Low-frequency vibrations of water molecules in DNA minor groove

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Abstract Water molecules around the DNA form the hydration shell having different structural and dynamical features in different regions of the double helix. In the DNA minor groove, water molecules are highly ordered and in the case of AT nucleotide sequence, the formation of a hydration spine is observed. In the present research, the vibrations of the hydration spine have been studied to establish the mode of translational vibrations of water molecules in the DNA low-frequency spectra (water-spine vibrations). Using the developed phenomenological model with the parameters determined for different nucleotides of the DNA fragment CGCGAATTCGCG, the frequencies of vibrations of the hydration spine have been obtained within $185 \pm 20 \text{ cm}^{-1}$ depending on type of nucleotide. The obtained frequencies are in the same region as the translational vibrations of water molecules in the bulk. To select the mode of water-spine vibrations from those modes that are present in the bulk water, the dynamics of DNA with different nucleotide contents has been analyzed, and the possible influence of heavy water has been estimated. The determined features of the mode of water vibrations in the hydration spine of DNA minor groove indicate that this mode may be observed in the experimental spectra.

1 Introduction

The natural DNA consists of two chains of nucleotides (adenine, guanine, thymine, and cytosine) winding around each other as the double helix [1]. The hydrophobic nucleotide bases form the complementary H-bonded pairs (A-T and G-C) inside the macromolecule to reduce the contact with water molecules. The negatively charged phosphate groups of the double helix backbone are exposed to the solution to be neutralized by the positively charged ions of metals. Starting with the very first X-ray and modeling studies of the DNA molecular structure, the ion-hydration environment was known to stabilize the macromolecule structure [2–4]. The ion-hydration shell of DNA ranges over several layers within 10–15 Å from the macromolecule and is considered as primary and secondary hydration shells [5–7]. The conformational dynamics of the DNA double helix and the dynamics of its hydration shell are interrelated [8,9] that is determinative for the mechanisms of nucleic-protein recognition and the interaction with the biologically active compounds [10–12]. Thus, to understand the physical mechanisms of DNA biological functioning the structure and dynamics of the hydration shell of the double helix should be studied.

In aqueous solution, the DNA double helix takes the canonical $B$-form with a hydration shell consisted of about 40 water molecules per nucleotide pair [6, 13,14]. These water molecules are localized in different compartments of the double helix: minor groove, major groove, and outside the macromolecule near the phosphate groups. The X-ray studies of crystal structure of short DNA fragments with nucleotide sequence AATT in the center of the macromolecule showed that in the minor groove of the double helix the ordered structure of water molecules is formed [15]. This structure is consisted of water molecules bridging N and O atoms of purines (A, G) and pyrimidines (C, T) nucleotide bases of opposite strands of the DNA, and it is now known as the water-hydration spine. The properties of water-hydration spine have been widely studied in further X-ray experiments [16], nuclear magnetic resonance (NMR) studies [17,18], and chiral nonlinear vibrational spectroscopy [19]. The formation of water-hydration spine in the DNA minor groove was also observed in molecular dynamics (MD) simulations [20,21].

The dynamics of hydration shell depends on location of water molecule in the DNA double helix and is characterized by different residence times. The experimental and simulation data [22,23] show that near phosphate groups the residence time of water molecules is about 10 ps, while in the bulk water it is about 1 ps. In the grooves of the double helix, the dynamics of water molecules is much slower. In the minor groove, the residence time is much longer (the range from 0.1 ns to
The vibrations of water molecules related to H-bond stretching and H-bond bending are observed in the frequency range 60–200 cm$^{-1}$, while librational motions are above 300 cm$^{-1}$ [28–39]. In the Raman spectra, the modes related to stretching and bending of H-bonds are observed as the bands at about 175 and 60 cm$^{-1}$ [28–31]. These vibrations are also observed in the infrared absorption (IR) spectra [32–34], neutron scattering experiments [35] and also obtained in the modeling [36], and MD simulations [37–39]. At the same low-frequency spectra range, the conformational vibrations of the DNA double helix, characterizing motion of the DNA atomic groups as the whole, are observed [40–43]. In general, the DNA low-frequency spectra are characterized by the narrow peak about 20 cm$^{-1}$, a broad band near 85 cm$^{-1}$ [40–43], and the counterion-dependent modes at higher frequencies (100–200 cm$^{-1}$) [44,45].

To describe the low-frequency spectra of DNA, different analytical approaches were developed [46–50]. In particular, the detailed interpretation of the DNA low-frequency spectra was done within the framework of the approach of the conformational vibrations of the double helix [47,48]. According to this approach, the lowest mode around 20 cm$^{-1}$ is interpreted as the vibrations of DNA backbone, while the broad band near 85 cm$^{-1}$ characterizes the vibrations of H-bonds stretching in the base pairs and intranucleoside vibrations. The counterion-dependent modes in DNA low-frequency spectra [44,45] were attributed to the vibrations of counterions with respect to the phosphate groups of the double helix backbone (ion-phosphate vibrations) [52–55]. To determine the modes of water molecules vibrations in the DNA low-frequency spectra, new theoretical approach should be developed.

The goal of the present study was to determine the low-frequency vibrations of water molecules in the DNA minor groove. To solve this problem, the analytical model has been elaborated based on the phenomenological approach of the DNA conformational vibrations [47]. The developed model is described in Sect. 2. In Sect. 3, the parameters of the model have been determined. In Sect. 4, the frequencies and amplitudes of vibration of DNA with water molecules have been estimated. As the result, the modes of atter translational vibrations in the DNA minor groove has been established within the frequency range from 160–210 cm$^{-1}$, depending on nucleotide sequence. In Sect. 5, the obtained frequencies of vibrations have been compared with the experimental spectra of DNA in an aqueous environment. The frequencies of water vibrations in the DNA minor groove are obtained in the same spectra range as translational vibrations of bulk water. To distinguish the vibrations of water molecules in the DNA minor groove from those in the bulk, the vibration of DNA with heavy water has been considered, and the dependence on nucleotide sequence is discussed.

2 Model of water vibrations in DNA minor groove

To build the model of vibrations of water molecules in the hydration spine of DNA minor groove, the approach for the description of the conformation dynamics of DNA double spine developed by Volkov and Kosevich [47] has been used. In the present model, the strands of sugar-phosphate backbone of the double helix are modeled as rigid walls. The nucleosides of mass $M$ are presented as the physical pendulums with the reduced length $\ell$, suspended to the backbone of DNA. The suspension points of pendulum-nucleosides are related to the $C_2$ atoms of deoxyriboses of the DNA backbone. The pendulum-nucleosides rotate in the plane orthogonal to the helical axis within the equilibrium positions characterized by the angle $\theta_0$. The pendulum-nucleosides of different chains of the model are linked by spring, modeling the H-bonded nucleotide pairs of the DNA double helix. Water molecules are represented as the masses bonded to the pendulum-nucleosides, bridging the nucleotide bases of one strand with the nucleotide base of another strand. In Fig. 1, the schematic structure of the Drew–Dickerson fragment with the spine of hydration is presented according to [15,16]. In the model, the hydrogen atoms of water molecule are not considered explicitly. All atoms of water molecule are presented as a point mass $m$, localized in defined position of the structure of the hydration spine of the DNA minor groove. The nucleosides of opposite strands bridged by water molecule form the monomer link in our model (Fig. 2a). In the further consideration, the nucleotides interacting with the water molecules and belonging to different nucleotide pairs will be referred as “water-bounded pairs”. In the present work, to obtain the analytical solutions for the vibrational frequencies, the average parameters $\theta_0, \ell$ and $M$ for the nucleotides of different types (adenine, thymine, guanine, and cytosine) are used.

To consider the dynamics of structural elements of the model, the following system of coordinates has been used. The center of coordinates is related to the water molecule that is bonded to the nucleotides of different strands (Fig. 2b). The axis $OZ$ is directed along the axis of the double helix. The axis $OY$ is directed to the major groove. The axis $OX$ is orthogonal to the plane $YOZ$. The nucleotides pairs are placed in
the plane $XOY$, where axis $OX$ defines the positive direction for each nucleoside to the outside of the double helix. The vibrations of pendulum-nucleosides with respect to the phosphate groups are described by deviations $\theta_{i,n}$ from the equilibrium angle $\theta_0$, where $n$ enumerates the monomer link ($n = 0, \pm 1, \ldots, \pm N$) and $i$ is the number of DNA strand ($i = 1, 2$). The position of water molecule in the monomer link is described by the parameters $a$ and $b$, characterizing the distances from the center of coordinate system to suspension point ($C'_3$ atom of deoxyribose) of nucleosides mass in $OX$ and $OY$ direction, respectively (Fig. 2b). The parameter $\phi_0$ is the angle that is formed by the water molecule and nucleotides with which it is bound. The displacements of water molecules from the equilibrium positions in the monomer link are described by the deviation $r_n$ (Fig. 2b). The coordinates of the displacements for the system are presented as follows:

$$X_{i,n} = a - \ell \cos(\theta_0 + \theta_{i,n}); \quad (1)$$
$$Y_{i,n} = \ell \sin(\theta_0 + \theta_{i,n}) - b; \quad (2)$$
$$u_{x,n} = r_n \cos \phi_0; \quad (3)$$
$$u_{y,n} = r_n \sin \phi_0. \quad (4)$$

Within the framework of the introduced coordinates, the energy of vibrations of structural elements of the double helix and water molecules may be written as follows:

$$E = \sum_{n} [K_n + U_n + U_{n-1}], \quad (5)$$

where $K_n$ and $U_n$ are the kinetic and potential energies of the monomer link $n$; $U_{n-1}$ describes the interactions in the complementary pairs and interactions of the staked bases along the chain.

Taking into account that in the present work, small displacements of the masses in the model are considered the coordinates, (1)–(4), the kinetic energy may be written in the following form:

$$K_n = \frac{1}{2} \sum_{i=1}^{2} M(\ell \dot{\theta}_{i,n})^2 + m r_n^2. \quad (6)$$
The potential energy of the monomer link in harmonic approximation may be written as follows:

\[ U_n = \frac{1}{2} \sum_{i=1}^{2} \left[ \beta \ddot{\theta}_{i,n}^2 + k (\theta_{i,n} - \ell C_1 + r_n C_2)^2 \right]. \]  

(7)

Here, \( C_1 = (a \sin \theta_0 - b \cos \theta_0) / R_0 \) and \( C_2 = (a \cos \phi_0 + b \sin \phi_0 - \ell \cos (\theta_0 - \phi_0)) / R_0 \), where \( R_0 \) is the equilibrium distance in water-bounded pair and \( R_0 = (a^2 + b^2 + \ell^2 - 2(a^2 \ell + b^2 \ell_0))^{1/2} \). \( \ell_a = \ell \sin \theta_0; \ell_b = \ell \cos \theta_0; \beta \) is the force constant related to the rotations of nucleosides with respect to the backbone chain in the plane of nucleosides (the constant of nucleoside vibrations); and \( k \) is the force constant describing the interaction of water molecule and nucleoside (the constant of water vibrations).

The potential energy of displacements in complementary nucleotide pairs and the energy of interaction along the chain may be written as follows:

\[ U_{n-1} = \frac{\alpha}{2} \ell_a^2 (\theta_{1,n} + \theta_{2,n-1})^2 + \sum_{i=1}^{2} \left[ g (\theta_{i,n} - \theta_{i-1,n}) - k (\theta_{i,n} - \ell C_1 + r_n C_2)^2 \right], \]  

(8)

where \( \alpha \) is the force constant of H-bonds stretching in complementary pairs; \( \ell_a (\theta_{1,n} + \theta_{2,n-1}) \) describes H-bonds stretching in base pairs; and \( g \) is the force constant of interactions between the stacked adjacent base pairs.

Using the formulae (6)–(8), the following equations of motion have been obtained:

\[ \begin{cases} 
M \ell^2 \ddot{\theta}_{1,n} + \beta \dot{\theta}_{1,n} + \alpha \ell_a^2 (\theta_{1,n} + \theta_{2,n-1}) + 
g(\theta_{1,n-1} - 2\theta_{1,n} + \theta_{1,n+1}) + 
+ k \ell C_1 (\theta_{1,n} - \ell C_1 + r_n C_2) = 0; \\
M \ell^2 \ddot{\theta}_{2,n} + \beta \dot{\theta}_{2,n} + \alpha \ell_a^2 (\theta_{1,n+1} + \theta_{2,n}) + 
g(\theta_{2,n-1} - 2\theta_{2,n} + \theta_{2,n+1}) + 
+ k \ell C_1 (\theta_{2,n} - \ell C_1 + r_n C_2) = 0; \\
m \ddot{r}_n + k C_2 (\theta_{1,n} \ell C_1 + r_n C_2) + 
+ k C_2 (\theta_{2,n} \ell C_1 + r_n C_2) = 0.
\end{cases} \]  

(9)

The system of Eqs. (9) consists of three differential equations of the second order. The solutions of these equations may be found in the following form:

\[ \begin{align*}
\theta_{i,n} &= \tilde{\theta}_i e^{i(\omega t - \kappa n)}, & r_n &= \tilde{r} e^{i(\omega t - \kappa n)},
\end{align*} \]  

(10)

where \( \kappa \) is the projection of the wave vector to the axis \( Z; \tilde{\theta} \) and \( \tilde{r} \) are the amplitudes of vibrations.

In the present work, the modes, observed in the experimental vibrational spectra, are in the scope of interest. Therefore, we are interested in finding the vibrations of optic type in long-wave limit. Taking this into consideration, the wave vector \( \kappa \) in Eqs. (9) can be equaled to zero. Using new variables

\[ \tilde{\theta}_1 + \tilde{\theta}_2 = \tilde{\theta}, \quad \tilde{\theta}_1 - \tilde{\theta}_2 = \tilde{\xi}, \]  

(11)

Eqs. (9) in long-wave limit (\( \kappa \to 0 \)) take the following form:

\[ \begin{align*}
&\{ \ddot{\theta} \left( \omega^2 - \beta_0 - 2\alpha_0 \sin^2 \theta_0 - k_0 C_2^2 m \right) - k_0 2C_0 C_2 m \ddot{\theta} = 0; \\
&-\theta_0 k_0 C_1 C_2 + (\omega^2 - 2k_0 C_2^2) \ddot{\theta} = 0; \\
&\tilde{\xi} \left( \omega^2 - \beta_0 - k_0 C_2^2 m \right) = 0,
\end{align*} \]  

(12)(13)

where \( \alpha_0 = \alpha/M; \beta_0 = \beta/M \ell^2; k_0 = k/m. \)

The system of equations (9) splits into equations (12) and (13). The equations in (12) form the system of coupled equations, characterizing the symmetrical vibrations of pendulum-nucleosides (variable \( \tilde{\theta} \)) and water molecules (variable \( \tilde{r} \)). Equation (13) describes the asymmetrical motions of pendulum-nucleosides.

Using the existence condition for a solution of equations (12), the equation for frequencies of long-wave vibrations has been determined in the following form:

\[ \omega^4 - \omega^2 \left( \beta_0 + 2\alpha_0 \sin^2 \theta_0 + k_0 \left( 2C_2^2 + C_1^2 m/M \right) \right) + 2k_0 C_2^2 (\beta_0 + 2\alpha_0 \sin^2 \theta_0) = 0. \]  

(14)

From Eq. (13), the following equation for frequency has been determined:

\[ \omega^2 - \beta_0 - k_0 C_2^2 m/M = 0. \]  

(15)

The solutions of Eq. (14) may be written in the following form:

\[ \omega_{W,H}^2 = \frac{1}{2} \left\{ \beta_0 + 2\alpha_0 \sin^2 \theta_0 + k_0 \left( 2C_2^2 + C_1^2 m/M \right) \right\} \pm \left\{ \left( \beta_0 + 2\alpha_0 \sin^2 \theta_0 + k_0 \left( 2C_2^2 + C_1^2 m/M \right) \right)^2 - 8k_0 C_2^2 (\beta_0 + 2\alpha_0 \sin^2 \theta_0) \right\}^{1/2}. \]  

(16)

The solution of Eq. (15) has been obtained as follows:

\[ \omega_N^2 = \beta_0 + k_0 C_2^2 m/M. \]  

(17)

Taking into account that ratio between the masses of nucleoside \( (M) \) and water \( (m) \) may be considered as negligibly small \( (m/M \to 0) \), Eqs. (16), (17) may be written in the following approximation:

\[ \omega_W^2 \approx 2k_0 C_2^2, \]  

(18)

\[ \omega_H^2 \approx \beta_0 + 2\alpha_0 \sin^2 \theta_0, \]  

(19)

\[ \omega_N^2 \approx \beta_0. \]  

(20)

The analysis of Eqs. (18) and (20) shows that the mode \( \omega_W \) depends only on the constant of water.
vibrations and \( \omega_N \) depends on the constant of nucleoside vibrations. Thus, it may be concluded that these modes characterize the vibrations of water molecules and pendulum-nucleoside vibrations, respectively. Further, the mode of water translation vibrations in the hydration spine of the DNA minor groove (\( \omega_W \)) will be referred as the mode of water-spine vibrations. As follows from Eq. (20), the mode \( \omega_H \) depends on constants of H-bonds stretching in base pairs and nucleoside vibrations with respect to the backbone, therefore, this mode may be considered as the mode of hydrogen bonds stretching vibrations.

To analyze the character of coupled vibrations of water molecules in the hydration spine of the DNA minor groove, the amplitudes of vibrations of the system should be analyzed. In the present work, the values of amplitudes of vibrations have been estimated accordingly to the approach [47], where the Boltzmann hypothesis about the uniform energy distribution by degrees of freedom was used. Following the work [47], the potential energy \( (7), (8) \) has been averaged over the time, and expressions for the energy have been obtained in the form:

\[
\langle U \rangle = \frac{1}{8} [U^+ + U^-],
\]

where

\[
U^+ = 2\alpha \ell^2 \theta^2 + \beta \tilde{\theta}^2 + k \left( \tilde{\theta}C_1 + 2\tilde{r}C_2 \right)^2, \tag{21a}
\]

\[
U^- = \beta \tilde{\theta}^2 + k \left( \tilde{\theta}C_1 \right)^2. \tag{21b}
\]

According to the Boltzmann hypothesis, the average energy per one degree of freedom is equal to \( k_B T/2 \), where \( T \) is the temperature and \( k_B \) is the Boltzmann constant [57]. Taking this into consideration, and using Eq. (21), the amplitudes of water-spine vibrations can be determined as follows:

\[
\tilde{r} = 2 \sqrt{\frac{k_B T}{U^+_r}}. \tag{22}
\]

Here, \( U^+_r \) has the form:

\[
U^+_r = 2\alpha \sin^2 \theta_0 \left( \frac{\tilde{\theta} \ell}{\tilde{r}} \right)^2 + \beta \left( \frac{\tilde{\theta} \ell}{\tilde{r}} \right)^2 + k \left( \frac{\tilde{\theta} \ell}{\tilde{r}} C_1 + 2C_2 \right)^2.
\]

The ratio of amplitudes of vibrations \( \tilde{\theta} \) and \( \tilde{r} \) may be obtained from system of Eqs. (12) in the following form:

\[
\frac{\tilde{\theta} \ell}{\tilde{r}} = \frac{2k_C C_1 C_2 \omega^2}{\omega^2 - \beta_0 - 2\alpha_0 \sin^2 \theta_0 - k_0 C_1^2 \omega^2}. \tag{23}
\]

Using the formulae (16), (17), (21) and (22), the frequencies and amplitudes of the vibrations may be determined.

### 3 Model parameters

To estimate the frequencies and amplitudes of vibrations of the system, the structural parameters \( (\theta_0, \ell, \phi_0, M \) and \( m \) and the force constants \( (\alpha, \beta, k) \) of the model should be determined. The parameters \( \theta_0, \ell, \alpha, \) and \( \beta \) for B-DNA double helix have been taken from [47,48]. Thus, the force constant of H-bonds stretching in the complementary base pairs \( \alpha \) and the force constant of nucleoside vibrations \( \beta \) are equal to 80 kcal/mol \( \AA^2 \) and 40 kcal/mol, respectively. The values of equilibrium angle \( \theta_0 \) and reduced length \( \ell \) are equal to 28° and 4.9 Å, respectively. The mean mass of nucleoside \( M \) has been taken equal to 199 u.m.a.

The position of water molecule in the monomer link of the model has been determined by the parameters \( a \) and \( b \) that are the distances from selected center of coordinate system (water molecule) to the suspension point of nucleoside (\( C'_3 \) atom of deoxyribose). Taking into consideration the structure of the DNA double helix and the structure of the hydration spine in the minor groove, the values of \( a \) and \( b \) have been taken equal 7.3 Å and 1.7 Å, respectively (Fig. 2b). The angle \( \phi_0 \) has been calculated using the X-ray data [16] for the structure of B-DNA. The values of the angle \( \phi_0 \) have been averaged over all type of water-bonded pairs in the structure. The obtained mean value of \( \phi_0 \) is equal to 39°. The mass of water molecule \( m \) is 18 u.m.a.

In the present work, the force constant of water vibrations \( k \) has been estimated using the information about the potential of mean force (PMF) that may be obtained from molecular dynamics simulations. Water molecules are trapped in the potential well that may be characterized by PMF. The PMFs for water molecules in each water-bonded pair have been calculated from the definition [58]:

\[
W = -k_B T \ln(g(r)), \tag{24}
\]

where \( k_B \) is the Boltzmann constant, \( T \) is the temperature, and \( g(r) \) is the radial distribution function (RDF).

The RDFs have been derived using molecular dynamics simulations trajectories obtained in [56]. In the work [56], the simulation systems contained canonical B-DNA double helix in water solution with counterions. The sequence of nucleotides in the DNA fragment was d(CGCGAATTCGCG). The systems were simulated at temperature 300 K and pressure about 1 bar. The length of each simulation trajectories was 200 ns. In the present work, the simulation trajectory of the system of DNA with K+ counterions was used for the analyses. The RDFs have been built for oxygen atoms of water molecules with the respect to reference atoms of nucleotides: \( O_2 \) of cytosine and thymine and \( N_1 \) of guanine and adenine. The radial distribution functions have been calculated using the plugin [59] implemented to the VMD software [60]. The obtained RDFs for water molecules with respect to the reference atoms of the selected bases in the minor groove
The obtained frequencies of water-spine vibrations \( \omega \) have been estimated for each nucleotide in the minor groove of the Drew–Dickerson dodecamer according to Eqs. (27). The values of the constant \( k \) have been averaged over the nucleotides forming the water-bonded pairs. The obtained constants of water vibrations may be used in the developed model as the case of infinite DNA macromolecule with homogeneous nucleotide sequence, for example, the poly(A)-poly(T) and poly(G)-poly(C). The calculated force constants for water molecules with nucleotide bases in water-bonded pairs in the minor groove are shown in Table 1.

The constants of water vibrations \( k \) have been estimated from the potentials of mean force, derived through molecular dynamics simulations. Therefore, the information about the state of the system is embedded to the constant. In particular, these are the temperature, pressure, the properties of the solution featured by water model. The changes of simulation parameters will induce the changes of the potential of mean force as well as the constant \( k \).

### 4 Frequencies and amplitudes of vibrations

The values of frequencies of vibrational modes have been estimated using the formulae (16), (17) and the parameters determined in the previous section (Sect. 3). The calculated frequencies of vibrations are presented in Table 2.

The obtained frequencies of water-spine vibrations \( \omega_W \) range from 166 cm\(^{-1}\) to 205 cm\(^{-1}\) depending on nucleotide type. In the case of G-G and C-A water-bonded pairs that are in the ends of polynucleotide, the frequencies of vibrations are the highest. The mean value for G4-G22 and G10-G16 is about 201 cm\(^{-1}\), while for A5-C21 and C9-A19 it is 203 cm\(^{-1}\) (Table 2). In the following step of water-bonded nucleotide pair (A-T), the frequency \( \omega_W \) drastically decreases for about 20 cm\(^{-1}\). The mean value of the frequency in the case of A6-T20 and T8-A18 water-bonded pairs is 182 cm\(^{-1}\).
The minimum value of $\omega_W$ is observed in the case of T-T water-bonded pair that is in the center of considered DNA fragment (lower than 170 cm$^{-1}$). The dependence of frequency of water vibrations on nucleotide sequence is almost symmetrical with respect to the central nucleotide pair (T7-T19). The values of frequencies $\omega_W$ in symmetrical water-bonded pairs vary within 2 cm$^{-1}$ around the mean values that is within the accuracy of our calculations. The dependence of the frequency of water-spine vibrations on sequence of nucleotides is related to both the structure of the DNA double helix and the hydrations shell of the macromolecule.

The frequency of the mode of H-bond stretching vibrations ($\omega_H$) is about 47 cm$^{-1}$ that is about twice lower than in the case of the approach of the four-mass model used as the basis of our model (about 85 cm$^{-1}$) [47,48]. According to the four-mass model, the H-bond stretching occurs due to the symmetrical rotations of nucleosides around phosphates and motions of the masses of phosphate groups. In the present model, the phosphates are fixed and in this case, the H-bonds stretching vibrations in complementary pairs are caused only by pendulum-nucleosides vibration around the phosphate groups. To check whether there is any effect of fixing phosphate groups for the vibrations of water molecules, the calculations of the frequencies of DNA with water molecules have been performed by taking different values of the constant of H-bond stretching vibrations. The results of such an analysis have shown that constraining the dynamics of phosphate groups does not significantly affect the dynamics of water molecules.

The frequency of the mode of the vibrations of nucleosides as physical pendulums ($\omega_N$) is within the range 14–16 cm$^{-1}$ depending on nucleoside type. The calculated frequency values are in good agreement with results of four-mass model [47,48], where this mode is referred to vibrations of DNA backbone. The obtained frequency values of this mode are in good agreement with experimental studies that determine this mode as the lowest mode in the DNA low-frequency spectra. The detailed studies have shown that this mode depends on the frequency range of the hydration spine in the minor groove of the DNA double helix.

Thus, the water-spine vibrations are interrelated with the conformational vibrations of the DNA structural elements in the nucleotide pairs. The obtained frequencies of vibrations show that dynamics of water molecule depends on nucleotide type.

### 5 Theory and experiment

The obtained results show that the water-spine vibrations are localized within the frequency range from about 160 cm$^{-1}$ to about 210 cm$^{-1}$ depending on sequence of nucleotides (Table 2). The experimental detection of the mode of water vibrations is difficult due to the problem of distinguishing this mode among other modes that are observed in the DNA low-frequency spectra. In particular, in the spectra range lower than 250 cm$^{-1}$ the modes of DNA conformational vibrations [40–45,51] as well as the modes of water translational vibrations [28–32,35] are observed.

The experimental data show that in the low-frequency Raman spectra of liquid water, the modes of translational vibrations of water molecules are observed as a broad band around 180 cm$^{-1}$ [28–31]. According to our results, the mode of water-spine vibrations is localized within this band. In the case of the samples of DNA polynucleotides at low humidity at the temperature 300 K, some other modes are also present in this spectra range [44,45]. In particular, in the peaks around 160 cm$^{-1}$, 170 cm$^{-1}$, 181 cm$^{-1}$, 195 cm$^{-1}$, and 214 cm$^{-1}$ were observed in the low-frequency spectra of poly(dA)-poly(dT), poly(dA-dT)-poly(dA-dT), and poly(dG)-poly(dC) dry films [44]. The modes around 170 cm$^{-1}$ are attributed to the lattice vibrations of NaCl crystals present in the sample [44] and to the vibrations of Na$^+$ counterions with respect to the phosphate groups of DNA backbone (ion-phosphate vibrations) [52–55]. The origin of the other modes was not established, but taking into consideration our results,
Table 3 The amplitudes of the DNA conformational vibrations with the water molecules which are located in the minor groove of double helix

| G4-G22    | θ (°) | ℓ (pm) | ξ (°) | δ (pm) |
|-----------|-------|--------|-------|--------|
| ω_W       | 0.045 | 14.0   | 0     | 0.18   |
| ω_H       | -2.97 | 3.85   | 0     | -11.9  |
| ω_N       | 0     | 0      | 8.9   | 0      |

| Ω          |        |        |       |        |
| A5-C21     | 0.044  | 13.9   | 0     | 0.18   |
| ω_W       | -2.97  | 3.84   | 0     | -11.9  |
| ω_N       | 0      | 0      | 8.8   | 0      |

| A6-T20     | 0.050  | 15.4   | 0     | 0.20   |
| ω_W       | -2.97  | 3.89   | 0     | -11.9  |
| ω_N       | 0      | 0      | 9.4   | 0      |

| T7-T19     | 0.055  | 16.8   | 0     | 0.22   |
| ω_W       | -2.97  | 3.94   | 0     | -11.9  |
| ω_N       | 0      | 0      | 9.8   | 0      |

| T8-A18     | 0.049  | 15.3   | 0     | 0.20   |
| ω_W       | -2.97  | 3.89   | 0     | -11.9  |
| ω_N       | 0      | 0      | 9.3   | 0      |

| C9-A17     | 0.043  | 13.6   | 0     | 0.17   |
| ω_W       | -2.97  | 3.83   | 0     | -11.9  |
| ω_N       | 0      | 0      | 8.7   | 0      |

| G10-G16    | 0.044  | 13.8   | 0     | 0.18   |
| ω_W       | -2.97  | 3.84   | 0     | -11.9  |
| ω_N       | 0      | 0      | 8.8   | 0      |

θ and ξ are the amplitudes of pendulum-nucleoside vibrations; ℓ is the amplitude of water molecule vibrations in water-bonded pairs; and δ is the value of H-bonds stretching in base pairs. ω_W, ω_H, ω_N are the frequencies of vibrations (Table 2).

These modes may be attributed to the vibrations of water molecules in the DNA minor groove.

To detect the mode of water-spine vibrations among the other modes that are observed in the low-frequency spectra of DNA, the specific properties of this mode should be taken into consideration. In particular, the isotopic shift due to the heavy water (D_2O) is possible. To analyze the possible value of isotopic frequency shift, the frequency of vibration of heavy water in the DNA minor groove has been calculated using the developed approach. Based on the X-ray and neutron diffraction studies of DNA structure [63, 64], the polar hydrogen atoms of DNA may be replaced by deuterium atoms in heavy water. Such exchange is observed for hydrogen atoms that are bonded to nitrogen and oxygen atoms, while H-atoms attached to the carbon atoms are not replaced by deuterium. In our estimations of the frequency of vibration of DNA with heavy water, the H atoms of nucleosides have been replaced by D atoms (on average three H atoms per nucleoside). As a result of exchange, the average mass of pendulums-nucleoside increased to 202 u.a.m.. The frequency of heavy water vibrations has been obtained within the range 158–195 cm^{-1} depending on nucleotide sequence. The comparison of H_2O and D_2O vibrations has shown that frequency decreases for about 10 cm^{-1}. The frequencies of vibrations of heavy water and light water in the DNA minor groove are shown in Fig. 3. The experimental data for liquid D_2O have shown that the mode of translational vibrations softens for about 10 cm^{-1} compared to the liquid H_2O [65].

Taking into consideration that the frequencies of water-spine vibrations essentially depend on nucleotide sequence, the samples of DNA with different contents of CG nucleotides may be used in experiments. For example, the DNA from bacterium Clostridium perfringens and the DNA from bacterium Micrococcus lysodeikticus contain 27 % and 72 % of CG nucleotides, respectively [66, 67]. In the spectra of DNA from Clostridium perfringens bacterium, the mode of water-spine vibrations is expected to be near 170 cm^{-1} due to the higher content of AT nucleotides. In this case, the mode of water-spine vibrations will be almost in the center of the broad band of water vibrations in the bulk, which will complicate the detection of this mode. In the spectra of DNA from Micrococcus lysodeikticus bacterium, the mode of water-spine vibrations is expected to be present near 200 cm^{-1}, since the number of CG is much higher than the number of AT nucleotides. In this case, the mode of
water-spine vibrations may be detected experimentally, since it is out the band of bulk water.

Thus, our analysis shows that the vibrations of water molecules in the hydration spine of the DNA minor groove may be detected in the experimental vibration spectra. The features of the mode of water-spine vibrations, determined in the present work, may be used to choose the most appropriate parameters of experiment. In particular, in the preparation of experimental samples the light and heavy water may be used, and the DNA with different contents of nucleotides may be taken. The comparison of the spectra of DNA with light and heavy water should allow to detect the isotopic shift that is expected to be about 10 cm$^{-1}$. The variation of the nucleotide content of DNA should make it possible to reduce the effect of the broad band of bulk water in the low-frequency spectra of DNA.

6 Conclusion

The low-frequency vibrations of water molecules in the hydration spine of the DNA minor groove (water-spine vibrations) have been studied. To determine the frequencies and amplitudes of vibrations of water molecules and DNA structural elements, an analytical model has been developed. The results have shown that the frequencies of water-spine vibrations are within the range 160–210 cm$^{-1}$. The vibrations of water molecules significantly depend on the conformational vibrations of the double helix and are modulated by the sequence of DNA nucleotides. The calculations have shown that the mode of water-spine vibrations is in the same spectra range as translational vibrations of water molecules in the bulk phase. To select the modes of water vibrations in the DNA minor groove from those modes that are present in the bulk, the dynamics of DNA with different nucleotide contents has been analyzed and the influence of heavy water on the frequency of water-spine vibrations has been estimated. The analysis has shown that the change of vibration frequency due to the variation of nucleotide sequence may reach 30 cm$^{-1}$ that is big enough to make the mode of water-spine vibrations out the broad band of bulk water. The estimations have shown that the frequency of heavy water vibrations is lower than in the case of light water for about 10 cm$^{-1}$. The determined features of the mode of water vibrations in the hydration spine of the DNA minor groove may be used for the detection of this mode in the experimental low-frequency spectra.

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Author contribution statement

TLB performed the analytical analysis and computations. SMP supervised the research. All authors discussed the results and contributed to the final manuscript.

Conflicts of interest The authors declare that they have no conflict of interest.

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