Ion-Phosphate Mode in the DNA Low-Frequency Spectra

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Abstract

The vibrational dynamics of a DNA molecule with counterions neutralizing the charged phosphate groups have been studied. With the help of elaborated model the conformational vibrations of the DNA double helix with alkaline metal ions have been described both qualitatively and quantitatively. For the complexes of DNA with counterions Li+, Na+, K+, Rb+ and Cs+ the normal modes have been found, and a mode characterized by the most notable ion displacements with respect to the DNA backbone has been determined. The frequency of countercion vibrations has been established to decrease as the ion mass increases. The results of theoretical calculation have been showed to be in good agreement with the experimental data of Raman spectroscopy.

Key words: DNA, ion, vibration, low-frequency spectra.

1 Introduction

Starting with the early research by Watson and Crick [1] it has been a well known fact that a DNA macromolecule in the natural form is a salt, a complex of nucleic acid and metal cations. The ion environment of the double helix plays the dominant role in the helical structure formation. The concentration of the counterions in DNA solution determines the macromolecule helix twisting, bending and the recognition of the DNA sites by proteins and drugs [2–5]. Therefore, metal cations are of paramount importance in the processes of DNA functioning in living systems.

Metal ions interacting with DNA may be divided in two groups [4,5]. The first group represents the ions belonging to the diffusion atmosphere of the macromolecule. Another group is the ions that are directly bound with different structural elements of the double helix. The interaction of the ions of this group is very specific and depends on their type. Transition and alkaline-earth metal ions are bound principally with nucleic base atoms, and the cations of alkaline metals being bound with phosphate groups of the helix backbone [5].

Under ordinary conditions the thermal fluctuations cause vibrations of DNA structural elements and counterions around their equilibrium positions. The vibrations of alkaline metal ions with respect to the DNA backbone phosphates (ion-phosphate modes) are likely to be visual and vastly intensive in vibrational spectra because of homogeneity of backbone phosphate groups and interacted cations. Determination of the character of these vibrations is of great interest for understanding the counterion role in the DNA helix mobility and conformational transformations.

The vibrations of the double helix structure elements may be observed in the low-frequency region because of the massiveness of DNA atomic groups and a relatively weak interaction between them. In fact, the DNA vibration spectra show the set of modes in the region lower then 250 cm−1 [6–17]. The low-frequency spectra of DNA
may be conditionally divided in three ranges. The lowest range (10 – 30 cm$^{-1}$) characterizes vibrations of the double helix backbone \cite{16,19}. The DNA frequencies in this range depend on counterion type \cite{13,15,16}, and humidity \cite{9,16}. The middle range (60 - 120 cm$^{-1}$) is generated by vibrations of the hydrogen bonds and intranucleoside mobility \cite{16,19}. A mode strongly depending on counte-

rior type has been observed in the range within 120 – 250 cm$^{-1}$ \cite{17}. In this frequency range an internal vibrational mode of the nucleic bases can be also observed \cite{14,18}. Therefore, it is important to estimate a possible range of the DNA ion-phosphate modes and their dependence on ion type.

To describe the low-frequency vibrational spectra of DNA macromolecule the theoretical approach has been proposed \cite{19,20}. However, in this approach the counterion vibrations have not been taken into consideration. The problem of ion effect on the DNA low-frequency modes has been studied in works \cite{12,21,22}. The results have showed that the DNA low-frequency vibrational spectra depend on counterions, but the specific ion mode has not been found.

The purpose of this paper is to describe the low-frequency vibrations of DNA with counterions, as well as to determine a place of ion-phosphate mode and its dependence on counterion type.

### 2 Model of DNA with counterions

In frame of the approach \cite{19,20} the improved model of the DNA vibrations is elaborated \cite{23}. The model presents DNA as a double chain of the backbone masses $m_0$ (PO$_2$+2O+C$_5$) with connected pendulum-nucleosides $m$ (sugar+base). The counterions are modelled as masses ($m_a$) bonded to the backbone. The nucleoside bases of different chains connected by hydrogen bonds (Fig.1). The heterogeneity of the DNA nucleosides is important for H-bond stretching vibrations in base pairs and for intranu-

cleoside mobility \cite{19,20}. In present paper we intend to find the place of the ion mode in the haul DNA low-frequency spectra, and on this stage the heterogeneity of nucleosides and the intranucleoside mobility are not considered.

Let us write the energy of the system:

$$E = \sum_n \sum_{i=1}^{2} (K_{ni} + U_{ni}) + \sum_{n,n-1} U_{n,n-1}, \quad (1)$$

where $K_{ni}$, and $U_{ni}$ are the kinetic and the potential energy of $n$-th monomer link of the system, and $U_{n,n-1}$ is the interaction along the chain.

The expression for kinetic energy of the $n$-th monomer can be written in the following way:

$$K_{ni} = \frac{1}{2} M Y_{ni}^2 + \frac{1}{2} I \theta_{ni}^2 + m_l \dot{Y}_{ni} + \frac{1}{2} m_a (2 \dot{Y}_{ni} \dot{\xi}_l + \xi_l^2), \quad (2)$$

where $M = m_0 + m + m_a$; $Y_n$ – the displacement of $n$-th nucleoside and phosphate group mass; $I = ml^2 + ma r_0^2$ – the inertia moment of nucleotide with counterion; $l$ is the reduced length of the pendulum-nucleoside, and $r_0$ is the equilibrium distance between ion and phosphate group; $\theta_n$ – the angle of displacement of $n$-th nucleoside from equilibrium state $\theta_{eq}$; $l_s = l \sin \theta_{eq}$; $\xi_n$ – the displacement of $n$-th ion from the equilibrium state.

For small displacements the potential energy of the monomer link may be presented as a sum of three terms describing the energy of H-bond stretching in the pair, the energy of torsion motions of nucleoside around the

![Figure 1: The four mass model with counterion. (a) The monomer links of the DNA. I – the counterions that directly bind to the DNA structure elements, II – the diffusion atmosphere of the macromolecule (b) The displacements of the atomic groups and ions in monomer link](image)
The equation for frequencies is obtained:

$$U_{ni} = \frac{1}{2}(\alpha \delta_n^2 + \beta \theta_n^2 + \gamma \xi_n^2).$$ (3)

Here $\alpha$ is the force constant of hydrogen bond stretching in pairs, $\delta_n = I_n(\theta_1 + \theta_2) + Y_1 + Y_2$ is the base pair stretching, $\beta$ – is the force constant of nucleoside vibration relatively phosphate group, $\gamma$ is the constant of ion-phosphate vibration.

In frame of the DNA conformational vibrations model (Fig. 1) we are looking for the normal modes of the lattice of double helix with counterions. To compare our calculations with experimental data let us consider a limited long-range vibrations of optic type that have to be seen in a spectra of real objects. In this case, it is enough to consider the homogeneous displacements of the system monomer links, where the interaction between monomers along the chain ($U_{n,n-1}$) may be waved.

Using the expressions for the energy (11), (2), and (3) let us write the Lagrange equations of motion for this system. For the conveniens of the following consideration we introduce the variables:

$$Y = Y_1 + Y_2, \quad y = Y_1 - Y_2,$$
$$\theta = \theta_1 + \theta_2, \quad \eta = \theta_1 - \theta_2,$$
$$\xi = \xi_1 + \xi_2, \quad \rho = \xi_1 - \xi_2.$$

In variables (4) the equations of motion for whole system brake up into two systems of connected vibrations:

$$\ddot{Y} + \frac{ml_s}{M} \frac{M}{M} \frac{y}{I} = -\alpha_0(l_s \theta + Y);$$
$$\ddot{\theta} + \frac{ml_s}{I} \frac{M}{M} \frac{\eta}{I} = -\beta_0 \theta - \alpha_0 \frac{ML_s}{I}(l_s \theta + Y);$$
$$\ddot{\eta} + \frac{ml_s}{M} \frac{\eta}{I} = -\beta_0 \eta;$$
$$\ddot{\rho} + \frac{ml_s}{I} \frac{\rho}{I} = -\beta_0 \rho.$$ (5)

Here is $\alpha_0 = 2\alpha/M, \beta_0 = \beta/I, \gamma_0 = \gamma/m_{\text{agt}}$.

The normal modes of the system (6) and (7) let us find in form: $q = q_0 e^{-i\omega t}$. From the system of equations (5) the equation for frequencies is obtained:

$$\omega^2 = \frac{m_{\text{agt}}}{M} \frac{ML_s}{I} \frac{\alpha_0 - \omega^2}{\alpha_0 - \omega^2 m/M^2} - \frac{\alpha_0}{\alpha_0 - \omega^2 m/M^2} \left(\frac{p_0}{p_0 - \omega^2} - \frac{ML_s^2}{I} \frac{\gamma_0 - \omega^2}{\gamma_0 - \omega^2 m/M^2} \right) \approx 0.$$ (7)

Here $p_0 = \alpha_0 ML_s^2/I + \beta_0$. The solutions of equation (7) are the modes $\omega_1, \omega_2,$ and $\omega_3$.

From (6) the following equation is obtained:

$$\omega^2 \mu + \omega^2 (\beta_0' + \gamma_0') + \gamma_0' \beta_0 = 0.$$ (8)

Here $\beta_0' = \beta_0(m_{\text{agt}}/M - 1)$, $\gamma_0' = \gamma_0(m_{\text{agt}}^2 I^2/MI - 1)$, $\mu = 1 - m_{\text{agt}}/M - m_{\text{agt}}^2 I^2/MI$. The solutions of (5) are the modes $\omega_4$ and $\omega_5$:

$$\omega_4^2 = \frac{-(\beta_0' + \gamma_0') \pm \sqrt{(\beta_0' + \gamma_0')^2 - 4\mu \gamma_0' \beta_0}}{2\mu}.$$ (9)

Let us analyze the modes $\omega_{4,5}$. Taking into account that for all counterion type $m_{\text{agt}}/M$ and $m_{\text{agt}}^2 I^2/MI$ are rather small (about 0.1), formula (9) may be transformed:

$$\omega_4^2 \approx \gamma_0,$$ (10)

$$\omega_5^2 \approx \beta_0.$$ (11)

Expressions (10) and (11) show that the modes $\omega_4$ and $\omega_5$ depend, respectively, on ion vibration constant, and constant of backbone vibration. Analyzing the ratio between amplitudes obtained from (6):

$$\frac{y_0}{\eta_0} = \frac{(\beta_0 - \omega^2)I}{\omega^2 m_{\text{agt}}},$$ (12)

$$\frac{\rho_0}{\eta_0} = \frac{(\beta_0 - \omega^2)I}{(\gamma_0 - \omega^2 m_{\text{agt}})},$$ (13)

it is clear that on the mode $\omega_4$ the amplitude of ion vibration ($\rho_0$) is much larger in comparison with the amplitudes of phosphate ($y_0$) and nucleoside ($\eta_0$) motions. So the mode $\omega_4$ characterizes mostly by ion displacements. Therefore we consider that this mode is the mode of ion-phosphate vibrations.

Let us analyze the equation (7). As seen, the form of equation (7) depends on the value of counterion mass ($m_{\text{agt}}$). Taking into account that for light ions ($Li^+$ and $Na^+$) the ratio $m_{\text{agt}}/M$ is very small (about 0.05), the last term in equation (7) may be waved:

$$\frac{\gamma_0 - \omega^2}{\gamma_0 - \omega^2 m_{\text{agt}}^2} \left[(\alpha_0 - \omega^2)(p_0 - \omega^2) - \frac{ML_s^2}{I} \left(\alpha_0 - \omega^2 m_{\text{agt}}^2\right)^2 \right] \approx 0.$$ (14)

One of the solution of (14) is $\omega_1 \approx \sqrt{\gamma_0}$. The amplitude of ion vibration on the mode $\omega_1$ is the largest in comparison with the amplitudes of phosphate ($y_0$) and nucleoside ($\eta_0$) motions. So we have found that for light counterions
the mode $\omega_1$ may be also considered as a mode of ion vibration. It means that for light counterions in the DNA low-frequency spectra there is a twice degenerated mode of ion-phosphate vibrations ($\omega_1 = \omega_2 \approx \sqrt{\gamma_0}$).

The analysis for heavy ions ($\text{Rb}^+$ and $\text{Cs}^+$) shows that on the mode $\omega_1$ the amplitude of H-bond stretching is the largest. So the structure of the DNA low-frequency spectra is qualitatively different for light and heavy counterions.

For further analysis of the ion mode let us determine the constant of ion vibration. Taking into account that counterions form the regular structure around the sugar-phosphate backbone of the DNA such system may be considered as the ion crystal. According to the classical study, the energy of ion interaction in crystal can be presented by potential:

$$V(r) = -\frac{M_\alpha e^2}{4\pi\varepsilon_0 r} + B \exp\left(-\frac{r}{b}\right)$$ (15)

where $M_\alpha$ is a Madelung constant, $e$ is the ion charge, $\varepsilon$ is the dielectric constant, $r$ is the distance between charges, $B$ and $b$ characterize the repulsion between ions. The first term describes the electrostatic attraction and the second – Born-Mayer repulsion. Expanding the energy in the row on small displacements from their equilibrium positions $\xi = r - r_0$, $V \approx \gamma \xi^2/2$ the constant of ion vibrations is obtained:

$$\gamma = \frac{M_\alpha e^2}{4\pi\varepsilon_0 r_0^3} \left(\frac{r_0}{b} - 2\right).$$ (16)

Using the expression for the constant of ion vibration and the approximate formula for the mode of ion vibration is obtained:

$$\omega_{\text{ion}} \approx \sqrt{\frac{M_\alpha e^2}{4\pi\varepsilon_0 M_\alpha r_0^3} \left(\frac{r_0}{b} - 2\right)}.$$ (17)

Analyzing we can see that the ion-phosphate mode strongly depends on the equilibrium distance $r_0$, and ion mass $m_\alpha$. Thus we can make the conclusion that the ion mode has to decrease with increasing of the ion radius:

$$\omega_{\text{Li}} > \omega_{\text{Na}} > \omega_{\text{K}} > \omega_{\text{Rb}} > \omega_{\text{Cs}}.$$ (18)

The ion-phosphate mode is also depended on the Madelung constant $M_\alpha$. This constant is the lowest for dipole ($M_\alpha = 1$) and is big enough for the NaCl ion crystal ($M_\alpha = 1.748$). In DNA the value of the Madelung constant is not known, but we can say that the Madelung constant is depended on the ion concentration, and in dilute solution it will be another then in the saturated solution. It means that the ion-phosphate mode has to be depended of the ion force of the solution.

The constant of ion vibration also depends on the other parameters ($b, \varepsilon$) that will be considered in the following section.

### 3 Constant of ion vibration

In this paper we study the conformational vibrations of DNA with alkaline metals. So the equilibrium distance $r_0$ is estimated as a sum of Pauling radiiuses of ion and oxygen atom of the phosphate group (Table 1). The parameter $b$ is taken equaled to values that are known for ion crystals $\text{LiF}$, $\text{NaF}$, $\text{KF}$, $\text{RbF}$, $\text{CsF}$ [24] (Table 1).

| Parameter | $\text{Li}^+$ | $\text{Na}^+$ | $\text{K}^+$ | $\text{Rb}^+$ | $\text{Cs}^+$ |
|-----------|---------------|---------------|---------------|---------------|---------------|
| $r_0$ (Å) | 2.00          | 2.35          | 2.73          | 2.88          | 3.01          |
| $b$ (Å)   | 0.329         | 0.316         | 0.327         | 0.329         | 0.313         |
| $\varepsilon$ | 5.0          | 6.4           | 8.2           | 9.0           | 10.1          |
| $\varepsilon$ | 1.3          | 1.5           | 1.8           | 1.9           | 2.1           |

Let us estimate the dielectric constant. The value of this constant depends on the distance between ions and the nature of environment. The dielectric constant determination for the DNA presents some difficulties [25–30]. The value of vacuum dielectric constant ($\varepsilon = 1$) is not suitable for description of electrostatic interaction in DNA because in this case the potential near DNA is too high [27]. Very often for solving the Poisson-Boltzmann equation the dielectric constant of the DNA-solution system is considered between 2 and 4 [27]. Hingerty with coworkers developed an approach where the dielectric constant presents as a function of a distance [25]:

$$\varepsilon(r) = 78 - 77(r/2.5)^2 \exp(r/2.5)(\exp(r/2.5) - 1)^{-2}.$$ (19)

Lavery with coworkers were improved the function of Hingerty [26]:

$$\varepsilon(r) = \varepsilon_\infty - \frac{1}{2}[(sr)^2 + 2sr + 2]e^{-sr},$$ (20)

were $\varepsilon_\infty = 78$, and $s = 0.16$. There are also exist other distant dependent dielectric functions [27–29], but functions of Hingerty [19] and Lavery [20] are most common used. The dielectric constants calculated by formulas [19] and [20] are shown in Table 1.

Let us estimate the Madelung constant $M_\alpha$. This constant characterizes the interaction of one ion with the other charges of the system. In our model the charges of the phosphate groups with counterions that neutralize them are considered. Also it is taken into account that
in the solution there exist negatively charged ions of Cl\(^-\). This anions are situated at the distance about 7 Å \([31]\). As usual long-range electrostatic interactions in such systems as DNA are cut off on distance about 10 Å \([31]\) that is approximately equaled to the distance between two neighbor phosphate groups of one polymer chain. That is why only the charges of neighbor ion-phosphate pairs and Cl\(^-\) anions are considered in Madelung constant calculations. The following formula for Madelung constant is obtained:

\[
M_a = 1 + \frac{\epsilon(r_0) r_0}{\epsilon(r_t) r_t} + 2 \frac{\epsilon(r_0) r_0}{\epsilon(r_p) r_p} - 2 \frac{\epsilon(r_0) r_0}{\epsilon(r_a) r_a}
\]  

(21)

Here \(\epsilon(r)\) is the dielectric constant, \(r_t\) is the distance between cation and Cl\(^-\) anion of the solution, \(r_p\) is the distance between cation and neighbor phosphate group of the same polymer chain, and \(r_a\) – the distances between neighbor cations of the same polymer chain (Fig.1). The first term in \(21\) describes the interaction between cation and Cl\(^-\) anion of the solution, the second term describes the interaction between cation and neighbor phosphate group, and the third term describes the interaction between neighbor cations. The values of the Madelung constants calculated by formula \(21\) are shown in Table 1.

### 4 Ion-phosphate mode

Using the parameters shown in Table 1 and formula \(16\) the values of the constant of ion vibrations (\(\gamma\)) is estimated. The frequencies of ion-phosphate vibrations (\(\omega_1\)) calculated by expressions \(9\) are shown in Table 2.

**Table 2.** The frequencies of ion-phosphate vibration for B-DNA (cm\(^{-1}\))

| Method | Li\(^+\) | Na\(^+\) | K\(^+\) | Rb\(^+\) | Cs\(^+\) |
|--------|---------|---------|-------|--------|--------|
| \(\varepsilon = 2\) | 444 233 162 112 93 |
| \(\varepsilon = 4\) | 314 165 114 79 66 |
| \(\varepsilon = 26\) | 488 237 151 100 80 |
| \(\varepsilon = 25\) | 252 115 70 46 37 |
| [17] | 237* 230* 150 110 95 |
| [14] | 235 |

Note: The asterisk * marks the value determined by us from the spectra of work [17]

Analyzing the results shown in Table 2 we can say that the best agreement with the experimental data gives the value of \(\varepsilon = 2\) and Lavery dielectric function [26]. In case of ion Li\(^+\) the calculated frequency of vibration differ sufficiently from the experimental data. The reason of this situation may be connected with effects of ion hydratability. The ion Li\(^+\) has a very small weight (7 a.u.m.) and radius (0.6 Å) in compare with molecules of water.

Therefore, the influence of water on the lithium vibrations may be very large. Our estimation Li\(^+\) frequency when it is in complex with one (\(\omega_1^d = 267\) cm\(^{-1}\)), two (209 cm\(^{-1}\)), and three (180 cm\(^{-1}\)) molecules of water show that the frequency value became sufficiently lower. As seen if one consider that lithium ion moves in the solution together with water molecules the frequency become very close to the experimental value.

For understanding of the low-frequency spectra dependence on counterion type the frequencies of all five branches of vibrations \(\omega_1, \omega_2, \omega_3, \omega_4,\) and \(\omega_5\) are calculated (Fig. 2). As we can see all low-frequency modes obtained with the help of proposed approach decrease with increasing of counterion mass. The ion mode (\(\omega_1, \omega_4\)) is the most sensitive to counterion type. Our calculations show the splitting of the ion mode for heavy ions that was qualitatively obtained above. The theoretical results for the lowest mode (\(\omega_{2,5}\)) and for the ion mode (\(\omega_4\)) correlate with the experimental data. The counterion dependence of the H-bond stretching mode (\(\omega_3\)) is not studied experimentally.

In the conclusion we can say that the specific mode of ion-phosphate vibration was found. It is in frequency range 90 – 250 cm\(^{-1}\) and decrease with increasing of ion radius. This mode is very sensitive to the counterion type and to the ion force of the solution. As the results presented in fig. 2 show all low-frequency modes of the DNA macromolecule depend of counterion type.
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