Anisotropy of Electrical Polarizability of a DNA Fragment

Hitoshi Washizu and Kazuo Kikuchi*
Department of Life Sciences (Chemistry), Graduate School of Arts and Sciences, The University of Tokyo, Komaba, Meguro-ku, Tokyo 153

(Received February 20, 1997; CL-970126)

Metropolis Monte Carlo Brownian dynamics simulations are performed on model DNA solutions. It is shown that the induced dipole moment responsible for the orientation of a DNA fragment in an applied electric field may have its origin in the displacement of Manning's condensed counterions along the DNA rod axis.

The origin of the induced dipole moment of polyelectrolytes that is strong enough to orient the polyions in an electric field is still poorly understood even if simple models are assumed for the geometry of the polyions.

The Metropolis Monte Carlo (MC) method when applied to part of the degrees of freedom of a system, e.g. colloidal particles embedded in a solvent continuum, turns into a simulation procedure of the Brownian motion of the solute particles.[1,2,4]

Recently we have applied the Metropolis MC method to the study of the response of rodlike polyelectrolytes to an external electric field and obtained some new insights into the behavior of counterions.[3,4] For example, it has been shown that the counterions in the immediate vicinity of the polyion are so firmly bound to it that their contribution to the induced dipole moment is small, whereas those far apart from it are easily polarized and even stripped from the electrostatic influence of the polyion at high electric fields.

It is, however, the anisotropy of the counterion polarizability, i.e. the difference between the polarizabilities parallel and perpendicular to the long axis of the polyion that causes the polyion to rotate along the applied electric field. Since the contribution to the polarizability tensor of the diffuse ion cloud far away from the polyion is more or less isotropic, its polarization under the influence of an external electric field may not generate a torque strong enough to orient the polyion however large a dipole moment may be induced.

During the course of our simulation studies of model DNA fragments in solution we always obtained snapshots of counterion distribution which is very adequately described by Manning's counterion condensation theory.[5] There is a layer of condensed counterions on the DNA surface that neutralize most of the phosphate charge. Surrounding this layer is a more diffuse ion atmosphere that may be treated in the Debye-Hückel approximation. In this communication we show that these two kinds of counterions are also distinguished by their polarization behavior and that the induced dipole moment responsible for the orientation of a DNA fragment in an applied electric field may have its origin primarily in the displacement of Manning's condensed counterions along the DNA rod axis.

A 64 base-pair fragment of the double-stranded DNA is modeled as an impenetrable cylinder of radius 0.85 nm with 128 negative charges spaced at 0.17 nm intervals along its axis. The hydrated univalent counterions are modeled as hard spheres of radius 0.15 nm so that the radial distance of closest approach of an ion to the axis of the DNA is 1.0 nm. The cylinder is extended 0.17 nm beyond the terminal charges at both ends. The solvent is treated as a dielectric continuum with the relative permittivity of pure water at 25 ℃ (78.3) and no salt is added. The MC cell is a sphere of radius 0.8 times as long as the DNA cylinder in which the DNA fragment is placed along the z-axis with its center in common with that of the MC cell, or the origin of the coordinate axes. The energy of configurations is calculated as a sum of interactions of each counterion in the MC cell with all the other counterions and DNA charges in the cell. The value of 0.2 nm is used as the maximum counterion displacement allowed for an MC move along each coordinate direction. When a counterion escapes from the cell during a move in the Metropolis sampling process, another counterion is put to the symmetrical position about the center of the MC sphere.

Manning's counterion condensation theory predicts that 76% of the DNA phosphate charge is neutralized by condensed ions, i.e. in the present case out of 128 counterions 98 are classified as condensed and 30 as constituting a diffuse ion atmosphere. As one way to show that the counterion distributions obtained in our simulations are well described by Manning's theory, we numerically sort counterions in increasing order of the sum of their distances from both ends of the polyion. Two groups of counterions, the first 98 counterions sorted in this way or the innermost counterions and the rest of 30 or the outer counterions are clearly recognizable in different spatial distributions.[6]

These two groups of counterions are distinguished also by their polarization behavior. The fluctuation of the dipole moment of the system is related to the polarizabilty.[7,8] At every simulation step we sort counterions in the above manner and calculate the contribution to the dipole moment of the first n counterions in the sorting list ($\mu_x(n)$, $\mu_y(n)$, $\mu_z(n)$) as follows

$$\mu_x(n) = \sum_{i=1}^{n} ex_i,\ \mu_y(n) = \sum_{i=1}^{n} ey_i,\ \mu_z(n) = \sum_{i=1}^{n} ez_i \qquad (1)$$

where e is the protonic charge and x_i, y_i, z_i are the coordinates

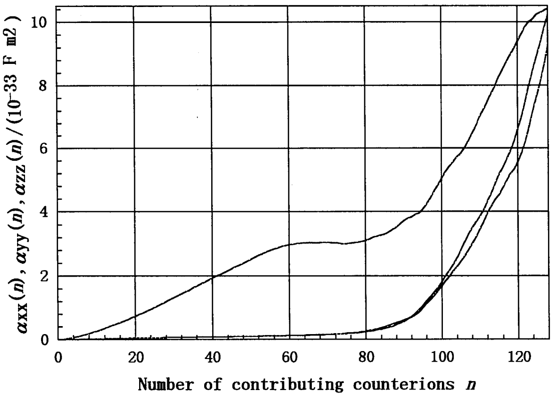

Figure 1. Principal polarizability components $\alpha_{xx}(n)$, $\alpha_{yy}(n)$ (lower curves) and $\alpha_{zz}(n)$ (upper curve) as functions of number of contributing counterions n. They are calculated from a trajectory consisting of 100000 steps.

of the i-th counterion. We then define the partial polarizability tensor due to the n counterions with its components $\alpha_{rs}(n)$ given by

$$\alpha_{rs}(n) = \left(\langle \mu_r(n)\mu_s(n)\rangle - \langle \mu_r(n)\rangle\langle \mu_s(n)\rangle\right) / k_{\mathrm{B}}T \quad (2)$$

where $r, s = x, y, z$, k_{B} is the Boltzmann constant, T is the absolute temperature, and $\langle\ \rangle$ denotes the time average. n runs from 1 to 128 and the anisotropy of the electrical polarizability $\Delta\alpha$ to be determined is expressed as

$$\Delta\alpha = \alpha_{zz}(128) - (\alpha_{xx}(128) + \alpha_{yy}(128)) / 2 . \quad (3)$$

Figure 1 plots principal components of the partial polarizability tensor as functions of n. With increasing number of the counterions contributing to the polarizability, α_{zz} first increases, reaches a plateau value while both α_{xx} and α_{yy} remain very small and at around $n = 80$ all the components begin to increase first slowly and then rapidly.

The dependence of the partial polarizability on n is explained as reflecting differences in the polarization behavior among counterions. α_{zz} increases until the DNA phosphate charge is neutralized by about 60 counterions. Note that it is calculated at every simulation step by selecting the innermost counterions. Then fluctuations of the z-component of the dipole moment $\mu_z(n)$ will increase with n as far as n is small because selected counterions may distribute randomly along the polyion rod axis. When the number of the selected counterions increases over 60, fluctuations of $\mu_z(n)$ no longer increase with n until n reaches about 80. Since most of the condensed counterions firmly bound in the immediate vicinity of the polyion are selected they distribute uniformly along the DNA. When n exceeds somewhere around 80, first outer part of the condensed counterions which are less firmly bound to the polyion and then the diffuse ion atmosphere begin to contribute to $\mu_z(n)$ with their diffuse spatial distribution reflected in the rapidly increasing fluctuation of $\mu_z(n)$. Fluctuations of both $\mu_x(n)$ and $\mu_y(n)$ remain very small when $n \leq 80$ because ions are condensed in a layer over the DNA surface. When $n > 80$, first outer part of the condensed counterions and then the diffuse ion atmosphere start to contribute to both $\mu_x(n)$ and $\mu_y(n)$ resulting in their rapidly growing fluctuation. Although polarizability components change with n smoothly due to the presence of less firmly or somewhat loosely bound condensed counterions in the transition region, different polarization behaviors of the two groups of ions are clearly distinguished.

It seems, however, difficult to obtain definite values of $\Delta\alpha$ from Eq.3. In salt-free solutions the density of the Debye-Hückel ion atmosphere is so small that the determination of each component of the polarizability tensor on the right hand side of Eq.3 is not free from statistical errors, i.e. $\Delta\alpha$ is given in Eq.3 as a difference of large, fluctuating quantities. In fact a discrepancy is observed between α_{xx} and α_{yy} when n is large in Figure 1 which shows polarizability components calculated from a trajectory consisting of 100000 steps. Although this kind of error is resolved in principle by statistically averaging a large number of trajectories, Figure 1 also shows a possibility that the distribution of the diffuse ion atmosphere might be influenced by the boundary conditions of our simulation cell.

Under these circumstances we cannot determine $\Delta\alpha$ without some simplifying assumptions. Since the potential experienced by ions constituting the diffuse ion atmosphere is a screened Coulomb potential of the polyion shielded by the condensed counterions and since they are sparsely distributed over a large volume distant from the polyion, it is expected that their motion is more or less free. We then assume as a first approximation that their contribution to the polarizability tensor is isotropic[9] and neglect the correlation between their contribution to the dipole moment and that of the condensed counterions. Then $\Delta\alpha$ is equated with the difference of the longitudinal and transverse partial polarizabilities due to the condensed counterions. This is a kind of two-phase or two-state approximation often used in analytical studies but in our simulation studies the diffusive nature of the counterion distribution is retained by the outer part of the condensed counterions which are somewhat loosely bound to the polyion.

Our simulation yields a $\Delta\alpha$ of 3.2×10^{-33} F m^2 for a 64 base-pair DNA fragment at a concentration of 9.4 mM nucleotide residues. The DNA concentration is calculated assuming that 128 nucleotide residues occupy an effective volume the size of the simulation cell. This may be compared with the experimentally determined $\Delta\alpha$ of 2.0×10^{-33} F m^2 for a 64 base-pair DNA fragment at a concentration of 20 μ M nucleotide residues in a buffer system of 1mM sodium cacodylate, 1mM NaCl, and 0.2 mM EDTA at pH 7.1 by Diekmann et al.[10] In spite of the large difference in the DNA concentrations, both systems have similar ionic strengths. Since the distribution of the condensed counterions is expected to be influenced primarily by the ionic environment, our simulation result is encouraging.

References and Notes

1 K. Kikuchi, M. Yoshida, T. Maekawa, and H. Watanabe, *Chem. Phys. Lett.*, **185**, 335(1991).

2 K. Kikuchi, M. Yoshida, T. Maekawa, and H. Watanabe, *Chem. Phys. Lett.*,**196**, 57(1992).

3 M. Yoshida, K. Kikuchi, T. Maekawa, and H. Watanabe, *J. Phys. Chem.*, **96**, 2365(1992).

4 M. Yoshida and K. Kikuchi, *J. Phys. Chem.*, **98**,10303(1994).

5 G. S. Manning, *J. Chem. Phys.*, **51**, 924(1969).

6 See the diagram in our graphical abstract showing 98 condensed counterions as filled circles and part of the ion atmosphere, 19 ions out of 30, as open circles.

7 R. Kubo, *J. Phys. Soc. Jpn.*,**12**, 570(1957).

8 F. Oosawa, *Biopolymers*, **9**, 677(1970).

9 Manning has shown by linear analysis that the dipole moment induced in the ion atmosphere of a polyion by application of an external electrical field is isotropic as far as the field of the polyion is treated to be small. G. S. Manning, *J. Chem. Phys.*, **90**, 5704(1989).

10 S. Diekmann, W. Hillen, M. Jung, R. D. Wells, and D. Pörschke, *Biophys. Chem.*, **15**, 157(1982).