=3\phi M_w/(4\pi a_{\text{eff}}^3 10^3 N_A)$, where $M_w=13\,022$ g mol^{-1} is the molecular weight of the DNA fragments. The effective radius resulting from the Stokes-Einstein relation applied to the measured diffusion coefficient at infinite dilution is $a_{\text{eff}}=2.0$ nm. However, since the excluded volume interaction of the effective spheres is influential at high salinity only, from comparing our results with the high-salt measurements of Wilk *et al.*, we have determined $a_{\text{eff}}=3.4$ nm$=L/2$ to provide the best overall fit, independent of the salt concentration. An effective radius of half the molecular length has some parallels with the excluded-volume calculations of rodlike particles in the isotropic state. Since the bare charge is given by the number of ionizable groups on the DNA molecule, $a_{\text{eff}}=L/2$ is the only adjusted parameter.

The effective charge for our model of the DNA fragments, calculated via the RJA in a closed system as in the experiment, is presented in Fig. 1. For low-salt systems, Z_{eff} shows a nonmonotonic dependence on ϕ. At very low ϕ, there is also a nonmonotonic dependence of Z_{eff} on the salt concentration (cf. Fig. 1), with the limit that $Z_{\text{eff}} \rightarrow Z_{\text{bare}}$ when $n \rightarrow 0$ and $n_s \rightarrow 0$. This zero-ϕ nonmonotonicity of Z_{eff} is also seen in its expansion in terms of the bare charge Z_{bare}. If Z_{bare} is sufficiently large, Z_{eff} becomes independent of the bare charge. This is the so-called saturated effective charge, $Z_{\text{eff}}^{\text{sat}}$. In our system, $|Z_{\text{bare}} L_B/a_{\text{eff}}| \approx 9$, which is well into the non-
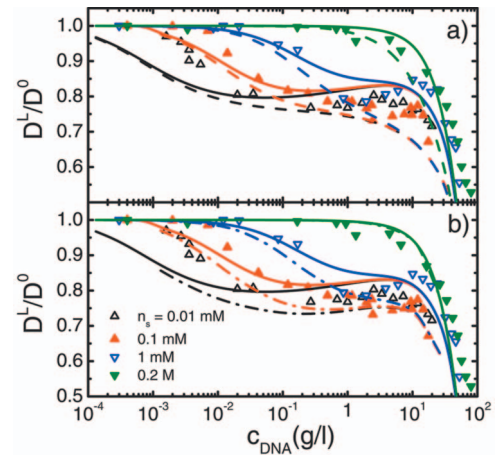

FIG. 2. (Color) Self-diffusion coefficient D^L of the DNA model vs weight concentration for salt concentrations as indicated. Symbols are experimental results taken from [1]. (a) Comparison with theoretical results using Z_{eff}. Solid lines are results with HIs; dashed lines are without HIs. (b) Comparison with theoretical results with HIs. Solid lines are again results using Z_{eff}; dashed lines are results with fixed charge $Z=-42$.

linear regime, but Z_{eff} is less than 66% of $Z_{\text{eff}}^{\text{sat}}$, so that saturation is not yet reached. Even though the κ_{eff} depends on Z_{eff}, it shows no nonmonotonic ϕ dependence.

The measured D^L of the 20-mer DNA and the comparison with the results of our spherical model are shown in Fig. 2. In Fig. 2(a), we include the results of our scheme when far-field HIs are included (solid lines) or ignored (dashed lines), with the values Z_{eff} and κ_{eff} used in both cases. The nonmonotonic dependence of D^L on ϕ in the experiments is also seen in the theoretical predictions when HIs between the particles are included. If the HIs are ignored, D^L shows a monotonic ϕ dependence, for all considered salt concentrations. In Fig. 2(b), a comparison is made between the theoretical results for D^L, including the effects of HIs, where instead of a ϕ-dependent Z_{eff} (solid lines again), we use a fixed charge of $Z=-42$ (dash-dotted lines). For both sets of results a nonmonotonic ϕ dependence is seen. The nonmonotonicity, however, is much stronger when a nonconstant Z_{eff} is used. This suggests that the nonmonotonic ϕ dependence of the experimental D^L results from a simultaneous interplay between the hydrodynamic enhancement caused by far-field HIs and the nonmonotonic Z_{eff} in low-salt systems. The strong decline in D^L at large ϕ seen in Fig. 2 is due to electrosteric caging, which becomes stronger with increasing ϕ. The single–macro-ion EF effect described in Booth's theory [13] cannot explain the nonmonotonicity of D^L since it is significant only for $\phi < 10^{-4}$ and $n_s \approx 0.01$ M [3], which is a salt concentration much larger than those where the DNA-D^L behaves nonmonotonically.

The hydrodynamic enhancement of the diffusion of particles repelling each other over long distances results from the fact that the dominant far-field HIs advect neighboring particles that may otherwise have hindered the motion of the considered one. Near-field HIs, on the other hand, have the opposite effect of slowing the diffusive motion. Hydrodynamic enhancement of D^L has been seen before in suspen-

sions of charged and magnetically interacting colloidal particles [19,24] and in simulations with HIs of charged nanosized poly-ions [25], but without a visible nonmonotonic ϕ dependence. A nonmonotonic $D^L(\phi)$ was found in simulations of salt-free polyelectrolyte solutions [26]. In these simulations, however, HIs have been neglected and the values for D^L/D^0 are smaller than 0.1, which is the value where the freezing transition of charged spheres and rods occurs [27].

In summary, we have shown that the nonmonotonic concentration dependence of D^L in low-salt suspensions of DNA fragments can be understood by the influence of far-field HIs and charge renormalization. According to our scheme, the nonmonotonicity of D^L is a generic effect for any low-salt suspension of strongly charged small colloids or biomolecules. We have obtained this result using a simplified mode-coupling scheme. This scheme is a marked improvement on previous methods, since its many-component version includes the far-field HIs between all ionic species. Its analytic simplicity allows the study of electrokinetic phenomena such as the EF effect on self-diffusion and collective diffusion for nonzero concentrations.

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