Published in final edited form as:

Chemphyschem. 2009 November 9; 10(16): 2871–2875. doi:10.1002/cphc.200900525.

DNA Condensation by Field-Induced Non-Equilibrium Noise

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Abstract

DNA molecules under good solvent conditions condense when subjected to strong AC electrical fields. It is shown that AC electrical fields couple charge fluctuations to molecular shape fluctuations, which produces a non-equilibrium noise source that dominates over equilibrium thermal noise in the long wavelength limit. These field-induced excess charge fluctuations amplify the Asakura-Oosawa fluctuation attraction force between neighboring chains, providing a mechanism for field-induced DNA condensation.

Gel electrophoresis of DNA molecules is an important tool for the separation of DNA molecules of different length. For the electrical field strengths typically used in electrophoresis experiments, the DNA molecules are stretched-out along the field direction¹. This is consistent with theoretical studies of the polarization energy of polyelectrolyte molecules, which find that it should increase as the cube of the length of a molecule if it is aligned with the field direction². It was a surprise therefore that for AC electrical fields in the 10^4 - 10^5 V/m range and frequencies in the 300-700 Hz range, λ -phage DNA molecules confined in channels seemed to *collaps*³. Condensation phenomena of DNA solutions in AC electrical fields had actually been reported earlier^{4,5}. Interestingly, the condensation is observed only over a limited frequency range and a limited range of field strengths. In particular, for fields above 10^5 V/m, the molecules were stretched⁶. The condensation was attributed by the authors of Ref.3 to polarization attraction between sections of the DNA molecule with opposite curvature.

Under conditions of thermodynamic equilibrium, condensation of DNA can be induced by adding low concentrations of polyvalent counterions⁷ to the solution. It is believed that correlated, out-of-phase charge fluctuations of the counterions condensed on neighboring chains generate an effective attractive force, a mechanism - first proposed by Asakura and Oosawa (AO) in 1958⁸ - that is akin to van der Waals attraction. For monovalent counterions, this attraction is not strong enough to overcome the electrostatic repulsion, at least under ambient conditions. We will demonstrate below that AC electrical fields in a limited frequency window and a limited field strength window do generate enhanced coupled charge-curvature fluctuations. These field-enhanced fluctuations significantly amplify the AO fluctuation attraction mechanism and is, we argue, responsible for the observed collapse. Before discussing the field-enhanced fluctuations, we first examine the time-averaged polarization energy of a semi-flexible polyelectrolyte molecule under AC conditions and discuss why the electrophoretic stretching effect⁹ weakens as the drive frequency increases. Next, we show that curvature and charge fluctuations are strongly coupled under AC conditions, followed by a discussion of the AO attraction under these conditions, after which we conclude.

The paper certainly does not present anything like an exact theory of this problem. DNA molecules in AC electrical fields are subject to viscous drag, dielectrophoretic effects¹⁰ and field-induced hydrodynamic flows¹¹. Specifically, we will make a number of simplifying

assumptions to illustrate the mechanism that is being proposed: (i) the collection of condensed counterions along the DNA backbone is treated as a conducting, one-dimensional ionic “wire” with no charge exchange with the surrounding medium, (ii), we neglect electrokinetic effects apart from those associated with the condensed counterions, (iii) we assume that the frequency is sufficiently high so the center of mass of the DNA molecule does not “follow” the AC electrical field¹². We also will follow the worm-like chain model of DNA and treat it as a uniform semi-flexible polyelectrolyte with a persistence length l_p of about 500 Å and a “bare” negative charge per unit length $\rho_0 = -e/b$, with $b \sim 1.7$ Å. Because of Manning condensation⁷, positively charged, mobile counterions are condensed along the molecule with a charge per unit length $e/b - e/l_b$. The effective charge per unit length $-e/l_b$ of the molecule is significantly smaller than the bare charge per unit length. The Bjerrum length l_b is defined here by the condition $e^2 / \epsilon_w l_b = k_B T$. The remaining neutralizing counterions are not bound.

Under these restrictions, an applied AC electrical field will drive an oscillating electrical current of counter-ions along the curving DNA molecule. Let s be the arc distance along the molecule, $\hat{t}(s,t)$ the local tangent unit vector and $\rho(s,t)$ the counterion charge-density along the molecule induced by a time-dependent AC electrical field $\vec{E}(t)$. If there is no ion exchange between the condensed counterions and the aqueous medium then $\rho(s,t)$ must obey a one-dimensional Nernst-Planck (NP) equation. For $\rho(s,t)$ small compared to ρ_0 the NP equation can be linearized, giving:

$$\frac{\partial \rho}{\partial t} = \frac{\partial}{\partial s} \left(D \frac{\partial \rho}{\partial s} - \mu \rho_0 e \vec{E}(t) \cdot \hat{t}(s,t) \right) \quad (1)$$

Here, μ is the counterion mobility related to the ion diffusion coefficient D by $D = \mu k_B T$. The term in brackets is (minus) the counter-ion current

For now assume that the molecule has a fixed, time-independent shape. For an AC electrical field with frequency Ω , the general solution of Eq. (1) for a time-independent shape of the molecule is easy to find:

$$\rho_\Omega(s) = -e^{-i\pi/4} \frac{\rho_0 e \vec{E}_\Omega}{2kT} \sqrt{\frac{D}{\Omega}} \int ds' \exp \left(-e^{i\pi/4} \sqrt{\frac{\Omega}{D}} |s - s'| \right) \left(\frac{d\hat{t}(s')}{ds'} \right) \quad (2)$$

with $\rho(s,t) = \text{Re}\{\rho_\Omega \hat{b}(s) \exp(i\Omega t)\}$, as can be verified by substitution. In order to satisfy the zero current boundary conditions at any endpoints of the molecule, solutions of the

homogeneous equation $i\Omega \rho_\Omega = D \frac{d^2 \rho_\Omega}{ds^2}$ have to be added but we will assume a circular DNA molecule without endpoints. Note that the curvature of the chain acts as a “source” term for the induced charge density. It follows from Eq.(2) that the length scale $\xi = \sqrt{D/\Omega}$ plays the role of a *correlation length*: induced polarization charges are correlated with the chain

curvature $\frac{d\hat{t}(s)}{ds}$ within arc distances less than ξ . For a 300 Hz AC field, ξ is in the range of microns, assuming Na^+ counterions.

The central role of this correlation length, which was emphasized earlier by Cohen¹³, can be better appreciated by considering a special conformation: a *kink* in the DNA molecule, which would be generated by stretching the DNA loop along the field direction (it could also be produced by certain DNA-binding proteins or by specific DNA sequences). First assume

that the DNA molecule has the shape of a single kink, located at $s=0$, connected to two infinite, perfectly straight sections. The appropriate solution of Eq.2:

$$\rho_{\Omega}(s)/\rho_0 \sim e^{-i\pi/4} \frac{e \vec{E}_{\Omega} \cdot \Delta \hat{t} \xi}{2kT} \exp\left(-e^{-i\pi/4} |s|/\xi\right) \quad (3)$$

is proportional to the change $\Delta \hat{t}$ of the tangent vector on opposite sides of the kink. For field strengths of 10^4 V/m and frequencies in the 100 Hz range, the RHS is of the order of one at $s=0$, i.e., sufficient for charge reversal of the DNA chain. For higher field strengths, the linearization approximation is apparently invalid. The charge density decays, in an oscillatory fashion, over a distance of the order of ξ . The amplitude of the charge oscillation localized around the kink is

$$Q_{\Omega} \sim \frac{\rho_0 e \vec{E}_{\Omega} \cdot \Delta \hat{t} \xi^2}{2kT} \quad (4)$$

For ξ one μm and a field strength of 10^4 V/m, this corresponds to about 10^4 elementary charges distributed over a distance of the order of ξ .

Next, assume a DNA loop has a length L large compared to the correlation length. The loop is stretched along the field direction, with two kinks on opposite ends separated by two strands of length $L/2$. Polarization charges with opposite sign accumulate at the two kinks at

the two ends of the loop, producing an effective *tension* $T_{\Omega} \sim E_{\Omega} Q_{\Omega} \sim \frac{\rho_0 e \xi^2}{2k_B T} E_{\Omega}^2$ that is proportional to the square of the field strength and inversely proportional to the drive frequency. As discussed in the Appendix A, the introduction of such a tension is equivalent to the statement that under AC conditions the DNA chain is effectively a string of polarizable dielectric “units”, each with a length ξ , whose dipole moment tries to align with the field (see also Ref.13). If one increased the length of the loop from zero to L then the work done by the field would be of the order of $T_{\Omega} L / 2$. In Appendix A we compute the polarization energy by standard methods and confirm that it indeed is of order $T_{\Omega} L$. For field strengths of the order 10^4 V/m and 300 Hz frequencies, the tension is of the order of picoNewtons (pN). Next, fold the loop to form a smaller *double* loop, and stretch the double loop along the field, so there are two positively charged kinks and two negatively charged kinks linked by four parallel strands with a length $L/4$. The total work $2 \times (T_{\Omega} L / 4)$ done by the field separating the polarization charges is the same as before. In terms of polarization energy, there is thus an approximate degeneracy between the single and double loop (see also Ref.13). The argument can be extended to multiple doublings until the separation between the kinks is of the order of the correlation length. In Appendix A we show that if the correlation length is larger than L , then the single loop has a much lower polarization energy. One might expect the total *free* energy of the single loop to be lower than that of the folded loops, since that would seem to interfere least with conformational chain fluctuations. That, as we shall see below, need not be the case.

Charge-Curvature Fluctuations

We will examine time-dependent charge and curvature fluctuations in the presence of thermal noise, focusing on the simple case of two dimensions where the conformation fluctuations can be described by just a single angle variable $\theta(s, t)$ between the tangent and the field direction. The charge and shape fluctuations will be described by two coupled Langevin equations for $\theta(s, t)$ and $\rho(s, t)$. Starting with the charge fluctuations, we will assume that, in the absence of the applied AC electrical field, the equilibrium fluctuation

spectrum of the charge degree of freedom is Gaussian: $\langle \rho(q)^2 \rangle_{eq} / \rho_0^2 \sim L \frac{k_B T}{B}$ with B the line compressional modulus of the system of counterions. In the Poisson-Boltzmann (P-B) approximation the compressional modulus is of the order of $k_B T \rho_0 / e \sim k_B T / b$. In the presence of the AC field, the line density is assumed to obey a NP equation with conserved noise:

$$\frac{\partial \rho}{\partial t} = \frac{\partial}{\partial s} \left(D \frac{\partial \rho}{\partial s} - \mu \rho_0 e \vec{E}(t) \cdot \hat{t}(s, t) + \eta(s, t) \right) \quad (5)$$

with $\eta(s, t)$ representing equilibrium voltage fluctuations along the chain. The thermal voltage fluctuations are in series with an effective, non-equilibrium noise source

$\chi(s, t) \equiv \mu \rho_0 e \vec{E}(t) \cdot (\hat{t}(s, t) - \langle \hat{t} \rangle)$, which we will examine below in more detail. The thermal noise spectrum follows in the usual way from the fluctuation-dissipation theorem.

From the Fourier transform $\rho(q, \omega) = \frac{i q \eta(q, \omega)}{(i \omega + D q^2)}$ with respect to arc length and time, for $\vec{E}(t) = 0$, one obtains an equilibrium spectrum:

$$\langle |\rho(q)|^2 \rangle = \int d\omega \langle |\rho(q, \omega)|^2 \rangle = \int d\omega \frac{q^2 \langle |\eta(q, \omega)|^2 \rangle}{(\omega^2 + D^2 q^4)} \quad (6)$$

This is consistent with $\langle \rho(q \rightarrow 0)^2 \rangle / \rho_0^2 \sim L \frac{k_B T}{B}$ if one imposes a white-noise spectrum

$$\langle |\eta(q, \omega)|^2 \rangle \sim L \rho_0^2 \frac{D k_B T}{B} \quad (7)$$

(we will set $L=1$ below). The “propagator” for charge fluctuations is thus

$$\langle |\rho(q, \omega)|^2 \rangle / \rho_0^2 = \frac{D k_B T}{B} \frac{q^2}{(\omega^2 + D^2 q^4)} \quad (8)$$

For the Langevin equation of the shape fluctuations of the chain, we will use the Rouse model, which is believed to be reasonable for stretched DNA molecules¹⁴. For the lateral displacement u of the chain in the direction perpendicular to the field, with $\theta \sim u / s$, the equation of motion is:

$$\frac{\partial u}{\partial t} = \zeta \left(k_B T l_p \frac{\partial^4 u}{\partial s^4} + T_\Omega \frac{\partial^2 u}{\partial s^2} \right) + \psi(s, t) \quad (8)$$

Here, ζ^{-1} is the drag coefficient per unit length (of the order of the fluid viscosity). Note that we can interpret ζT_Ω as an effective diffusion coefficient for shape fluctuations and that the charge degree of freedom only enters the Langevin equation through the effective tension

$T_\Omega \sim \frac{\rho_0 e \xi^2}{2 k_B T} E_\Omega^2$. The spectrum of the thermal noise $\psi(s, t)$ follows again from the fluctuation-dissipation theorem:

$$\langle |\psi(q, \omega)|^2 \rangle \sim \zeta k_B T \quad (9)$$

The propagator for angle fluctuations is thus:

$$\langle |\theta(q, \omega)|^2 \rangle \sim \frac{\zeta k_B T q^2}{\omega^2 + \zeta^2 [(k_B T l_p) q^4 + T_\Omega q^2]^2} \quad (10)$$

The wavenumber $q_T = (T_\Omega / (k_B T l_p))^{1/2}$ for the cross-over from the quartic bending mode spectrum to the quadratic tension mode spectrum will play an important role below. If the tension is in the range of a pN, then the associated wavelength is about five nm. Note that for long wavelengths, the angle and charge propagators have the same mathematical form.

The angle fluctuations determine the spectrum of the non-equilibrium noise source

$\chi(s, t) \sim \frac{1}{2} \mu \rho_0 e E_x(t) (\theta^2(s, t) - \langle \theta^2 \rangle)$. The fact that this is a *non-linear* function of the angle variable introduces rather interesting but distracting mathematical complications that have to be addressed using the method of Feynman diagrams. If, however, the strand is maintained at a finite average angle $\langle \theta \rangle$ with respect to the field direction by some external constraint, such as a channel confining the molecule, then one can employ a linearization approximation $\theta^2(s, t) - \langle \theta^2 \rangle \sim \langle \theta \rangle^2 - \langle \theta^2 \rangle + 2 \langle \theta \rangle \delta \theta(s, t)$. In this case, after a Fourier Transform, one obtains $\chi(q, \omega) = \chi_+(q, \omega) + \chi_-(q, \omega)$ with

$$\chi_\pm(q, \omega) \sim \mu \rho_0 e \langle \theta \rangle E_\Omega \delta \theta(q, \omega \pm \Omega) \quad (11)$$

The power spectrum of the non-equilibrium noise is then proportional to that of the angle fluctuations. Adding equilibrium and non-equilibrium contributions:

$$\langle |\rho(q, \omega)|^2 \rangle / \rho_0^2 \sim \frac{q^2}{(\omega^2 + D^2 q^4)} \left\{ \frac{D k_B T}{B} + \frac{(\mu e E_\Omega)^2 \langle \theta \rangle^2 \zeta k_B T q^2}{(\omega \pm \Omega)^2 + \zeta^2 [(k_B T l_p) q^4 + T_\Omega q^2]^2} \right\} \quad (12)$$

The first term is the thermal equilibrium contribution to the charge fluctuations. It is immediately clear that the non-equilibrium noise term cannot be absorbed by introducing an effective “noise temperature”. For example, the power spectrum has a pronounced maximum when the drive frequency is set equal to plus or minus the drive frequency Ω , the analog of Stokes and anti-Stokes lines. The non-equilibrium noise term diverges at that point

as $\frac{(\mu e E_\Omega)^2 \langle \theta \rangle^2 k_B T}{\zeta T_\Omega^2 q^2}$ in the long wavelength limit, while the equilibrium contribution stay finite. Quite similar non-equilibrium noise-enhancement phenomena have been discussed, for example, for the case of active motor proteins interacting with polymer networks¹⁵ and of active membranes¹⁶. After integrating over frequency, one obtains in the limit of small Ω the following steady-state fluctuation spectrum:

$$\langle |\rho(q)|^2 \rangle / \rho_0^2 \sim \frac{k_B T}{B} + \frac{k_B T (\mu e E_\Omega \langle \theta \rangle)^2 q^{-2}}{D [T_\Omega + (k_B T l_p) q^2] (D + \zeta [T_\Omega + (k_B T l_p) q^2])} \quad (13)$$

This expression is valid only for low frequencies. Below, we will encounter a wavenumber “infrared” cut-off, denoted by $q_{\min}$. If the drive frequency Ω exceeds $\zeta [(k_B T l_p) q_{\min}^4 + T_\Omega q_{\min}^2]$, then the infrared divergence of the curvature fluctuations are weakened. We will denote the RHS of Eq.14 by $S^{-1}(q)$, where $S(q)$ plays the role of a non-equilibrium *structure factor* for charge fluctuations. The cross-over wavenumber below which the non-equilibrium noise dominates is:

$$\tilde{q}_\Omega = \begin{cases} \frac{eE_\Omega \langle \theta \rangle}{k_B T} \sqrt{\frac{DB}{T_\Omega (\zeta T_\Omega + D)}} & q_T \gg \tilde{q}_\Omega \\ \left(\frac{B(eE_\Omega \langle \theta \rangle / k_B T)^2}{k_B T l_p} \right)^{1/4} & q_T \ll \tilde{q}_\Omega \end{cases} \quad (14)$$

Since the traction is proportional to the square of the field strength, q_Ω has a *maximum* as a function of field strength when $q_T \sim q_\Omega$. In the long-wavelength limit, the fluctuation spectrum can be approximated as

$$S^{-1}(q) \sim \frac{k_B T}{B} \left(1 + \frac{\tilde{q}_\Omega^2}{q^2} \right) \quad (15)$$

If the strand is aligned with the field, then the non-linear nature of the noise must be explicitly accounted for. It can be shown that, apart from replacing $\langle \theta \rangle^2$ by $\langle \theta^2 \rangle$, the above results do remain valid but only for short wavelengths and high frequencies. For long wavelengths and low frequencies there are important differences. If, for example, one sets ω

$= \Omega = 0$, then the non-equilibrium noise diverges as $\frac{(\mu e E_\Omega)^2 k_B T}{\zeta T_\Omega^2 |q| (T_\Omega / k_B T)}$ in the long wavelength limit, not as $1/q^2$. The infrared divergence is thus weakened if the molecule is fully aligned with the field direction.

Fluctuation Attraction

We are now in a position to study DNA condensation induced by the AO mechanism. Recall that we found that the single loop and the doubled loop have approximately the same polarization energy. In this section we will show that there is a fluctuation attraction that favors the folded loop structure over the single loop and that favors rotation the strand in the direction perpendicular to the field. Specifically, by pairing a section with negative curvature of one chain with a section having positive curvature of another chain, there can be a Coulomb attraction between the induced charges of the two chains.

Assume an array of parallel DNA chains spaced by a distance d . The effective quasi-equilibrium Hamiltonian for the interaction between just two of the chains (1 and 2) would be:

$$H(\{\rho(s_1)\}, \{\rho(s_2)\}) = \frac{k_B T}{2} \int S^{-1}(q) \rho_0^{-2} \left\{ |\rho_1(q)|^2 + |\rho_2(q)|^2 \right\} dq + \frac{1}{2\epsilon_W} \iint ds_1 ds_2 \frac{\rho_1(s_1) \rho_2(s_2)}{\sqrt{(s_1 - s_2)^2 + (d + u(s_1) - u(s_2))^2}} \quad (16)$$

The first two terms describe the field-dependent charge fluctuations of the two chains as Gaussian with a variance equal to the structure factor. The second term is the (unscreened) Coulomb interaction between the chains with $u(s_1)$ and $u(s_2)$ the chain displacements in the direction normal to the chains. It is known that in order to maintain a mean orientation for a parallel array of strands, long-wavelength curvature fluctuations must be suppressed¹⁷. In the study of shape fluctuations of arrays of linear molecules or membranes this done by imposing an infrared cut-off $q_{\min}$ on the curvature fluctuations so $\langle u^2 \rangle = d^2$. The inverse of $q_{\min}$, also known as the “Odijk collision length”, is large compared to the spacing d between the chains and there is an entropic repulsive force per unit length between the chains, due to confinement, that is of the order of $k_B T q_{\min}$. In the present case, this cut-off is determined

by the condition $\frac{k_B T}{(k_B T l_p) q_{\min}^3 + T_{\Omega} q_{\min}} \sim d^2$. This cut-off also truncates the infrared divergence of the non-equilibrium charge-curvature fluctuations. It follows that $q_{\min} \sim \frac{k_B T}{T_{\Omega} d^2}$ if $q_{\min}$ is larger than q_T while $q_{\min} \sim \left(\frac{1}{l_p d^2}\right)^{1/3}$ in the opposite case. If one now computes the free energy

$$F = -k_B T \ln \int D(\{\rho(s_1)\}) D(\{\rho(s_2)\}) \exp(-H(\{\rho(s_1)\}, \{\rho(s_2)\}) / k_B T) \quad (17)$$

by expanding, to second order, in powers of the interaction term, one obtains a chain-chain attractive energy per unit length:

$$U(d) \sim -\frac{k_B T e^4}{2\pi \varepsilon_w^2 B^2} \left\{ \frac{1}{d} \int_0^{\infty} dx K_0^2(x) + \int_{q_{\min}(d)}^{\infty} dq \left(2(\tilde{q}_{\Omega}/q)^2 + (\tilde{q}_{\Omega}/q)^4 \right) K_0^2(qd) \right\} \quad (18)$$

with $K_0(x)$ a Bessel function. Note that the infrared cutoff only applies to the charge-charge curvature fluctuations. The first term inside the curly brackets provides an attractive energy

per unit length of the order of $-\left(\frac{l_b}{b}\right)^2 \frac{k_B T}{d}$. This is the usual OA fluctuation attraction, which is inversely proportional to the spacing. As mentioned, under ambient conditions with monovalent counterions, this attraction is not able to overcome electrostatic repulsion. The second term is due to the non-equilibrium charge fluctuations. It actually *increases* in strength as the inter-strand spacing d grows, although it obviously will be limited by the electrostatic screening. This dependence is due to the fact that the infrared cutoff decreases with increasing d . The condition for the non-equilibrium attractive force to exceed the equilibrium attractive force is for $q_{\Omega}^4 / q_{\min}(d)^3$ to be large compared d^{-1} so we can view $dq_{\Omega}^4 / q_{\min}(d)^3$ as a dimensionless coupling constant that measures the relative strength of the non-equilibrium fluctuation attraction. This coupling constant exceeds one if d exceeds a characteristic distance, which for 10^4 V/m and 100 Hz is in the 10 nm range.

Does this mechanism provide a framework for interpreting the observations discussed in the introduction? In particular, is it operative only over a limited field and frequency range?

First, recall that for a fixed field strength of 10^4 V/m, the traction $T_{\Omega} \sim \frac{\rho_0 e \xi^2}{2kT} E_{\Omega}^2$ is about one pN in the 300 Hz range. Since the traction is inversely proportional to frequency so reducing the frequency to 30 Hz, would increase the traction force to 10 pN range, which would quite strongly suppress curvature fluctuations. Separately, at low frequencies viscous drag effects by electrophoretic center of mass motion must be included that also add to the tension¹⁹. In terms of the dimensionless coupling constant $dq_{\Omega}^4 / q_{\min}(d)^3$, both characteristic wavenumbers are inversely proportional to the traction in that regime so the coupling constant itself is proportional to frequency in the low frequency limit. For frequencies large compared to 300 Hz on the other hand, the traction force is negligible while the characteristic frequencies are independent of frequency for high frequencies, according to our results. Increasing would seem to amplify the non-equilibrium noise. However, as noted below Eq.13, for frequencies above $\zeta(k_B T l_p) q_{\min}^4$ transverse long-wavelength curvature fluctuations are suppressed because they no longer can “follow” the field (recall that longitudinal center-of-mass motion cannot follow the field for frequencies above 10^2 Hz). For spacings in the range of 100 Angstrom, this cross-over frequency is about 10^4 Hz. There is thus indeed an optimal frequency range for collapse.

Next, if one varies the electrical field strength for a frequency fixed at 300 Hz, then for field strengths exceeding 10^4 V/m, ζT_Ω exceeds the diffusion coefficient D . The wavenumber scale q_Ω is inversely proportional to the traction force and hence inversely proportional to

the square of the field strengths while $q_{\min} \sim \frac{k_B T}{d^2 T_\Omega}$ also is inversely proportional to the square of the field strength. It follows that the strength of the fluctuation attraction decreases with field strength as $1/E_\Omega^2$. In the opposite limit of very low field strengths, where ζT_Ω is less than D , the coupling constant $dq_\Omega^4 / q_{\min} (d)^3 q_\Omega$ decreases proportional to field strength because $q_{\min}$ is independent of field strength at low tractions in this regime. There is thus indeed an intermediate range for condensation both in terms of field strengths and frequency.

Verifying the model presented in this paper should be straightforward. The coupling constant for fluctuation attraction $dq_\Omega^4 / q_{\min} (d)^3$ is proportional either to $\langle \theta \rangle$ or to $\langle \theta \rangle^4$. That means that in the condensed state, the fluctuation force exerts a *rotary torque* that attempts to rotate the strands in the direction perpendicular to the field. The strands are thus expected to show a zig-zag pattern in the condensed state. Recall that if the strands really are perfectly aligned with the field, then the fluctuation attraction is weakened. One thus expects there to be two states, one with the strands aligned with the field with weak fluctuation attraction no condensation and a second state with the strands at an angle and strong fluctuation attraction and condensation. As the field strength is adjusted, the relative fraction of these two states should shift, which should be clearly visible by microscopy.

Acknowledgments

RB would like to acknowledge support by the NSF under DMR Grant No. 04-04507.

Appendix A

In this Appendix, we compute the polarization energy of the chain by standard statistical mechanics methods. First, perform a Fourier transform of the relation between the charge and curvature of the molecule (Eq.(1)), giving

$$\rho_\Omega(q) = i \frac{\rho_0 e}{2kT} \frac{D}{\Omega} \vec{E}_\Omega \cdot \delta \vec{\theta}(q) \left(\frac{1}{1 - i \frac{D}{\Omega} q^2} \right) \quad (\text{A1})$$

with $\delta \vec{\theta}(q)$ the Fourier transform of the local curvature vector $\frac{d\hat{t}(s)}{ds}$. The low frequency limit $\rho(q) \sim -\frac{\rho_0 e}{2kT} \vec{E}_\Omega \cdot \vec{r}(q)$ is the equilibrium excess charge density induced by a DC field obtained by expanding the Boltzmann distribution to first order in the field. The induced oscillating dipole moment is

$$\vec{P}_\Omega(t) \propto \text{Re} \{ \exp(i\Omega t) \int ds \rho_\Omega(s) \vec{r}(s) \} \quad (\text{A2})$$

Performing a Fourier transform of both charge density and displacement in this expression, use Eq.(A1) and perform a time-average. The result can be expressed in the form of polarization tensor:

$$\alpha_{ij} \sim \frac{\rho_0 e}{kT} \int dq \frac{\langle \delta \vec{\theta}_i(q) \delta \vec{\theta}_j(-q) \rangle}{\xi^{-4} + q^4} \quad (\text{A3})$$

with $P_i = \alpha_{ij} E_j$. The time-averaged polarization energy is $-\frac{1}{2} \alpha_{ij} E_{i\Omega} E_{j\Omega}^*$.

In the very low frequency limit, where the correlation length is large compared to the chain length, ξ^{-4} can be set to zero. After a reverse Fourier transform, the polarizability tensor:

$$\alpha_{ij}(\Omega \rightarrow 0) \sim \frac{\rho_0 e}{k_B T} \int ds \langle r_i(s) r_j(s) \rangle \quad (\text{A4})$$

reduces to the usual result that α_{ij} is proportional to the second moment of the displacement vector of a molecule. If the DNA molecule is a random coil with the shape of a prolate ellipsoid having long axis $R_{\parallel}$ along the field direction and short axes $R_{\perp}$ perpendicular to

the field then the polarizability tensor is a uniaxial tensor with components $\alpha_{\perp} \sim \frac{\rho_0 e L}{k_B T} R_{\perp}^2$ and $\alpha_{\parallel} \sim \frac{\rho_0 e L}{k_B T} R_{\parallel}^2$ so the polarization energy is of the order of $-\frac{\rho_0 e L}{k_B T} E_{\Omega}^2 R_{\parallel}^2$. The polarization energy favors stretching the ellipsoid along the field direction, which is opposed by entropic elasticity:

$$F(R_{\parallel}) \sim \frac{k_B T}{l_p} R_{\parallel}^2 - \frac{\rho_0 e L}{k_B T} E_{\Omega}^2 R_{\parallel}^2 \quad (\text{A5})$$

For electrical field strengths greater than $E_c(\Omega \rightarrow 0) \sim k_B T \frac{1}{L} \sqrt{\frac{1}{e \rho_0 l_p}}$ the polarization energy overcomes the entropic elasticity and the molecule will stretch out. For a 30 μm DNA chain, this field strength is of the order of one V/m, which is very modest compared to the electrical field strengths used during electrophoresis, so based on the polarization energy alone the molecules indeed should be stretched out along the field direction. In that case, the

polarizability $\alpha_{\parallel} \sim \frac{\rho_0 e L^3}{k_B T}$ is proportional to the *cube* of the chain length, another well-known result¹⁸. That means that if a loop is doubled to form two loops of half the size – as discussed in the main text – then the polarization is reduced by a factor four. In the DC limit, viscous drag opposing electrophoresis adds on top of this another contribution that tends to stretch the molecule¹⁹.

For finite frequencies where the correlation length is less than the chain length, the polarizability tensor is reduced since the integral over wavenumber in the polarizability tensor no longer diverges as $1/q^4$. In effect, the previous description still can be applied but now only on length scales less than the correlation length. The molecule must be viewed as a *dielectric* string of L/ξ polarizable segments with each segment a one-dimensional ionic

conductor. The total polarizability tensor is then of the order of $\alpha_{\parallel} \sim \frac{\rho_0 e L}{k_B T} r_{\parallel}(\xi)^2$ with $r_{\parallel}(\xi)$ the typical spatial dimension of one of the segments. Repeating the earlier argument, but now for a segment of length ξ , it follows that for field strengths above

$E_c(\Omega) \sim k_B T \frac{1}{\xi} \sqrt{\frac{1}{e \rho_0 l_p}}$ the segments – and hence the molecule – will be elongated along the field direction. For a 30 μm DNA chain at 100 Hz, this field strength is of the order 10² V/m, still well below the experimental field strengths. In the stretched state, the AC

polarizability $\alpha_{\parallel} \sim \frac{\rho_0 e L \xi^2}{k_B T}$ is proportional to the chain length, not the cube of the chain

length so the doubled loop has the same polarization energy as the loop itself. The

corresponding polarization energy $\frac{\rho_0 e L \xi^2}{k_B T} E_\Omega^2$ is the result $T_\Omega L$ obtained for the work done by the field separating the polarization charges at the end of the stretched loop.

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