

SHORT-RANGE DISORDER IN POLYELECTROLYTES:
REPLICAS AND CONSTRAINED ANNEALING COMPARISON

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The general formalism describing polyelectrolyte behavior in presence of sequence disorder is presented. The Edwards and Poisson–Boltzmann equations are obtained. The possible effect of the boundary conditions is discussed. Comparison between replica and constrained annealing approaches is made.

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Introduction. The structure and properties of macromolecules are governed by interactions over different length scales including van der Waals and electrostatic, hydrogen bond forming, etc. In the present study we will focus mainly on the biological polymers, which are heteropolymers comprised of monomers of different types. At the same time, biological macromolecules are polyelectrolytes, i.e. contain ionizable groups [1] able to disassociate in water, leaving charges on polymer chains and releasing counter ions in solution.

Polyelectrolytes are ubiquitous in nature and exhibit rich phase behavior. Some of them (e.g. proteins) are polyampholytes and bear both cationic and anionic repeat groups. The others (e.g. nucleic acids) are polyanions, carrying negative charges on the nucleotides.

Polyelectrolytes have been extensively investigated both theoretically [2–15] and experimentally [16]. Great progress was made in understanding their characteristics in solutions at different concentrations ranging from dilute to dense.

The phase behavior of the polyelectrolytes substantially depends on the fact, whether the heterogeneity is coupled with the short or long-ranged interactions. For instance, a collapse transition for a neutral chain of a polyampholyte (heteropolymer with long-range interactions) in three-dimensions has been reported in presence of salt [17]. However, a modulated or frozen phase for the polyampholytes has not been observed, even at very low temperatures. This is different from the well-known phase behavior of the heteropolymers with short-range interactions [18], where freezing transition is known to happen at temperatures low enough.

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Systems containing biological polyelectrolytes are often governed by both long-range (electrostatic) and short-range interactions. In particular, when considering the problems of RNA folding, self-assembly of viruses etc. [19, 20] non-specific electrostatic repulsion between chain segments of single-stranded RNA (ssRNA) or single-stranded DNA (ssDNA) competes with the sequence-specific Watson–Crick base pair formation. Such an interplay needs to be properly accounted for and in this paper we present an example of such consideration.

Polyelectrolytes with Short-Range Disorder. We consider a generic flexible polyelectrolyte comprised of equally charged monomers with disorder, which is conditioned by the short-range features only (e.g., ssRNA or ssDNA). The charge per monomer is assumed to be equal to pe , where e is the electron charge and $0 < p < 1$. The position of a monomer is considered in a continuous way as $\mathbf{r}(\tau)$, where $\tau \in [0, N]$ and N is the dimensionless length of the chain. The random sequence of the chain assumes that the type of the τ -th monomer is described by the variable ξ_τ . $\{\xi\}$ s are considered to be independent random variables drawn with the same probability law. Thus, the overall probability distribution of the sequence $\{\xi\}$ is

$$\mathcal{P}\{\xi\} = \prod_{\tau} p(\xi_{\tau}), \quad (1)$$

where the sequence disorder is supposed to be Gaussian

$$p(\xi_{\tau}) = \frac{\exp(-\frac{\xi_{\tau}^2}{2\xi^2})}{\sqrt{2\pi\xi^2}}. \quad (2)$$

The Hamiltonian of the system in this case reads

$$\beta\mathcal{H} = \frac{3}{2\ell^2} \int_0^N d\tau (\partial_{\tau}\mathbf{r}(\tau))^2 + \frac{\beta}{2} \int_0^N d\tau \int_0^N d\tau' v_{\tau\tau'}(\mathbf{r}(\tau) - \mathbf{r}(\tau')) + \beta V\{\mathbf{r}\}, \quad (3)$$

where ℓ is the length of the Kuhn segment, $V_{el}\{\mathbf{r}\}$ describes the interaction between polyelectrolyte, counter-ions, viral capsid, etc., and

$$v_{\tau\tau'}(\mathbf{x}) = v_0 \xi_{\tau} \xi_{\tau'} \delta(\mathbf{x}) \quad (4)$$

with the positive interaction constant $v_0 > 0$. Thus, the different monomers will attract, but the similar ones will repel.

The partition function of the polyelectrolyte for every fixed sequence $\{\xi\}$ writes

$$Z\{\xi\} = \int \mathcal{D}\mathbf{r} e^{-\beta\mathcal{H}}. \quad (5)$$

In the limit of $N \rightarrow \infty$, the free energy of a disordered system obeys the principle of self-averaging [21]:

$$\mathcal{F} = -k_B T \langle \ln Z\{\xi\} \rangle_{\mathcal{P}}, \quad (6)$$

where $\langle \dots \rangle_{\mathcal{P}}$ means averaging with the distribution function (1). Self-averaging physically means that the distribution of the free energy has a very narrow peak in the vicinity of the point of maximum, corresponding to the mean value of free energy (6).

Free Energy Calculation: Replica Trick and Constrained Annealing.

The quenched free energy (6) can be estimated using the replica trick [21]

$$-\beta\mathcal{F} = \lim_{n \rightarrow 0} \frac{\langle Z\{\xi\}^n \rangle_{\mathcal{P}} - 1}{n}, \quad (7)$$

where $\beta = (k_B T)^{-1}$. Now we need to calculate the n -replica partition function as

$$\begin{aligned} \langle Z\{\xi\}^n \rangle_{\mathcal{P}} &= \int \mathcal{D}\mathbf{r} e^{-\frac{3}{2\ell^2} \sum_{a=1}^n \int_0^N d\tau (\partial_\tau \mathbf{r}^a(\tau))^2 - \beta \sum_{a=1}^n V_{el}\{\mathbf{r}^a\}} \times \\ &\times \int \mathcal{D}\xi \mathcal{P}\{\xi\} e^{-\frac{\beta v_0}{2} \int_0^N d\tau \int_0^N d\tau' \xi_\tau \xi_{\tau'} \sum_{a=1}^n \delta(\mathbf{r}^a(\tau) - \mathbf{r}^a(\tau'))}. \end{aligned} \quad (8)$$

After some algebra the average over the distribution function (1) in the Eq. (8) is transformed as

$$\langle Z\{\xi\}^n \rangle_{\mathcal{P}} \propto e^{-\frac{nV}{2} \ln(2\pi\beta v_0)} \int \mathcal{D}\Psi \mathcal{D}\rho \mathcal{D}\hat{\rho} \mathcal{D}q \mathcal{D}\hat{q} e^{G(\Psi, \rho, \hat{\rho}, q, \hat{q}) + \ln \zeta(\hat{\rho}, \hat{q})}, \quad (9)$$

where

$$\begin{aligned} G(\Psi, \rho, \hat{\rho}, q, \hat{q}, \varphi, c^\pm) &= -\frac{1}{2\beta v_0} \sum_a \int d^3\mathbf{x} \Psi_a(\mathbf{x})^2 - \beta \sum_{a=1}^n W_{el}(\rho_a, \varphi_a, c_a^\pm) - \\ &- \frac{\xi^2}{2} \sum_a \int d^3\mathbf{x} \Psi_a(\mathbf{x})^2 \rho_a(\mathbf{x}) - \xi^2 \sum_{a<b} \int d^3\mathbf{x} \int d^3\mathbf{x}' \Psi_a(\mathbf{x}) \Psi_b(\mathbf{x}') q_{ab}(\mathbf{x}, \mathbf{x}') + \\ &+ \iota \sum_a \int d^3\mathbf{x} \rho_a(\mathbf{x}) \hat{\rho}_a(\mathbf{x}) \iota \sum_{a<b} \int d^3\mathbf{x} \int d^3\mathbf{x}' q_{ab}(\mathbf{x}, \mathbf{x}') \hat{q}_{ab}(\mathbf{x}, \mathbf{x}'), \end{aligned} \quad (10)$$

$W_{el}(\rho_a, \varphi_a, c_a^\pm)$ is the electrostatic contribution into the free energy [20]:

$$\begin{aligned} W_{el}(\rho_a, \varphi_a, c_a^\pm) &= \int d^3\mathbf{x} \left\{ -\frac{\varepsilon \varepsilon_0}{2} (\nabla \varphi_a(\mathbf{x}))^2 \varphi_a(\mathbf{x}) \left[e c_a^+(\mathbf{x}) - e c_a^-(\mathbf{x}) - \right. \right. \\ &- p e \rho_a(\mathbf{x}) + \rho_{surf}(\mathbf{x}) \left. \right] + \sum_{i=\pm} \left[k_B T (c_a^i(\mathbf{x}) \ln c_a^i(\mathbf{x}) - c_a^i(\mathbf{x}) - (c_0^i \ln c_0^i - c_0^i)) - \right. \\ &\left. \left. - \mu^i (c_a^i(\mathbf{x}) - c_0^i) \right] \right\}, \end{aligned} \quad (11)$$

where c^\pm are the concentrations of \pm monovalent salt ions with c_0^\pm being their bulk concentrations, and μ^\pm their chemical potentials, ε is the permittivity of water and ρ_{surf} is the fixed charges distribution. Here

$$\begin{aligned} \ln \zeta(\hat{\rho}, \hat{q}) &= -N \min_{\Psi} \left\{ \int d^{3n}\mathbf{x} \Psi(\mathbf{x}_1, \dots, \mathbf{x}_n) \times \left(-\frac{\ell^2}{6} \sum_a \nabla_a^2 + \iota \sum_a \hat{\rho}_a(\mathbf{x}_a) + \right. \right. \\ &\left. \left. + \iota \sum_{a<b} \hat{q}_{ab}(\mathbf{x}_a, \mathbf{x}_b) \right) \times \Psi(\mathbf{x}_1, \dots, \mathbf{x}_n) - E_0 \left(\int d^{3n}\mathbf{x} \Psi(\mathbf{x}_1, \dots, \mathbf{x}_n)^2 - 1 \right) \right\}, \end{aligned} \quad (12)$$

where E_0 is the ground state energy and $\Psi(\mathbf{x}_1, \dots, \mathbf{x}_n)$ is the corresponding eigenfunction of the ‘‘quantum-like’’ Hamiltonian

$$\hat{\mathcal{H}}_n = -\frac{\ell^2}{6} \sum_a \nabla_a^2 + \iota \sum_a \hat{\rho}_a(\mathbf{x}_a) + \iota \sum_{a<b} \hat{q}_{ab}(\mathbf{x}_a, \mathbf{x}_b).$$

In the $\sim \mathcal{O}(\xi^4)$ approximation saddle-point approximation of the partition function (9) gives the following system of the Edwards–Poisson–Boltzmann equations for any integer n

$$\frac{\ell^2}{6} \nabla^2 \psi(\mathbf{x}_1, \dots, \mathbf{x}_n) = \left[-\beta p e \sum_a \varphi(\mathbf{x}_a) - \varepsilon_0 - \xi^4 (\beta v_0)^2 \left(\sum_a \rho(\mathbf{x}_a) + \sum_{a < b} q_{ab}(\mathbf{x}_a, \mathbf{x}_b) \right) \right] \psi(\mathbf{x}_1, \dots, \mathbf{x}_n) \quad (13)$$

and

$$\varepsilon \varepsilon_0 \nabla_r^2 \varphi(\mathbf{r}) = 2e c_0 \sinh(\beta e \varphi(\mathbf{r})) - \rho_{surf}(\mathbf{r}) + p e \rho(\mathbf{r}). \quad (14)$$

We need to solve the system of Eqs. (13, 14) and to estimated the free energy (7). Next step requires the introduction of assumptions about the particular form of charge distribution $\rho_{surf}(\mathbf{r})$ to solve the system of Eqs. (13, 14), followed by taking the limit of $n \rightarrow 0$ for the number of replicas. Solution is also strictly dependent on the boundary conditions. The proposed approach allows to consider the effect of the short-range disorder on the polyelectrolyte chain behavior in different geometries.

The alternative way to estimate the quenched free energy (6) is so called *constrained annealing* approach. Following [22], the free energy of the polyelectrolyte with quenched random sequence $\{\xi\}$ can be estimated on the basis of annealed averages of the partition function with appropriate constraints using inequality

$$f \geq g(T, \mu) \geq f_A, \quad (15)$$

where $f = \frac{1}{N} \mathcal{F}$ and $f_A = -\frac{k_B T}{N} \ln \langle Z\{\xi\} \rangle_{\mathcal{P}}$ are the reduced quenched and annealed free energy per monomer correspondingly, and

$$g(T, \mu) = -\frac{k_B T}{N} \ln \langle Z\{\xi\} e^{-N\mu \alpha\{\xi\}} \rangle_{\mathcal{P}}. \quad (16)$$

$Z\{\xi\}$ is the partition function of the polyelectrolyte with given sequence realization $\{\xi\}$, and $\alpha\{\xi\}$ is the appropriate self-averaging quenched quantity. Thus, we can get the best lower bound of the free energy (7) maximizing the Gibbs-like potential (16)

$$\mathcal{F} \approx \max_{\mu} g(T, \mu). \quad (17)$$

Let us choose $\alpha\{\xi\}$ as follows

$$\alpha\{\xi\} = \frac{1}{N} \int_0^N d\tau \xi_{\tau}. \quad (18)$$

The average of the partition function (5) over the distribution function (1) with constraint (18) after some algebra gives

$$\begin{aligned} -\frac{Ng(T, \mu)}{k_B T} &= \frac{N}{2} (\mu \xi)^2 - \frac{\beta v_0}{2} (\mu \xi^2)^4 \int d^3 \mathbf{x} \frac{\rho(\mathbf{x})}{1 + \beta v_0 \xi^2 \rho(\mathbf{x})} - \\ &- \frac{1}{2} \int d^3 \mathbf{x} \ln(1 + \beta v_0 \xi^2 \rho(\mathbf{x})) + \iota \int d^3 \mathbf{x} \rho(\mathbf{x}) \hat{\rho}(\mathbf{x}) - \beta W_{el}(\rho, \varphi, c^{\pm}) - \\ N \min_{\psi} &\left\{ \int d^3 \mathbf{x} \psi(\mathbf{x}) \left(-\frac{\ell^2}{6} \nabla^2 + \iota \hat{\rho}(\mathbf{x}) \right) \psi(\mathbf{x}) - E_0 \left(\int d^3 \mathbf{x} \psi(\mathbf{x})^2 - 1 \right) \right\}. \quad (19) \end{aligned}$$

In the saddle point approximation the Gibbs-like potential (16) gives the following system of the Edwards–Poisson–Boltzmann equations:

$$\begin{aligned} \varepsilon\varepsilon_0\nabla^2\varphi(\mathbf{x}) &= 2c_0\sinh(\beta e\varphi(\mathbf{x})) - \rho_s(\mathbf{x}) + qeN\psi(\mathbf{x})^2, \\ E_0\psi(\mathbf{x}) &= \left[-\frac{\ell^2}{6}\nabla^2 - \beta qe\varphi(\mathbf{x}) + \frac{(\mu\xi)^2}{2} \right] \psi(\mathbf{x}). \end{aligned} \quad (20)$$

Just like the case of replica approach we need to solve the system of Eqs. (20). Solution is strictly dependent on the boundary conditions and charge distribution $\rho_{surf}(\mathbf{r})$. Then, we need to put the obtained solution into the Gibbs-like potential (19) and to maximize it over Lagrangian multiplier μ .

Each of the above mentioned methods has its own advantages. In both cases we need to solve the system of Edwards and Poisson–Boltzmann equations. While the replica approach requires to take the limit $n \rightarrow 0$ for the number of replicas, the constrained annealing method needs to maximize the Gibbs-like potential (16). The proposed approaches allow to consider the effect of the short-range disorder on the polyelectrolyte chain behavior that is important for the interactions between DNA (or RNA) and nanoparticles of the various origin.

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