Importance of hydrodynamic shielding for the dynamic behavior of short polyelectrolyte chains

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The dynamic behavior of polyelectrolyte chains in the oligomer range is investigated with coarse-grained molecular dynamics simulation and compared to data obtained by two different experimental methods, namely capillary electrophoresis and electrophoresis NMR. We find excellent agreement of experiments and simulations when hydrodynamic interactions are accounted for in the simulations.

We show that the electrophoretic mobility exhibits a maximum in the oligomer range and for the first time illustrate that this maximum is due to the hydrodynamical shielding between the chain monomers. Our findings demonstrate convincingly that it is possible to model dynamic behavior of polyelectrolytes using coarse grained models for both, the polyelectrolyte chains and the solvent induced hydrodynamic interactions.

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INTRODUCTION

Electrophoresis methods are widely used to separate (macro)biomolecules such as peptides, proteins, and DNA, as well as synthetic polymers. Short polyelectrolytes (PEs) can conveniently be separated in free solution without the aid of a gel by capillary electrophoresis (CE). Additionally, CE is employed to characterize the hydrodynamic properties of charged biomolecules, in particular the electrophoretic mobility, \( \mu \), the diffusion coefficient, and the hydrodynamic radius.

Alternatively, these properties can be determined by pulsed field gradient (PFG) NMR. With a combination of diffusion NMR and electrophoretic NMR, the charge of macromolecules, the influence of ionic strength and the dielectric constant of the solution have been investigated.

Several studies of PEs of well defined length in the short chain regime have shown that the free-solution mobility \( \mu \) exhibits a characteristic behavior: from the monomer mobility, \( \mu_0 \), onwards, \( \mu \) increases towards a maximum, \( \mu_{\text{max}} \), that occurs for chains of a specific degree of polymerization, \( N_{\text{max}} \). After this maximum, \( \mu \) decreases slightly to reach a constant value, \( \mu_{FD} \), the so-called free draining mobility. Very little is known about the origin of the maximum, yet the knowledge of the precise dynamical behavior of a PE is a prerequisite for designing possible applications in microfluidic devices, such as electrophoretic separation or gene sequencing.

Whether or not a mobility maximum appears and the precise value of \( N_{\text{max}} \) seems to depend on the flexibility of the chain. While a maximum has been observed for flexible PEs such as single stranded DNA or sulfonated polystyrene (PSS) at values around 10 repeat units for \( N_{\text{max}} \), semi-flexible double-stranded DNA does not exhibit it. The small number for \( N_{\text{max}} \) and the strong influence of the persistence length shows that a short chain behavior must be responsible for this. Furthermore, it has been shown that the \( \mu_{\text{max}} \) is diminished under elevated salt conditions.

Existing theories have been successful in describing the qualitative behavior of an initially rising mobility as well as the constant long-chain limit, but they have not been able to reproduce this maximum or explain its origin.

To provide a fundamental understanding of the involved dynamics of PEs, we propose a coarse-grained Molecular Dynamics model that takes all charged particles (i.e., PE repeat units, counter ions, and additional salt) and electrostatic and hydrodynamic interactions (HI) between them into account. In the following we demonstrate that this model reproduces experimental results obtained by two completely different experimental techniques. In addition we suggest a microscopic interpretation of the size-dependence of \( \mu \) for short PE chains, based on hydrodynamic shielding, which gives fundamental insight into the interplay of hydrodynamic friction and charge correlations for charged macromolecules.

SIMULATIONS

Model. We simulate a flexible PE using a bead-spring model employing the ESPResSo package ([17]). All pa-
parameter values are chosen to match the properties of PSS used in the experiments and given in reduced units with \( kT = 1.0 \) and \( \sigma_0 = 2.5 \AA \) being the energy and the relevant length scale. The beads (chain monomers) are connected by FENE bonds with stiffness \( k = 30 \), and maximum extension \( R = 1.5 \). Additionally a truncated Lennard-Jones or WCA potential with depth \( \epsilon = 0.25 \) and width \( \sigma = 1 \), is used for excluded volume interactions. Each monomer has a charge of \( q = -1 \) in units of \( e \). Monovalent counter ions, \( q = 1 \), and monovalent positive and negative salt ions are subjected to the same LJ potential giving all particles the same size. The simulations are carried out under periodic boundary conditions in a rectangular simulation box of size \( L \times L \times L \). All electrostatic interactions are calculated with the P3M algorithm. The Bjerrum length \( l_B = e^2/4\pi \varepsilon kT \) is \( 2.84 \) in simulation units corresponds to \( 7.1 \) Å (the Bjerrum length for water at room temperature). Together with the model’s average bond length of \( b = 0.91 \), we compute a Manning factor of \( \xi = l_B/b = 3.12 \). The inclusion of HI is done via frictional coupling of the beads to a Lattice Boltzmann (LB) fluid as detailed in \([18]\). The Bjerrum length for water at room temperature. Together with the model’s average bond length of \( b = 0.91 \), we compute a Manning factor of \( \xi = l_B/b = 3.12 \). The inclusion of HI is done via frictional coupling of the beads to a Lattice Boltzmann (LB) fluid as detailed in \([15]\). The modeled fluid has a kinematic viscosity \( \nu = 3.0 \), a fluid density \( \rho = 0.864 \), and is discretized by a grid with spacing \( a = 1.0 \). The coupling parameter is \( \Gamma = 20.0 \). The simulation time step is \( \tau = 0.01 \).

To determine the impact of HI, we compare the results to simulations with a simple Langevin thermostat that does not recover long-range hydrodynamic interactions between the monomers, but only offers local interaction with the solvent.

**Transport coefficients.** We determine two different transport coefficients for the model PE that are likewise determined in the associated experiments. The single chain diffusion coefficient is obtained from the center of mass velocity auto correlation function: \( D = \frac{1}{3} \int_0^\infty d\tau \langle v_C^2(\tau) v_C(0) \rangle \).

In CE experiments, the electrophoretic mobility \( \mu \) of the solute is determined by \( \mu = v/E = L/I/Vt \), where \( v \) is the velocity, \( E \) is the electric field, \( V \) is the applied voltage, \( L \) is the total length of the capillary, \( I \) is the migration (or effective) length up to the detector and \( t \) is the detection time of the solute.

In the simulations, we use a Green-Kubo relation to obtain \( \mu \) at zero electric field. This approach has been successfully applied in simulations to determine the electrophoretic mobility of charged colloids \([19]\). The chain mobility is calculated from the correlation function between the center of mass velocity of the polyelectrolyte chain and the velocities of all charged particles in the system: \( \mu = \frac{1}{3k_B T} \sum_i \int_0^\infty \langle v_i(0) \cdot v_i(\tau) \rangle d\tau \). This method guarantees that no conformational changes of the chain structure or the ion distribution are induced by an artificial high external field, which is sometimes used in other simulations to separate the directed electrophoretic motion from Brownian motion within reasonable computing time. Our method enables us furthermore to obtain both transport properties from the same simulation trajectories without additional computational effort \([21]\).

### EXPERIMENTS

**Capillary electrophoresis (CE)** is an analytical separation technique based on the differential migration of ionic species under electric field \([1]\).

The CE experiments were performed using an Agilent technologies capillary electrophoresis system (Agilent, Waldbronn, Germany). Capillaries of \( 33.5 \) cm (25 cm to the detector) length, and \( 50 \) µm diameter were prepared from bare silica tubing purchased from Supelco (Bellefonte, PA, USA). New capillaries were conditioned by performing the following flushes: \( 1 \) M NaOH for 30 min, \( 0.1 \) M NaOH for 10 min, and water for 5 min. Samples were introduced hydrodynamically (~ \( 4 \) nL) at \( 0.5 \) g/L concentration (~ \( 2.5 \) mM monomer concentration). The electrolyte was pure water. Solutes were detected at \( 225 \) nm. The electric field was kept constant at \( 224 \) V/cm (\( V = +7.5 \) kV). The polarity of the applied voltage on the inlet side of the capillaries was positive. All the experiments were performed at \( 27 \) °C. Electro osmotic mobilities were determined from the migration time of a neutral marker (mesityl oxide, ~ \( 0.1\% \) (v/v) in the electrolyte). The sodium polystyrene sulfonate standards \( (M_n 1.430 \times 10^3, 5 \times 10^3, 8 \times 10^3, 16 \times 10^3, 31 \times 10^3, 41 \times 10^3, 88 \times 10^3, 177 \times 10^3, 350 \times 10^3; \) \( M_n/M_w \) ca 1.1) were purchased from American Polymer Standards Corp. (Mentor, OH, USA). These standards have verified sulfonation rates larger than 88% and are almost fully charged. Purified water delivered by an Alpha-Q system (Millipore, Molsheim, France) was used to prepare all electrolytes and sample solutions.

**In electrophoretic NMR,** diffusion and electrophoretic motion are separated by the design of the experiment \([21]\). No gel has been used, so that self diffusion and free electrophoresis are measured. The PSS samples have been obtained from Fluka. To minimize the effects of variations of the ionic strength \([10]\), samples have been dialyzed against water (cut off volume 0.5kDA), and subsequently dried under vacuum. For all experiments a monomer concentration of \( 5 \) mM in deuterated water has been used. The diffusion experiments have been performed on a Bruker Avance 500 NMR spectrometer operating at a Larmor frequency of 500MHz for protons equipped with a DIFF30 probe head generating a maximum pulsed field gradient strength of \( 12T/m \). The gradient pulse duration and diffusion times have been adjusted between 0.8 to 2ms and 8 to 20ms respectively for optimal resolution in each molecular weight resulting in different diffusion coefficients. Because of their narrow molecular
Diffusion. Recently, Stellwagen et al. [13] observed that the diffusion coefficient, $D$, of PSS can be approximated by a power law scaling $D = D_0 N^m$, where $D_0$ is the monomer diffusion coefficient, and $m$ is the scaling exponent. In Figure 1, we compare the diffusion coefficient obtained from simulations to the results from the NMR study. The simulated data is normalized by $D_0 = 0.052$ as obtained from the power law fit, and the experimental data by the monomer diffusion coefficient of $D_0 = 5.710 \times 10^{-10} \text{ m}^2/\text{s}$. The simulations with HI result in a scaling exponent of $m = -0.63 \pm 0.01$, which is in good agreement with value obtained from experiments, $m = -0.64 \pm 0.02$, and a previously reported result, $m = -0.617$, by [12]. Only for the very short chains, $(N < 5)$, is a deviation from the prediction observed and a higher diffusion coefficient found in the simulations. For intermediate chain length, the coarse-grained simulation model with HI, reproduces the experimentally observed behavior.

Without HI, the chains show the expected Rouse diffusion with an exponent of $m = 1.02 \pm 0.02$. This simple model is clearly not applicable to mimic the experimental behavior of short PE chains.

Electrophoretic mobility ($\mu$). The results for measurements of $\mu$ in pure water without additional salt are shown in Fig. 2. To account for the different viscosity of the solvents, we rescale the mobilities by the free-draining mobility $\mu_{FD}$ as obtained for long chains.

The experimental data sets agree within the accuracies of the individual methods and show the characteristic behavior of the mobility in dependence to chain length. A mobility maximum for $N = 10$ is observed with capillary electrophoresis. This maximum for intermediate chains as well as the long chain behavior is successfully reproduced in simulations with HI. For the first few oligomers, we observe a small difference which is in line with the deviation for the diffusion.

On the other hand, as illustrated in the inset of Fig. 2, the simulation without hydrodynamic interactions fails completely to describe the short chain behavior and can only be mapped to the experimental data in the long chain limit. Therefore, we infer that the mobility maximum can only be explained when taking into account HI between the PE and the surrounding solvent.

To further illustrate this, we estimate the effective hydrodynamic friction, $\Gamma_{eff}$, and the effective charge, $Q_{eff}$, in dependence of its length. During electrophoresis, the electrical driving force $F_E = Q_{eff} E$ is balanced by the
frictional force with the solvent $F_F = \Gamma_{\text{eff}} v$, where $v$ is the migration velocity induced by the electric field $E$. For the mobility, we then obtain: $\mu = Q_{\text{eff}} / \Gamma_{\text{eff}}$. The PE is surrounded by oppositely charged counter ions, some of which moving with the chain and thus reducing its effective charge. We estimate this charge reduction by subtracting the number of counter ions that are found within 2 units of the chain from the bare charge $N$. This estimate is used together with the obtained mobility to calculate the effective friction as shown in Fig. 3. The effective charge for long chains is in agreement with the Manning prediction at infinite dilution, yielding $Q/N = 1/\xi = 0.32$. From Fig. 3 we see the impact of HI that results in the mobility maximum. Additional monomers are partly shielded from the flow by the other monomers decreasing the effective friction per monomer with chain length. This shielding is effective on short length scales and leads to a stronger initial decrease of the friction than the counter ion condensation reduces the effective charge. This leads to an increasing mobility for intermediate chains. While the effective friction levels off quickly, the effective charge per monomer keeps decreasing slowly, reducing the mobility and causing the maximum. For long chains, effective charge and effective friction per monomer become constant, leading to the well-known free-draining behavior.

**CONCLUSION**

We performed a detailed study investigating the dynamic behavior of short PE chains via MD simulations of a coarse grained model and via two different experimental approaches. The results of experiments and simulations can be quantitatively matched and agree with the existing theory and predictions, as long as the simulation model correctly includes long-range HI. A simulation model that neglects HI fails to reproduce the short-length scale behavior of the diffusion coefficient and of the electrophoretic mobility.

To our knowledge we demonstrated for the first time, that the transport coefficient of short PEs can be quantitatively modeled by coarse grained simulation techniques. No chemical details are needed to explain the experimental results. Our model allows to simulate time scales otherwise out of reach for atomistic simulations and provides a microscopic understanding of the observed maximum in $\mu$. From our observation we conclude, that hydrodynamic shielding between the chain monomers is the major cause for this previously little understood behavior, and that it is vitally important to include HI to model such systems.

Having a simulation model at hand, that confirms the experimental data, opens new possibilities of investigating the electrophoretic behavior of short PEs, which so far has not been fully explained by the existing theories. We thank B. Dünweg, U. Schiller, and G. Slater for helpful remarks. Funds from the the Volkswagen foundation, the DAAD, and DFG under the TR6 are gratefully acknowledged.

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