Molecular dynamics simulations are used to study the local dynamics of counterion-charged polymer association at charge densities above and below the counterion condensation threshold. Surprisingly, the counterions form weakly-interacting clusters which exhibit short range orientational order, and which decay slowly due to migration of ions across the diffuse double layer. The cluster dynamics are insensitive to an applied electric field, and qualitatively agree with the available experimental data. The results are consistent with predictions of the classical theory only over much longer time scales.

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Many biochemical reactions involve local interactions between small molecules (ligands) and biological macromolecules such as DNA, which are polymers consisting of repeating ionizable groups known as polyelectrolytes [1]. When dissolved in a polar solvent such as water, polyelectrolytes ionize and counterions dissociate from the polymer, leaving an oppositely charged polymer backbone. The highly ionized polyelectrolyte in solution attracts small mobile counterions of opposite charge, partially screening the backbone charge. The approach of the small molecules to a polyelectrolyte is governed to a large degree by electrostatic interactions, which in turn depend on the local molecular environment, and in particular is sensitive to the instantaneous distribution of counterions around the polyelectrolyte. Thus, knowledge of the counterion distribution at atomic resolution is crucial for many aspects of DNA dynamics such as molecular assembly and inter-cellular transport.

The difficulty in studying polyelectrolyte solutions resides in the delicate interplay of the long range electrostatic interactions, short range intermolecular interactions, and thermal energy, which are comparable to each other in magnitude. Furthermore, typical polyelectrolytes are highly charged, which precludes straightforward application of the usual Debye-Hückel theory of electrolytic solutions. A key advance in understanding the equilibrium state of counterions associated with a charged polymer was the condensation theory of Manning [2], which treated the polyelectrolyte molecule as an infinite rigid rod of uniform charge density \(-z_pe/b\), as an approximation to discrete groups of equal charge \(-z_pe\) separated by a distance \(b\), and considered independent dissolved counterions of charge \(z_e e\) placed in a uniform bulk solvent of dielectric constant \(\epsilon\) about the molecule. Considering the two-dimensional partition function in the plane normal to the polyelectrolyte axis, Manning found that the free counterion configuration is unstable for sufficiently strong electrostatic interaction, when the dimensionless “Manning parameter” \(\xi \equiv z_p z_e l_B/b > 1\), where \(l_B = e^2/(\epsilon_e k_BT)\) is the “Bjerrum length” at which thermal energy \(k_BT\) equals electrostatic potential energy. He then hypothesized that counterions would condense uniformly on the polyelectrolyte backbone so as to reduce \(\xi\) to unity, while the remaining (dilute) unbound ions in solution could be treated in the Debye-Hückel approximation. Since the seminal work of Manning, several analytical and numerical investigations [4] have relaxed various assumptions in the original model. While the qualitative aspects of Manning’s predictions survive, the phase transition at \(\xi = 1\) is present only for an infinite rod.

In contrast to the average properties of the equilibrium state of condensed counterions, little is known about the local dynamics of counterion-charged polymer association, which trigger and control ion-exchange reactions and affect the binding affinity of polyelectrolytes by shielding local electrostatic forces. In particular, most previous theoretical work is of a mean-field nature, and certainly cannot address any issues relating to temporal or spatial fluctuations in the distribution of the counterions along a polyelectrolyte. The electrophoresis of polyelectrolytes raises the further issue of the response of the charge distribution to an applied electric field; previous treatments assume the counterion distribution is unchanged from its equilibrium state, but at least at high field strengths some modification will occur.

In order to understand the fine scale behavior in the distribution of the counterions in the vicinity of a polion, we employ molecular dynamics (MD) simulations [5] to investigate, for the first time, the dynamics of counterion condensation on a mobile and flexible polyelectrolyte in a solution. Previous numerical studies using MD, or Langevin dynamics [6] or Monte-Carlo methods [7] have focused instead on the average behavior of the charge distribution or on polymer dynamics issues. Our computational formulation is similar to that of Chang and Yethiraj [8], and is based on a bead-spring model of a flexible polymer chain [9] of Lennard-Jones monomers bound by FENE interactions, suspended in explicit solvent.
We consider a counterion to be “bound” to the polyelectrolyte chain contains \(N=50\) monomers carrying a total charge \(-Z_pe\) distributed uniformly along the chain. For computational tractability, the solvent molecules are modeled as Lennard-Jones (LJ) spheres, with the polarizability of water accounted for through its dielectric constant \(\epsilon_r=78\) in the Coulomb interaction between charges. The polyelectrolyte and dissolved ions are likewise treated as LJ spheres, with an appropriate charge at the center, and for simplicity all are assigned the same mass \(m\) and core size \(\sigma\). All dissolved ions are monovalent and the counterions from the salt and the polyelectrolyte are assumed to be identical. Accordingly, the system includes \(N_–=100\) coions of charge \(-e\) and \(N_+=N_–+Z_p\) counterions of charge \(+e\) so as to maintain electro-neutrality.

The simulations involve a total of 32,000 atomic units (monomers, co- and counter-ions and solvent) in a periodic simulation cube of side \(L=34.2\sigma\), giving a total number density \(\rho=0.8\sigma^{-3}\). Simulations for one case with a larger box size \(1.65L\) gives very similar results. From the density of water at room temperature, assuming for simplicity a cubic packing of spheres, one estimates \(\sigma\approx0.38nm\). The temperature in the simulations is maintained at \(T=1.0\epsilon/k_B=300\)K using a Nosé-Hoover thermostat (\(\epsilon\) is the depth of the LJ potential) and gives a Bjerrum length \(l_B\approx1.85\sigma\). Given \(N_–\) above, the salt concentration is approximately \(0.073M\), and the Debye length is \(l_D\equiv(4\pi l_B \sum z_i^2 \rho_i)^{-1/2}\approx2.7\sigma\), where \(z_i\) and \(\rho_i\) are the valence and the number density of the simple ion species \(i\). These parameters correspond to the typical experimental situation \(\sigma<l_B<l_D=R_g\), where \(R_g\) is the radius of gyration of the polyelectrolyte (found to be 5-10\(\sigma\)). To simulate the effects of external electric fields, a force which is proportional to the charge is added to every charged particle in the system. The natural MD unit of electric field strength \(E\) is \(\epsilon/e\sigma\approx67kV/mm\), and here we compare \(E=0\) and 1.0. We vary the polyelectrolyte charge \(Z_p\), such that the Manning parameter \(\xi\) for our system (with \(b\approx\sigma\), \(z_c=1\) and \(z_p=Z_p/N\)) spans a range above and below the critical value 1. Lastly, the characteristic time scale in the simulations is \(\tau=\sigma(m/\epsilon)^{1/2}\), about 1 ps here. Typical simulations equilibrate for 1000\(\tau\) and data is accumulated over a 3000\(\tau\) interval.

To quantify the spatial distribution of the charge near the polyelectrolyte, we form a tube of radius \(r\) around the polymer chain backbone by uniting all the spherical regions of radius \(r\) centered at every monomer in the chain, and count the number of ions inside the tube. We consider a counterion to be “bound” to the polyelectrolyte molecule whenever it is within a tube of radius \(l_B\); the Bjerrum length is the relevant length scale because within this distance the electrostatic interaction dominates Brownian motion and could bind the charges together. From the time-averaged probability distributions of the two nearest neighbor distances of a bound counterion to any polyelectrolyte monomer, shown in Fig. 1 we see that the bound counterions prefer to sit between two adjacent monomers forming a triangle. Indeed, the typical separations are very close to each other, as well as to the mean monomer separation (\(~1\sigma\)), and correspond to the three particles lying at the vertices of an equilateral triangle subject to modest thermal fluctuations. Note that the distributions sharpen as the polyelectrolyte charge increases, and that application of an electric field of even unit strength has little effect.

We can thus associate each bound counterion to its two nearest monomers in the polymer chain, which we term a monomer-ion triplet. Nearby triplets are strongly correlated at short length scales because the positively charged counterions tend to avoid each other. To characterize these orientational correlations, we consider the angle \(\theta\) between the normals to the planes formed by any two triplets; see Fig. 2(a), and compute the time-averaged value of \(\cos\theta\) as a function of the separation along the molecule, as defined by the difference \(\Delta_j\) in the label \(j\) \((j=1, 2, \cdots, N)\), of the first monomer in the triplet. As seen in Fig. 2(b), neighboring triplets are strongly anti-correlated out to a distance of about 5 monomers, while bound counterions separated by larger separations are independent. The correlations are weakly dependent on \(Z_p\), and not significantly affected by an electric field.

The counterion-monomer triplets exhibit dynamical clustering along the polyanion. We define a cluster of size \(n\) to consist of \(n\) adjacent triplets along the chain backbone with no intervening vacancies, and plot the probability distributions \(P(n)\) for clusters of size \(n\) for different polyanion charge \(Z_p\) in Fig. 3. Provided \(n\) is not too small, we find an exponential distribution \(P(n)\sim-n\), both with and without an electric field. Note that the range of charges \(0\leq Z_p\leq 60\) corresponds to \(0\leq \xi\leq 2.225\), and spans the Manning transition region. If we interpret this probability distribution as arising from a Boltz-
Furthermore, the binding of the counterions to the chain is transient rather than permanent. The direct evidence comes from snapshots of successive configurations from the simulations, where one sees that bound counterions continuously move in and out of the Bjerrum layer and do not remain adjacent to a particular monomer indefinitely. We quantify these observations through the charge autocorrelation function $C_{QQ}(t)$ of the total ionic charge $Q(t)$ within the Bjerrum layer. As shown in Fig. 4, $C_{QQ}$ decays over a time close to the Debye time $\tau_D$ and then fluctuates about zero, indicating counterion decorrelation and transport through the Bjerrum layer. The relevant decorrelation time scale is the time $\tau_D = l_B^2/D$ for an isolated counterion to diffuse through a Debye length, where $D$ is the diffusion constant of the counterions. The latter parameter was measured in independent simulations without a polion to be $D = 0.070 \sigma^2/\tau$, leading to $\tau_D \approx 0.1$ ns. Note in particular that there is no significant difference between a neutral and charged polyelectrolyte molecule, and again an applied electric field has little effect.

The connection between independence of the clusters and the exponential form of $P(n)$ can be seen in another way, by reference to the random sequential adsorption (RSA) model [10] for polymer reactions. If ions are independently adsorbed with probability $p$ and released with probability $q$ per unit time at different sites, then the probability of forming a cluster of size $n$ is proportional to $p^n/(p+q)^n$. The latter expression has the same exponential decay with $n$ as our simulation data, although this model is too simple to predict the slope correctly. If the ratio $p/q$ is adjusted to give the mean number of counterions within the Bjerrum layer separately for each $Z_p$ then the slope increases systematically with $Z_p$ as in our simulations, but does not have the correct numerical value.

FIG. 2: (a) Geometry defining the relative orientation between two triplets: $\theta$ is the angle between the normals $n_1$ and $n_2$ to the planes formed by two triplets. (b) Correlation in the relative orientations between triplets as a function of the separation along the molecule, with and without electric field.

FIG. 3: Probability of finding a monomer-ion cluster of size $n$ for (a) $E=0$ and (b) $E=1$.

FIG. 4: Autocorrelation functions $C_{QQ}(t) = \langle [Q(t)Q(0)] - \langle Q(t) \rangle \langle Q(0) \rangle \rangle^2 / \langle [Q(t)^2] - \langle Q(t) \rangle^2 \rangle^2$ for the net ion charge $Q(t)$ inside $r = l_B$ for a polyelectrolyte of length $N=50$ (a) in thermodynamic equilibrium and (b) translating in the presence of an applied field $E = 1.5 e \sigma / a$. Each curve is an average over 5 different realizations. The error bars shown correspond to 1 standard deviation for the case $Z_p = 60$.

Aside from the fluctuations apparent in $C_{QQ}$, the spatial distribution of charge within the Bjerrum layer is constant on average, and shows an approximate agreement with Manning’s predictions. Fig. 3 shows the total charge within a tube of radius $r$ about polyions of charge $Z_p = 20, 40$ and 60, over a time interval of $3000 \tau$ in the steady state. In the latter two cases, the linear charge densities of the polyion are above the critical value for Manning condensation. In the absence of an electric field, we see that the time-averaged total charge of the ions within the Bjerrum layer when $\xi > 1$ approximately agrees with Manning’s prediction. The original model was imprecise about exactly where the condensed counterions would be located; we find that the condensed charge in the region $r < 1.5 \sigma$ is very close to the prediction. Moreover, the number of the counterions within the Debye layer is found to be negligibly small as was as-
sumed in the theory. Furthermore, the slopes of the solid curves for $E = 0$ in Fig. 5b for the cases $Z_p=40$ and 60 above the transition point are almost the same for $r > l_D$. This fact is qualitatively consistent with Manning’s treatment, where the “unbound” counterions are treated by the linear Debye–Hückel theory, neglecting the effects of the polyelectrolyte charge. Also as indicated in Fig. 5 the effect of the applied electric field is to reduce the charge in the vicinity of the polyelectrolyte compared to the zero-field value, in contrast to Manning’s theory of the electrophoresis of polyelectrolytes for $\xi > 1$ [12] and its generalizations [13, 14, 15, 16].

Experiments have just begun to probe counterion structure and dynamics in polyelectrolyte solutions at nanometer and nanosecond scales. Small-angle neutron scattering measurements of the counterion-counterion structure factor [17] indicate that the counterions are strongly correlated with the polymer chain so as to mimic the pair correlations typical for the polymer, indicating that counterions are localized in the vicinity of the polyions. Similarly, small-angle neutron and X-ray measurements [18] provide evidence for counterion localization below the Debye layer, and inelastic X-ray scattering measurements [19] find phonon-like excitations in the counterion distribution, indicating the presence of a correlated structure. Electron paramagnetic resonance spectroscopy studies [20] of counterion dynamics gave direct evidence for the existence of preferred sites corresponding to the charged groups of the polyelectrolyte, where the counterions are electrostatically attached directly with no solvent molecule in between. Such “site bound” counterions presumably correspond to the bound counterions inside the Bjerrum layer observed in our simulations. We find that such counterions enter and leave the Bjerrum layer with a time scale around $\tau_D \approx 0.1$ ns, while the experiments find that the exchange rate constant for the the “site-bound” counterions is significantly larger than $10^5$ s$^{-1}$, implying a lifetime shorter than 1 ns, consistent with our result. Lastly, recent experimental findings related to polyelectrolyte electrophoretic mobility [21] argue that an ion pairing mechanism (Bjerrum association [22]) resembling triplet formation may play a role in the process of counterion condensation.

In summary, our simulations provide insight into the previously unexplored local dynamics of counterion condensation on a mobile and flexible polyelectrolyte, both above and below the condensation transition. We find that strong long-ranged Coulomb interactions cause counterions to form weakly-interacting transient clusters around the polyelectrolyte, which exhibit short range orientational order. The counterion clustering is robust to changes in the degree of ionization as well as to the application of an external electric field, and the cluster decay results from ion diffusion in and out of the charged double layer about the polyelectrolyte. Both the presence of clusters and their finite lifetime is qualitatively consistent with experimental data. The classical counterion condensation theory is only consistent with the local charge distribution at much longer time scales. Our results provide a framework for further theoretical and experimental studies of the dynamics of counterion-charged polynner association at nanometer and nanosecond scales, information essential for understanding the electrophoretic behavior of these molecules, as well as the interaction and binding of ligands to biological polyelectrolytes.

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\[\text{FIG. 5: Charge distribution around a polyion for } Z_p=20, 40 \text{ and } 60 \text{ with and without an applied electric field. The horizontal arrows indicate the charge of condensed counterions predicted by Manning’s theory in each case for } \xi > 1.\]

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