

Counterion Condensation in DNA Systems: The Cylindrical Poisson–Boltzmann Model Revisited

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Nucleic acids are highly charged systems and counterions condense on the negatively charged phosphates, imparting electrostatic stability to the system.¹ This counterion condensation (CC) hypothesis enjoys wide support from numerous experimental and theoretical studies.^{2–7}

Earlier efforts to capture this phenomenon with Poisson–Boltzmann (PB) methodology as applied to cylinders^{8–18} led to the conclusion that a fraction of the counterions lie within the vicinity of the cylinder. These are called condensed counterions; their fraction depends on the linear charge density of the polyion and they do not contribute to colligative properties to any significant extent.^{1,11,12} The extent of counterion condensation, however, depended upon the added salt concentration, at variance with the constancy of the condensed fraction as predicted by the CC theory¹ and inferred from ²³Na nmr experiments.¹⁹ More precisely, the PB equation predicted that the counterion fraction enclosed in a coaxial cylinder of fixed radius around the polyion varied with added salt, or conversely, the radius of the coaxial cylinder containing the fixed counterion fraction varied with added salt. Extensive comparisons between cylindrical PB results and those emerging from computer simulations have shown that the neglect of small ion correlations in the former method leads to an underestimation of the condensed fraction, but the results in both approaches are qualitatively similar, and in particular, the condensed fraction varies with added salt.^{13–15,20} The constancy as implied by the CC theory and experiment is restored in simulations upon introduction of a dielectric saturation function for the polyion–small ion interactions.^{7,20,21} Given the success of the PB approach in characterizing several biophysical phenomena,^{22,23} the disagreement between the PB predictions and experiment with regard to counterion condensation is quite intriguing.

We were thus led to a reexamination of the cylindrical model of DNA with a very specific question: Are there any spatial scales that are invariant to added salt concentration in the cylindrical PB model system?

CALCULATIONS AND RESULTS

We have set up the nonlinear PB equation for a cylindrical model of DNA and solved numerically using Runge–Kutta method. The procedure is very similar to that of Record and co-workers.⁹ Radius of the cylinder is taken to be 9.5 Å and effective charge density on the cylinder ξ is equal to 4.2.¹ These values correspond to canonical B-DNA treated as a cylinder. Added salt concentration is reported as Debye length in Å {Debye length in Å = 1/0.329 [conc. (M)]^{1/2}}. Excess counterion concentration at a distance r from the cylindrical axis, $C^+(r)$, is calculated as $\{2C_{\text{bulk}} \sinh[\phi(r)e/kT]\}$. R_M is the radius of a coaxial cylinder containing 76% excess counterionic charge per phosphate.

Results on “Manning radius (R_M)” are shown in Figure 1A as a function of salt concentration, and these match with earlier observations based on the PB equation. In particular, R_M may be seen to vary with added salt. Also shown in the figure are the distances at which the surface concentration C^+ (surface), drops to 1/e of its value at various added salt concentrations. Curiously enough, this distance (denoted R_C) remains constant.

To investigate the sensitivity of the above result, the constancy of R_C as a function of added salt in particular, we repeated the above calculations for several values of the cylindrical radius ranging from 7 to 15 Å. In all cases R_C is seen to be independent of added salt (Figure 1B). The ion exclusion radius can be taken into account in the evaluation of R_C either by changing the cylindrical radius as above or by calculating the distance at which C^+ (surface + ion exclusion radius) drops to 1/e of its value in place of C^+ (surface) in this uniform dielectric model. The results are shown in Figure 1C for different ion exclusion radii. It may be noticed that R_C remains fairly constant, paralleling the above trends (shown in Figure 1A) for small counterions (radii < 3 Å).

DISCUSSION AND CONCLUSIONS

The numerical experiments presented here with the PB approach point to the existence of a characteristic scale

that is invariant to added salt concentration for B-DNA treated as a charged cylinder. The characteristic distance depends on the radius and charge density of the cylinder. In this study, we have found that R_C is independent of

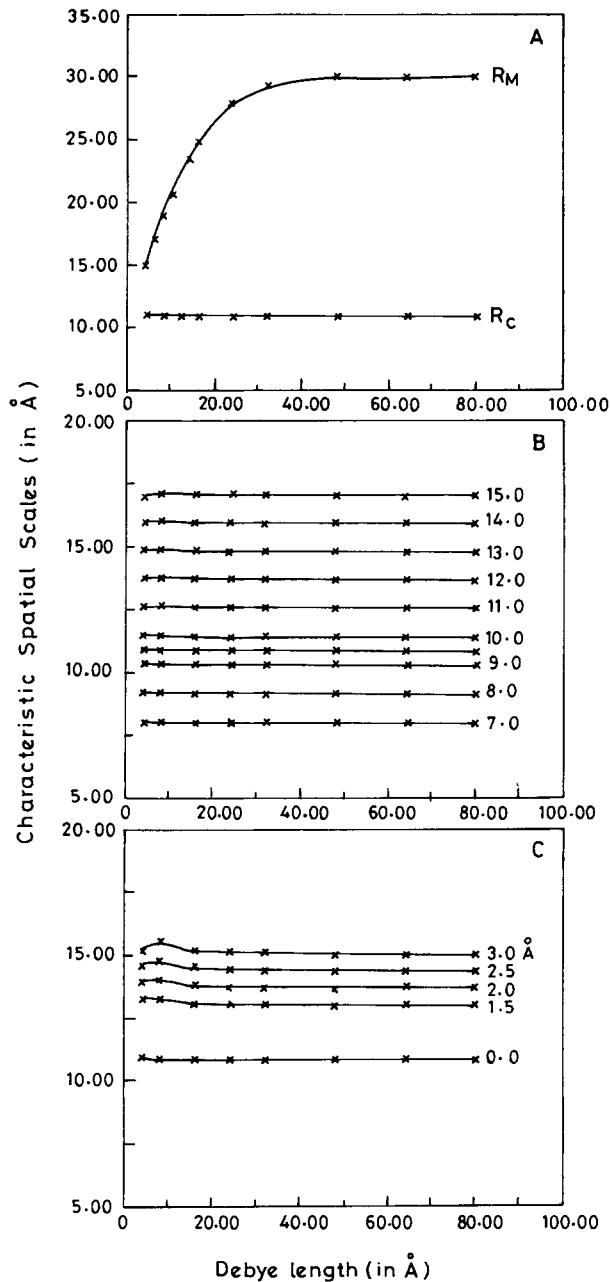


Figure 1. (A) Calculated Manning radius (R_M in Å) and characteristic distance (R_C in Å) at which the surface excess counterionic charge drops to $1/e$ of its value, are shown as a function of added salt concentration in terms of Debye length in Å. (B) Calculated R_C (in Å) for different cylindrical radii (indicated against each curve). (C) Calculated R_C (in Å) for different ion exclusion radii (indicated against each curve).

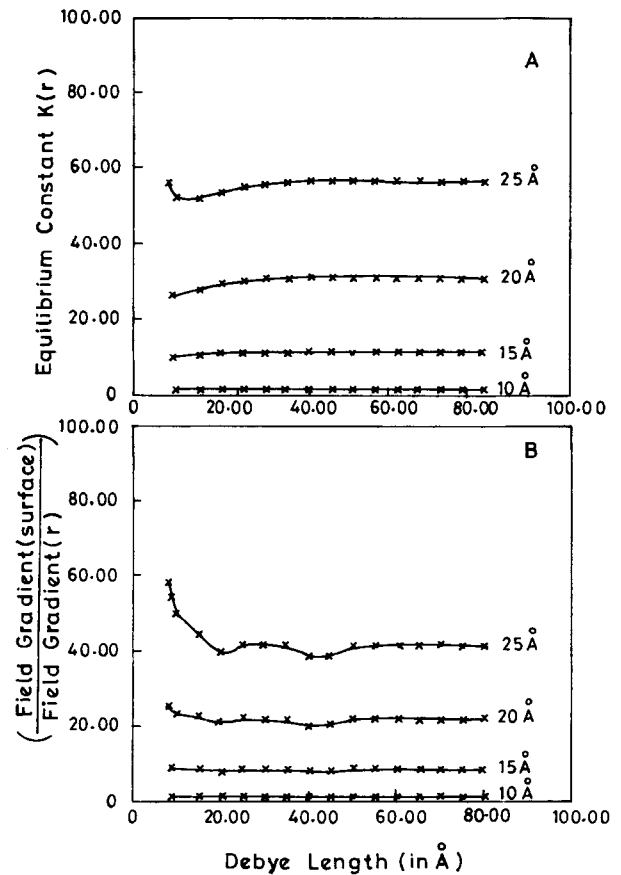


Figure 2. (A) Microscopic equilibrium constant $K(r)$ [defined in Eq. (2)] shown as a function of added salt concentration in terms of Debye length (in Å). (B) The ratio of field gradients at surface and distance r , shown as a function of added salt concentration in terms of Debye length (in Å).

added salt concentration for a charge density of 4.2 and for different values of cylindrical radii. We have also checked the behavior of R_C for different values of charge density (results not shown) and came to essentially similar conclusions for cylinders of high charge density ($\xi > 2$). An analysis of R_C profiles in terms of counterion and coion contributions indicated that the observed behavior at low concentrations (i.e., $C_{\text{bulk}} < 0.036M$ or a Debye length of $>16 \text{ \AA}$) is explicable in terms of counterion distributions alone but otherwise is a manifestation of the net effect of both counterions and coions over the entire concentration range studied. We have further investigated the behavior of R_C within the framework of LeBret and Zimm's theory¹² as an additional test of the above observation [by calculating R_C for a given ξ and different choices of κa for the case of no added salt using Eqs. (A1), (A2), and (29) in Ref. 12] and the results are in agreement with those presented above.

The existence of characteristic distance that is independent of added salt concentration suggests a relation:

$$C^+(r) = C^+(\text{surface}) \exp(-r/R_C) \quad (1)$$

This implies that the microscopic equilibrium constant, i.e.,

$$K(r) = C^+(\text{surface})/C^+(r) \quad (2)$$

at a given distance r , is independent of added salt concentration (Figure 2A). It is evident from Figure 2A that $K(r)$ remains invariant approximately up to 20 Å from the cylindrical axis even though the salt concentration varies a hundredfold. These observations are consistent with the ideas developed by Paulsen et al. on the cation competition coefficient.²⁴

According to the PB formalism, the ratio of field gradients at the surface and at a distance r in a homogeneous dielectric medium is proportional to the ratio of excess counterion concentrations (net charge densities), i.e., the microscopic equilibrium constant $K(r)$ defined above. Hence the ratio of the field gradients must also be independent of added salt within the vicinity of the cylinder. This observation appears to hold true (Figure 2B) up to a distance of 20 Å from the cylindrical axis. We wish to add parenthetically that the ratio of the observed rate constants for energy transfer between small ions (studied as in Ref. 25) depends on an equilibrium constant analogous to the one defined above [Eq. (2)]. Similarly, the quadrupolar relaxation rates (as investigated in Refs. 19 and 26) depend upon the field gradient fluctuations. A detailed examination of R_C , its relationship with the structural characteristics of the polyanion, and the implication of the constancy of the $K(r)$ field gradient ratio to the inferences based on ²³Na nmr and charge transfer experiments are under investigation.

We note in conclusion that, by definition, the characteristic distance (R_C) for net charge densities around highly charged polyions represented as cylinders is like the Debye length for potentials around point charges. The invariance of R_C with respect to added salt is a hitherto unnoticed/unreported feature of the solutions of the cylindrical PB equation.

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