Introduction of a Method for Computing Electrostatic Potential Distribution around a DNA Molecule by a Cylinder Model.

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A method was introduced for computing the three dimensional distributions of electrostatic potentials and forces in a DNA molecule with helically distributed electrical charges. A cylindrical model of DNA molecule composed of an inner region where a discrete charge does not exist, a middle region where there is an interaction between charges and the external region where the ions interact. The potential in each region was described by Laplace and Poisson equations. The Green function method was applied for the discrete helical charge distribution within a one helical turn of the finite cylinder. The calculated potentials and forces depended on the circumferential angles. The present method, when it was improved, will be available for evaluating the free energy of the DNA molecule.

Keywords: DNA, Electrostatic potential, Discrete charge, Debye-Huckel theory

1. Introduction

Characterization of molecular structure of DNA has been progressed for these two decades. Precise molecular properties have been reported particularly in their geometry (1). Fig 1 shows the side view of the double helix DNA molecule. The Top view Fig 2 shows how the phosphate charges are arranged along the helical loop with equal spacing. There are ten phosphates for each helical turn with a raise angle of 32 degree. Fig 3 shows spatial positioning of the electrical charges around the surface of the DNA cylinder. L is the length of the interhelical interval, φ is the latitudinal angle around the circular cross sectional plane of the DNA.

All these findings, however, are still in premature to be organized to understand the thermodynamic behavior of the DNA (2). Since a DNA molecule consists of neatly arranged charges, modeling analysis is the most reasonable approach. This should be directed to investigate the potential and electrical force to evaluate the electrochemical dynamic properties of the DNA. The present work introduces a simplest method (3) for computing three dimensional distributions of electrostatic potentials and force of modeled DNA.

2. Charge distribution in one helical turn.

We set following assumptions for modeling electrostatic potential in a DNA.

1. Phosphate charges locate helically on the surface of a cylindrical DNA.
2. The DNA cylinder (Fig 3) is impermeable to the screening ions (2).

Fig. 1. DNA
Fig 1 is side view

Each position of a charge was described on one helical turn on the surface of the DNA cylinder (3).

We set L as the periodic length of the helical loop (pitch of one helical turn). L is a repeat distance...
of one helical turn along the longitudinal axis.

(4) Only the interaction between screening ions and the DNA helix contributes to the intermolecular interaction \(^{(3)}\).

3. Geometric description of charge distributing in a one helical turn.

3.1 Circumferential angle in one helical turn.

Ten phosphates are arranged helically around the central axis of the DNA cylinder \(^{(1)}\) in one pitch. Each electrical charge makes a rotation of \(\phi = 2\pi/10\) around the central axis of the DNA. The \(k\)th charge on a cross sectional horizontal plane of the DNA in a given helical turn has a circumferential angle of

\[
\phi_k = \frac{2\pi k}{10}
\]

3.2 Side view of one helical turn. (Fig4)

We introduce a side view of the relative position of two successive charges on one helical turn. Superscript \(^t\) denotes the charge position on the helical loop. \(z'_k\) denotes the position of the \(k\)th charge on any given helical loop and is not the axial distance of the \(k\)th charge. \(zH_k\) is the position of the \(k\)th charge that has been projected from \(z'_k\) down on to the horizontal cross sectional plane of the DNA. \(zk\) is the vertical axial distance between \(z'_k\) and \(zH_k\) (Fig4). The relation between spatial positions of two successive \(k-1\)th and \(k\)th charges (Fig4) on the helical loop \((z'_k, z'_k-1)\) can be approximated by

\[
z_k - z_{k-1} = I|z'_k - z'_{k-1}| \sin \psi 
\]

where \(\psi\) is the rise angle ( Fig1 ) in a given helical turn. It describes how the charges are shifted from the horizontal cross sectional plane of the DNA cylinder.

3.3 Arrangement between adjacent charges.

Relation between the distances of two successive charge on the helical turn that are projected on the horizontal plane \((zH_k, zH_{k-1})\) and those which are projected on the helical loop \((z'_k, z'_{k-1})\) can be approximated by

\[
\cos \psi = \frac{Izk - zh_{k-1}I}{Iz'_k - z'_{k-1}I}
\]

From the triangular formula, we have

\[
\frac{Izk - zh_{k-1}I}{\sin(\phi_k)} = \frac{\rho_k}{\sin(\pi - 2\phi)}
\]

where \(\rho_k\) is the radial distance of the \(k\)th charge from the central axis of the DNA on the horizontal cross sectional plane. Then \(cos \psi\) can be expressed by 3 and 4. The distance between two successive charges on the helical loop can be approximated by

\[
Iz'_k - z'_{k-1}I = \frac{\rho_k \sin(\phi_k)}{\sin(\pi - 2\phi)} \cos \psi
\]

Hence the position of the \(k\)th charge in the axial direction is given by

\[
zk = \frac{k \rho_k \sin \phi_k}{\sin(\pi - 2\phi) \tan \phi}
\]

From the reported measured data \(^{(1)}\), we have

\[
\psi = 32^\circ \text{ and } \phi_k = 36^\circ
\]


According to the Debye-Huckel theory, the potential field created by the charged DNA is divided into three
DNA Potential

Fig. 4a. Circumferential positions.

Fig. 4a is the top view of DNA molecule showing the circumferential positions of the Phosphate charges on the horizontal cross sectional plane of the DNA. Each position was denoted by $z_{H0}, z_{H1}, z_{H2}, z_{H3} \ldots$. The circumferential angle between charges at $z_{H0}$ and $z_{H1}$ is expressed by $\phi_{k1}$. The angle from $z_{H0}$ to $z_{H2}$ is $\phi_{k2}$ etc. Since all the phosphate charges occupied their spatial positions in equivocal distances, we set all the circumferential angles between two neighboring charges $\phi_{k}$. 

Fig. 4b. Stereoscopic description.

Fig. 4b is the stereoscopic view of DNA molecule showing the positions of the phosphate charges on the helical loop around the DNA cylinder. $O$ is the center of the cylinder. $O - z_{Hk-1} - z_{Hk}$ is the horizontal cross sectional plane. On this plane, the phosphate charges at $z_{Hk-1}$ and $z_{Hk}$ on the helical loop were projected vertically. $O$ denotes the position of a charge on the helical loop and $H$ denotes the projected charge position on the horizontal plane.

Regions (Fig 5).

Region I is the DNA cylinder with radius $b$ and dielectric constant $D_h$. The points of discrete charges by phosphates locate in this region. This region is the main source of the potential of DNA.

Region II is the area of closest approach of screening ions. In the range of $b < \rho < d$, $(d - b)$ is the radius of screening ions. Since the radius of screening ion is constant and the radius of region I does not change, the number of ions that can enter to this region is automatically determined. In other words, in this region the movement of the screening ions is strongly constricted and their locations are almost fixed. The ions can not diffuse freely due to intense electro static interaction between the charged phosphates in the region I and screening ions.

In addition, the close positioning of screening ions would produce ionic pairwise interaction that would not occur in a dilute space where ions can take free positions. Since the action of ions in this region II differs from those of the ions in free volume space, we set another region III to discriminate the ions which are not constricted their movements.

Region III is a free field in which the screening ions can approach to the DNA cylinder. Region III is free diffusion space for ions. We set this region as a dilute space in which the concentration of the ions are so low that mutual interactions among the ions do not occur as in the dense solution or colloid solution. Region III differs from the region II only in the situation that the screening ions do not take the closest approach to the DNA cylinder. The ions in this region can move freely and the potential of this region goes to zero as the distance from the DNA cylinder increases. There may be a lot of non screening ions and counter ions in this region. The essential difference is the free movement and number of ions. The dielectric constants for region II
and III are assumed to be the same, D which is equal to that of the bulk solution.

We set following assumptions (4) and approximations which seem to be valid in this problem (5).

1. **Assumption 1.** "Each ion was represented by a rigid sphere and spherical ion can be replaced by a point charge at its center".

This assumption neglects ionic volumes and is only valid when the mean inter ionic distance is sufficiently large compared with their sizes meaning a dilute solution.

2. **Assumption 2.**

Near the central ions (region I), the concentration of positively charged ions differs from the concentration of negatively charged ions depending on the polarity of the central ions (region I). By the Debye-Huckel theory, this concentration difference takes the Boltzmann distribution. The ratio of the concentration of one kind of ion near the central ion to the concentration of far from the central ion equals to \(\exp(-w_{ij}(r)/k_B T)\). \(k_B\) is the Boltzmann factor. \(T\) is the absolute temperature. \(w_{ij}(r)\) is the work done to carry the ion from the infinity (\(\psi = 0\)) to the potential \(\psi\) prevailing at the point for which the concentration is to be computed. The work done is \(w = e \psi\) for a positive ion of charge \(e\) and \(w = -e \psi\) for a negative ion of charge \(-e\). The Boltzmann distribution gives the number \(n_i\) density of \(i\) ions around the ion \(j\) by

\[
n_i = n^0_i \exp\left[-w_{ij}(r)/(k_B T)\right]
\]

and hence the charge density of \(j\) ion is

\[
\rho_j(r) = \sum_i e z_i n_i \exp\left[-w_{ij}(r)/(k_B T)\right]
\]

The \(z_i\) is the valence of \(i\) ion. \(n^0_i\) is reference concentration of the salt solution. \(n - n^0_i\) is the average local excess of \(i\) ion at the position \(r\).

3. **Approximation 1.** The factor \(w_{ij}(r)\) can be replaced by the potential energy of an ion \(i\) which locates at a point of a potential \(\psi_j(r)\) due to ion \(j\).

\[
w_{ij}(r) \approx z_i e \psi_j(r)
\]

4. **Approximation 2.** We approximate

\[
\frac{z_i e \psi_j(r)}{k_B T} = \ll 1
\]

This means that the potential is sufficiently small at all the points where Poisson equation is to be used. This approximation owes to the linear property in dilute system that neglect mutual interactions among the ions. In the physiological circumstances, the central ions (region I) has sufficiently low charge density. Hence, the Approximation 2 is satisfied. Then, the basic form of solution for the region I can be given by the series of modified Bessel function

\[
\Psi_I = \sum_{m=1}^{\infty} A_I \cos \left(nc \left(z + \frac{u \pi}{2}\right)\right)
\]

where

\[
\kappa = 10^9
\]

5. **Mathematical description of the system.**

We introduce a method (11) only for the region I in detail. Phosphate groups produce a point charge density \(\rho_I(r)\) (\(r\) is a position vector) on the region I.

\[
\rho_I(r) = \sum_{j} e_j \delta(r - r_j)
\]

where \(r_j\) is the position vector of the \(j\)th charge. \(e_j\) is the \(j\)th discrete charge. The sum is all over the points of discrete charge in one helical turn (\(p = 10\)). Then, the Poisson equation is

\[
\nabla^2 \psi_I(r) = -\frac{4\pi}{D_h} \rho_I(r)
\]

The corresponding Laplace equation is

\[
\nabla^2 \psi_I(r) = 0
\]

The corresponding particular equation is

\[
\nabla^2 \psi_I(r) = \frac{4\pi}{D_h} \sum_j e_j \delta(r - r_j)
\]

Then, the basic form of solution for the region I can be given by the series of modified Bessel function

\[
\Psi_I = \sum_{m=1}^{\infty} \sum_{n=1}^{\infty} A_I \cos \left(nc \left(z + \frac{u \pi}{2}\right)\right)
\]

where
\[
\lambda = \frac{2\pi}{L} \quad (c = \frac{2\pi}{L}) \quad \ldots \quad (21)
\]

\(g_m\) is a Green function. It is a product of \(I_m\) (the modified Bessel function of the first kind) and \(K_m\) (the second kind). For \(\lambda \neq 0\)

\[
g_m(\rho, \rho_j) = 4\pi I_m(\lambda \rho)K_m(\lambda \rho_j) \quad \ldots \quad (22a)
\]

\[
go(\rho, \rho_j) = 4\pi I_0(\lambda \rho)K_0(\lambda \rho_j) \quad \ldots \quad (22b)
\]

and \(\lambda = 0\)

\[
g_m(\rho, \rho_j) = \frac{\pi}{m} \left(\frac{\rho_j}{\rho}\right)^m \quad \ldots \quad (23a)
\]

\[
go(\rho, \rho_j) = 2\pi \log \frac{1}{\rho} \quad \ldots \quad (23b)
\]

subscript \(j\) indicates a variable in the cylindrical coordinate of the \(j\)th charge in one helical turn.

The coefficients \(A_1, B_1\) and \(T_1\) are determined by the boundary conditions at \(\rho = b\)

\[
\psi_1(\rho = b) = 0 \quad \ldots \quad (24a)
\]

\[
D_h \frac{\partial \psi_1}{\partial \rho} = D \frac{\partial \psi_1}{\partial r} \quad \ldots \quad (24b)
\]

Applying these boundary conditions independently to each harmonic component of the potential, we have the potential for the inner region, \(\psi_1\) in an exact form by

\[
\psi_1 = \sum_{n=0}^{\infty} \sum_{m=0}^{\infty} Q_{nm} \cos(nc(z - z_j)) \cdot \cos[m(\phi - \phi_j)]I_m(ncp)I_m(ncp) + \sum_{j=0}^{\infty} S_m \cos[m(\phi - \phi_j)] \left(\frac{L}{d}\right)^m \left(\frac{\rho_j}{\rho}\right)^m \cdot \left(\frac{L D}{d^2}\right) \log \frac{d}{b} + \frac{z}{L D_h} \log(b) + \psi_0 \quad \ldots \quad (25)
\]

where \(oht\): one helical turn. Coefficients \(Q_{nm}\) and \(S_m\) are determined by the boundary conditions. Their exact forms are given by our previous technical report \((4)\). \(z_j\) and \(\phi_j\) specifies the discrete position of the \(j\)th charge in a given helical turn. Sum over \(j\) extends for all the points of discrete charges in one helical turn. The solution of the characteristic potential \(\psi_0\) is given by

\[
\psi_0 = \frac{8\pi}{LD_h} \sum_{j=1}^{\infty} \sum_{n=1}^{\infty} \cos(nc(z - z_j)) \cdot \left\{ I_0(ncp) \frac{K_0(ncp)}{2} \right. + \sum_{m=1}^{\infty} \cos[m(\phi - \phi_j)]I_m(ncp)K_m(ncp) \left. \right\} + \frac{\epsilon_0}{LD_h} \sum_{j=1}^{\infty} \sum_{m=1}^{\infty} \cos[m(\phi - \phi_j)] \left(\frac{p_m}{m}\right)^m \rho_m^m + \frac{\epsilon}{L D_h} \log \frac{1}{\rho} \quad \ldots \quad (26)
\]

where \(\rho_0\) is the radial position of the point charge. The potential for the second region \(\psi_{II}\) is

\[
\psi_{II} = \sum_{n=1}^{\infty} \sum_{m=1}^{\infty} \sum_{n=1}^{\infty} \cos(nc(z + \frac{\pi n}{2})) \cdot \cos[m(\phi + \frac{\pi m}{2})] \cdot [A_{II}I_m(ncp) + F_{II}K_m(ncp)] + \sum_{m=1}^{\infty} \left(\frac{B_{II}p_m + G_{II}m}{p_m^m}\right) \cdot \cos[m(\phi + \frac{\pi m}{2})] + T_{II} + \frac{H_{II}}{cp} \quad \ldots \quad (27)
\]

The coefficients of \(A_{II}, B_{II}, F_{II}, G_{II}, H_{II}\) and \(T_{II}\) are determined by the continuity of the boundary between the region II and region III. They are given in our technical report \((4)\). Since all the potentials involve the factors \(\cos(nc(z - z_j))\) and \(\cos[m(\phi - \phi_j)]\), we selected the positions \((z, \phi)\) for the potential computation as

\[
nc(z - z_j) = 0, \pi/2, \pi, 3\pi/2 \text{ and } 2\pi \quad \text{and} \quad m(\phi - \phi_j) = 0, \pi/2, \pi, 3\pi/2 \text{ and } 2\pi.
\]

Then, we computed the potentials in three regions at

\[
z = (0, \pi/2, \pi, 3\pi/2, 2\pi) / (n2\pi/L) + z_j \quad \phi = (0, \pi/2, \pi, 3\pi/2, 2\pi) / m + \phi_j
\]

For simplicity, we set \(z_j = 0\) and \(\phi_j = 0\). Other the biophysical parameters were set \((1),(3)\) as

\[
L = 33.8 \times 10^{-8} \text{ (cm)}, \quad b = 10 \times 10^{-8} \text{ (cm)} \quad d = 12 \times 10^{-8} \text{ (cm)} \quad \rho_0 = 9 \times 10^{-8} \text{ (cm)} \quad \frac{1}{\kappa} = 0.1 \times 10^{-8} \text{ (cm)} \quad D = 10, (3),(4) \quad \text{and} \quad D_h = 20, (3),(4).
\]

To present several examples of computed results, we simplified the computing process. All the potentials were normalized by \(e_0\), the phosphate charge. The number of charges per one helical turn was assumed to be ten according to the number of charges on one pitch of one helical loop. The computation was confined only for one helical turn.

An entire scope of the potential distribution can be computed when the potentials in all the helical turn were summed. As the circumferential and axial distributions of these potentials in one helical turn were characterized by the factors of \(\cos(nc(z - z_j))\) and \(\cos[m(\phi - \phi_j)]\), the potentials in \(z\) axis and circumferential directions oscillated like sinusoidal function. In the radial direction characterized by the modified Bessel functions with arguments of \(ncp\) and power of \(\rho\), the potential (the third region ) decreased monotonically.

The forces acting on the latitudinal direction were obtained by differentiating the potential with respect to the circumferential angle \(\phi\). The present computation confines only for one helical turn. Thus, we show only a limited interaction.
6. Results.

1. Potential distributions at the inner region (Fig 6-a) and at the middle region (Fig 6-b)

Fig. 6-a shows three dimensional distribution of the inner regional potential timed by the factor of 10^20 at radial position of \( R = 5 \times 10^{-8}\) cm. Along the axial positions with \( \pi/4 \) step, the potential oscillated to negative values at \( \pi/4 \) and at \( 3\pi/4 \). There were three peaks at \( z = 0 \), \( \pi/2 \) and at \( \pi \). In the latitudinal direction, the potential showed two peaks at \( \phi = 0 \) and \( 2\pi \).

The potential at the middle region was computed at the radial position of \( R = 11 \times 10^{-8}\) cm. Absolute values of the potential at the middle region (timed by the factor of 10^8) was considerably smaller than the inner potential (timed by the factor of 10^20). In contrast to the inner regional potential, all the potential values were positive. The oscillative natures of the potential was, however, similar to those of the middle regional potential.

2. Distribution of the forces at the inner region (Fig 7-a) and at the middle region (Fig 7-b).

The force at inner region (timed by the factor of 10^20) oscillated periodically. This originates from the distributions of the inner regional potential. The force attained the negative peak values at \( z = \pi/4 \) and \( 3\pi/4 \) in the axial coordinate and at \( \pi/2 \) and \( 3\pi/2 \) in the circumferential coordinate. These oscillative natures were in contrast to those of the potentials at the inner region. The distributions of middle regional force were quite different from those of the middle region potential. For the hemisphere of \( 0 \leq \phi \leq \pi \), the force directed in negative direction while for \( \pi \leq \phi \leq 2\pi \), the positive values. For the interval of \( 0 \leq z \leq \pi \), the oscillation of the force was weak.

7. Discussion.

The main part of the present work were based on electrostatic potential theory (1). The geometric consideration was founded on the basis of molecular biology. The spatial distribution of phosphate charges are neatly arranged, we can determine the distribution of charges by setting only a few parameters.

The present three layers modeling seem to be over complicated. The region I and II differed only because of the existence of charges in the region I. Thus, it may be possible to associate region I and II, because the region II envelopes region I and their charges. The difference between region II and region III originates in the mobility of screening ions. Since the sum of radius of the DNA and screening ion determines the number of the screening ion that can envelope the region II. Hence the degree of freedom of the screening ion in the region II is strongly limited. On the other hand, the region III is a free space where the ions can take any position.

We have no precise measured data for local distribution of potential in one helical turn. The boundary conditions in cylindrical symmetry and the charge distribution would result in symmetric distribution of the potentials. The present computed results, however, can not represent such symmetry. Since we have computed just only a portion of an entire helical turns, we could not reproduce such symmetric distribution pattern.

The difference of magnitude between the inner region potential and the outer region potential was large. This would originate in the difference of computed radial positions. For the inner region \( R = 5 \times 10^{-8}\) cm and for the middle region \( R = 11 \times 10^{-8}\) cm which is about twice the distance. Measuring the electro static potential around the DNA molecule will disclose minute distribution of electrical potential by nano technological approach such as nano electrode. The present computed data have to be compared to them.

There may be some limitations for the computational system. Particularly some computational error may exist regarding to the modified Bessel functions of the second kind in region I and those in Poisson Boltzman equation for region II. In the region II, the Debye parameter \( \kappa \) is so large 10^8 that the analytic solution may be inadequate. The large value \( \kappa \) would over estimate the modified Bessel functional. As a result, the potential remote from the center will become incorrect. The approximation solution for large \( \kappa \) will converge rapidly and may be more adequate.

The most critical point of the present study is the assumption of the helical distribution charge due to phosphate and its simple boundary condition. The boundary condition should be corrected in a helical coordinate system. Another point is the isotropic nature of the dielectric constant. This is because there is a lot of electric dipole perpendicular to the molecular axis and along the base ladder. Such large dipole would result in anisotropic dielectric constant along the helical axis. So the biological boundary conditions have to be more complicated than the ordinal electro static boundary conditions. In addition, we did not take into consideration of the secondary effects of counter ions, salt and water molecules. The counter ions contribute for neutralization of the electrical circumstances (1). Salt will contribute the the structural modification of the DNA because the melting point of the DNA is a function of the salt ion concentration (1). Thus a high concentration of salt will influence of the stiffness of molecular structure of the DNA (1). Water molecules can easily invade the DNA molecules and occupy the empty spaces among the bases. Such empty space occupation of the DNA molecule contribute to stabilize the molecular conformation of the double stranded DNA (1).

The present work introduced (1) an electro static computational method and its computed results. For more precise computation, one should use FEM or MD simulation systems.
Fig 6. Three dimensional distributions of the Inner regional potential Fig6-a (timed by the factor $10^{20}$) and of the middle regional potential Fig 6-b (timed by the factor $10^{20}$) in one helical turn of the DNA. They are normalized by $\varepsilon_0$, the phosphate charge. Circumferential plots were set by every $\pi/2$ from 0 to $2\pi$. The axial positions were selected every $\pi/4$ from 0 to $\pi$.

Fig 7. Three dimensional distribution of the Forces generated in the inner region Fig7-a (timed by the factor $10^{20}$) and in the middle region Fig7-b (timed by the factor $10^{20}$) in one helical turn of the DNA.
8. Conclusion

1. A computational method was introduced for potentials and forces in a DNA molecule with the helically arranged discrete electrical charges distribution on its surface. The potential and force at the inner and middle regions of the DNA cylinder were significantly influenced by circumferential angle.

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