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Hydration of nucleic acid components in dependence on nucleotide composition and relative humidity: a Monte Carlo simulation

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Abstract. What role does the nucleotide composition play in the process of formation of hydrated environment of nucleic acids? Can one estimate the hydration of nucleic acids on the level of their components? In order to resolve these questions we have completed an extensive computer simulation of the hydration of nucleic acids components – deoxynucleoside monophosphates distinguished by nucleotide composition. The energetic characteristics of systems containing deoxynucleoside monophosphates and water clusters of various dimensions are received. Our results demonstrate that deoxynucleoside monophosphates containing guanine and/or cytosine residues hydrated more strongly because of formation of more hydrogen bonds with water molecules in small water clusters, *i.e.* at low values of relative humidity. With increasing of number of water molecules in a water cluster the energetic preference of deoxynucleoside monophosphates containing guanine and/or cytosine residues decreases, and for water clusters corresponding to a state of a dilute aqueous solution the hydration of all types of deoxynucleoside monophosphates does not differ in a great degree. Deoxynucleoside monophosphates containing guanine and/or cytosine residues cause the greater destruction of the water structure compensated by the greater interaction with the nearest water molecules for all levels of relative humidity.

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1 Introduction

The DNA molecule is one of the most important biomolecules. The double-helical structure of DNA is crucial for its function – storing and transferring the genetic information. Any particular DNA structure (B-DNA, A-DNA or Z-DNA) is a result of a delicate balance of the following interactions: hydrogen bonding of nucleobases, stacking of bases and base pairs, interactions between the charged phosphate groups, environmental effects such as counterion composition, salt effects, presence of metal cation, specific hydration and hydrophobic interactions. The commonly accepted view is that hydrogen bonding and stacking interaction of DNA bases play an important role in the formation of any DNA structure. On the other hand it is known that the molecular mechanism of stabilization of the nucleic acids structure is mainly determined by their interaction with water environment. In the recent investigation [1] was demonstrated, that the basic contribution to the total energy of stabilization of the double helix is made by water molecules (up to 70%) and that the hydrogen bonds in Watson-Crick pairs and other types of interaction provide an energy contribution no more than 30%.

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The level of relative humidity (RH), the degree of the hydration and the type of counterions definite whether the DNA structure belongs to A- or B-families [2–5]. It was found by the investigation of A–B transition in natural DNA and some polynucleotides that minimum number of water molecules necessary to get the B-form also depends on the base composition of the DNA [6–9].

The structure of hydrated environment, the energetic parameters and conformation mobility of nucleic acids (NA) substantially depend on AT/GC content and nucleotide sequence of NA [10–13]. In experimental investigations devoted to studying the difference in behaviour of DNA–water systems for AT- and GC-enriched samples [1,10,11,14] the following results were obtained. By the methods of differential scanning calorimetry, IR-spectroscopy and piezogravimetry the energetic parameters of interaction of water molecules with hydrated centers of DNA with various AT/GC composition in dependence on water content in a sample (or RH) have been determined [1,8]. The increasing of the excess energy of DNA hydration in 1.5 times under the linear law at increase of quantity of GC-pairs from 0 up to 100% has been revealed. That fact enables one to define DNA composition from the calorimetrically measured values of dehydrated energy. It is also shown that the excess energy of

a hydration, as well as enthalpy of fusion of DNA, depends on its GC-content. These results allow authors to make a conclusion that the thermostability of DNA is determined not only by the electrostatic energy in Watson-Crick complementary AT- and GC-pairs, but also by various hydration of these base pairs.

The dependences of dynamic parameters of bound water: free volume, relaxation time of dipoles of water and coefficient of a surface diffusion on water content in a sample are found with the help of the experimental data and the model calculations. It is shown that at increasing relative content of GC-pairs in DNA the dynamic mobility of water molecules in hydrated shell decreases within the whole interval of a change of water content [5,14–16]. These results are in agreement with the last data of computer simulation of a hydration of various DNA sequences carried out by a method of molecular dynamics [12,13,17]. The authors of these works have shown that GC-pairs hydration is higher than AT-pairs hydration that is determined by greater "lifetime" of water molecules near GC-sequences in comparison with the value of this parameter for AT-sequences.

Despite the great number of works devoted to investigation of nucleic acids hydration in dependence on nucleotide composition, detailed description of process of formation of hydrated environment near to AT- and GC-sequences on molecular level are practically absence. We have tried to receive more detailed representation about water environment of nucleic acids with various nucleotide composition on the basis of analysis of the energetic characteristics of the model systems containing deoxynucleoside monophosphates (DMP) and water clusters obtained by means of a Monte Carlo method. The computer simulation of systems DMP–water is less expensive than simulation of extended sequences of DNA double helixes. Nevertheless, the information received from researching on such small systems is not less valuable and allows us to study in detail the interaction of nucleic acids with water environment at a level of their components. Knowing, for example, only the hydration points of separate nucleic bases and their hydrogen bonded pairs it is possible to reproduce precisely enough the hydration places of B-dodecamer of DNA [18,19]. Furthermore, the model systems containing DMP and water clusters of the various dimensions, reproduce the interaction of nucleic acids components with water at different levels of RH. Such approach has been used in molecular dynamic simulation devoted to investigation the hydration of DNA fragments [20]. It was shown, that the system containing the fragment of DNA with 10 base pairs and 500 water molecules (or 25 water molecules per nucleotide), corresponds to $\sim$ 86% RH, and system with 1 050 water molecules (or $\sim$ 52 water molecules per nucleotide) corresponds to $\sim$ 98% RH.

2 Methods and objects

The computer simulation of DMP hydration in water clusters of various dimensions was performed by a Monte Carlo method and the evaluation of the energetic characteristics of investigated systems was carried out. The application of a Monte Carlo method for study of the hydration of biomolecules and, in particular, of nucleic acids and their components, is described in detail in the literature [21–24]. In our investigation the calculations were carried out in the canonical (N, V, T) ensemble within the framework of Metropolis algorithm [25]. In each system DMP + water the number of water molecules was equal to 40, 80, 100 and 400, that allows us to simulate the systems with various degrees of RH. Temperature in the systems was 298 K.

For calculation of interaction energies the semiempirical atom–atom potential functions suggested by Poltev *et al.* were used [19,26]. The total interaction energy was taken as the sum of water–water interaction energy, water–DMP interaction energy and conformational energy of DMP. The water–water interaction energy was approximated by potential function of the 1-6-exp type [19] with parameters reproduced the energies of hexagonal crystal lattice of ice and force constant for the bending of hydrogen bonds in ice. The model proposed for water and chosen type of potential function was reproduced satisfactorily the thermodynamic and structural properties of liquid water and water solutions received experimentally.

The water–DMP interaction energy was approximated by atom-atom potential functions of 1-6-12 type [26,27] with parameters reproduced the lengths of hydrogen bonds between water molecules and bases, sugars and phosphate groups and experimental positions of water molecules in crystallohydrates of the bases, nucleosides and nucleotides.

The conformational energies of DMP were taken as the sum of the individual contributions from van der Waals interactions (solute–solute interactions) and torsion potentials. These energies were also approximated by a 1-6-12 atom–atom potential function and a function received for calculation of the energy at a change of torsion angles [28]. The parameters of this function were adjusted to reproduce intermolecular interactions of the nucleic acid bases and related substances. For example, the calculated energies of base pairs formation and stacked associates correlated with the experimental values obtained by field mass-spectrometry *in vacuo* [29,30]. As it was noted in [24], the potential functions we used here give reasonable energetic and structural characteristics for nucleic bases complexes in the gas phase, heats of sublimation and lattice constants of crystals and crystal hydrates, the hydration energy of the nucleic bases, their derivatives and complexes in water, and at the conformational analysis of nucleic acids fragments. So they are transferable and one set of parameters for atoms or groups of atoms can be used to construct potential functions for Monte Carlo simulations of different systems. The charges on atoms used in our calculations were reported previously in the literature [26,28].

As boundary conditions we used the cluster theory [31,32]. At such approaching the computational system was placed in a sphere with impermeable walls so that the center of mass of solute coincided with the center of

sphere. Initially there was only configuration of N water molecules in sphere. This configuration was generated using special program for creation of energetic favourable water structure of pure water for cluster of particular dimension. Radius of sphere was equal to radius of sphere received for such water structure. Then radius of sphere was increased by quantity necessary for water molecules, which were superseded by DMP from water "drop" when DMP was placed in the center of sphere.

In order to reach the equilibrium state of system DMP + water $4-6 \times 10^6$ elementary configurations were carried out, then $4-6\times10^6$ elementary configurations were generated for calculation of thermodynamical characteristics of investigated system on the equilibrium state. The statistical error due to the finite number of configurations that were considered was calculated with the help of a method of control functions. The entire set of elementary steps was divided into a finite number of intervals. For each interval the values of thermodynamic quantities (in our investigation it was a total energy of system) and the standard deviations were calculated. In our calculations the value of a statistical error did not exceed $\pm0.05-0.005$ in dependence on the dimensions of water cluster.

Actually, it is necessary to calculate the water–water, water–solute interactions and the conformation interactions in a molecule of solute on molecular level for the study of the hydration of various conformations of deoxynucleoside monophosphates in solution. This problem is complex enough because a complete conformational analysis involves the definition of the preferred energy of the most favourable conformation with the count of many bonds in DMP. Therefore we have used series of approximations based on the results of experimental study of DMP structure in crystals and solutions.

According to the experimental data, sugar rings in composition of nucleic acids can exist in several particular conformations. The data of X-ray diffraction and NMR studies [33,34] indicate that such conformations are C2′-*endo* and C3′-*endo* conformations. Therefore we chose these two preferable conformations of sugar in dependence on structural form of investigated DMP: A- or B-forms. According to the data of X-ray diffraction and NMR analyses [35,36] the most preferable orientation of sugar and base in DMP when they are located in a double helix of DNA or RNA is *anti*-conformation, *i.e.* we chose the particular values of torsion angle of rotation around glycosidic bond.

As a result of these two approximations the complete number of bonds, around which the rotation in DMP is possible, has decreased to 10. They are: C1′−N1(N9)−2 bonds, C3′−O3′−2 bonds, C4′−C5′−2 bonds, C5′−O5′−2 bonds, P−O5′ and P−O3′. In our calculations the change of these torsion angles was carried out on each steps of simulation in framework of Metropolis algorithm. The lengths of valence bonds and values of valence angles of DMP did not change during the simulations. DMP is divided into seven blocks: "a tailing" C5′−O5′H, two deoxyriboses, phosphate group O3′−PO_2^-−O5′, "tailing" C3′−O3′H and two bases. The complete conformational energy of DMP has been calculated as the sum of energies of interactions between separate blocks.

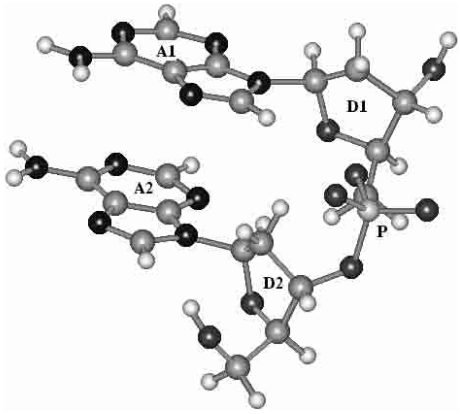

Fig. 1. Structural formula for dinucleoside monophosphate ApA: A1, 2 − adenine residues 1, 2; D1, 2 − desoxiriboses 1, 2; P − phosphate atom.

It is known, that DMP in solutions are charged negatively because of presence of phosphate groups, which are completely ionized under physiological conditions. The electroneutrality of system is provided for the presence of equivalent number of counterions, usually ions of Na^+. We did not take into account counterions in our calculations. However the requirement of an electroneutrality was kept. For this purpose the charges on phosphate groups were calculated to ensure an electroneutrality of DMP. The described approximation is similar to that of the conformation calculations of nucleic acids [28,37] and simulation of a hydration of fragments of nucleic acids in solution [38].

As the objects to be studied we have chosen different types of dinucleoside monophosphates XpY with X, Y = A, T, C, G, U. The starting configurations of DMP were constructed with the help of the RCA data. Such configurations were placed in water clusters and the simulation of their interaction with water environment in clusters with various number of water molecules was carried out on the procedure described above. In Figure 1 the detail structural formula of ApA is given and in Figure 2 all other dinucleoside monophosphates are represented.

3 Results and discussion

The calculated results of the energetic characteristics are reported in Table 1. Here are the average values of the total potential energy for system per one water molecule $U_{\mathrm{TOT}/1}$, water–water interaction energy per one water molecule $U_{\mathrm{WW}/1}$, DMP–water interaction energy per one water molecule $U_{\mathrm{WD}/1}$ and conformational energy of DMP U_{CONF}. N_{Hb} is the average number of water molecules making hydrogen bonds with DMP (±1 water molecule). Some additional results calculated on the basis of data received from the Monte Carlo simulations are presented in the three last columns in Table 1.

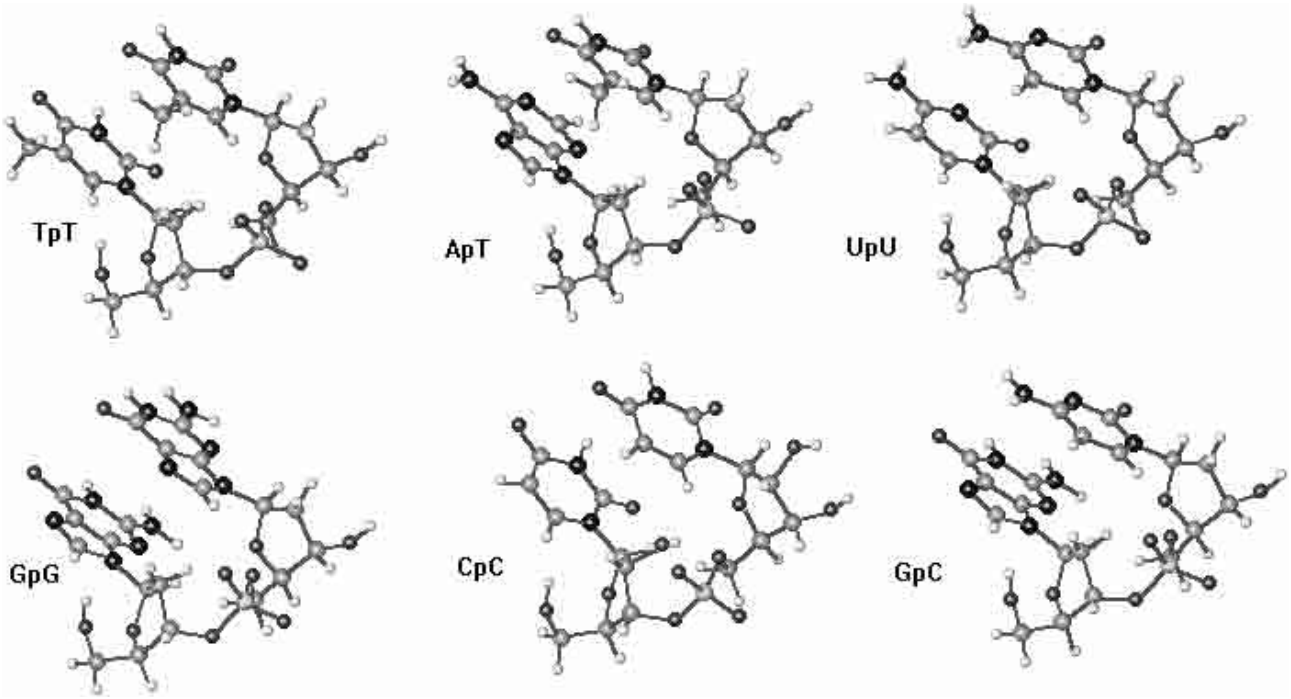

Fig. 2. Structural formulas for dinucleoside monophosphates TpT, ApT, UpU, GpG, CpC and GpC; A – adenine, C – cytosine, G – guanine, T – thymine, U – uracile.

The first conclusion following from data representing in Table 1 is that DMPs containing G or/and C residues are energetically more preferable than DMPs containing A or/and T (U) residues. Especially it is noticeable for systems with small number of water molecules (at low RH). The results from Table 1 allow us to determine, that this preference is caused by two types of interactions in the systems: the solute–solute interaction (conformational energy U_{CONF}) and the solvent–solute interaction (water–DMP interaction energy U_{WD}). With increasing RH, or for systems corresponding to a state of a dilute aqueous solution (water cluster with 400 water molecules), the difference between DMPs containing either A, T(U) or G, C residues is practically disappeared. The certain energetic preference of DMPs containing G or/and C residues is determined by the conformational component of the total energy of systems, especially for CpC DMP (see Tab. 1). The energetic preference for systems containing DMP CpC determined by a conformational energy of DMP is conserved irrespective of water content.

From data summarized in Table 1 one can estimate the change in water structure by comparing the water–water interaction energy in different DMP-water systems and systems with pure water (Tab. 1, H_2O^* terms). The greatest destruction in structure of water cluster is observed in systems containing ApA, GpG and GpC DMPs at low RH (water clusters with 40 and 80 water molecules). The tendency to greater destruction of solvent structure in systems containing G, C residues with increasing RH is conserved.

A comparison of the magnitudes for water–water interaction energies for all investigated types of DMPs allows us to make one more conclusion: the least destruction of water structure is observed for ApT DMP and water clusters of any sizes (the values of $U_{\mathrm{WW}/1}$ are the largest on an absolute value, see Tab. 1, column 5). This result is in agreement with known representation that the AT-rich sequences of nucleic acids have more ordered hydrated shell [39,40].

The destruction of the water structure is caused by the break of hydrogen bonds between water molecules and formation the hydrogen bonds with hydration centers of DMPs. These centers are: phosphate groups (PO_2^-) and atoms O3′, O5′ of sugar-phosphate backbone; atoms O4′ of desoxyribose rings; atom groups CO, NH_2 and atoms N of nucleic base residues. The analysis of values of water–DMP interaction energies is shown that in the systems with small water content (at low RH) the largest magnitudes of $U_{\mathrm{WD}/1}$ (on an absolute value) have GpG DMPs, then follow ApA and GpC DMPs (by decreasing of $U_{\mathrm{WD}/1}$, see Tab. 1, column 6). These DMPs also make greater hydrogen bonds with water molecules than other DMPs (see Tab. 1, values N_{Hb}). The values of $U_{\mathrm{WD}/1}$ for all types of DMPs differ to a lesser degree with increasing of water cluster (or increasing RH). The certain increasing of $U_{\mathrm{WD}/1}$ (on an absolute value) is observed for ApA DMP.

As we can see from data represented in Table 1 the contribution of conformational interactions in the total potential energies of systems in a considerably degree explains the energetic preference of one or another type of DMP. Nevertheless it is interesting to find out whether there is a dependence of differences in interaction of water environment and DMPs with various nucleotide composition not only on the conformational peculiarities of

Table 1. Energetic characteristics of systems containing DMP + H_2O and clusters of pure water (H_2O^*) of the various dimensions (kcal mol^{-1}).

n, H_2O	System	$U_{TOT/1}$	U_{CONF}	$U_{WW/1}$	$U_{WD/1}$	N_{Hb}	$U_{SUM/1}$	ΔU_{hyd}	τ_d, 10^{-11} s
40	ApA	-9.30 ± 0.05	-51.4	-4.48	-3.57	12	-8.05	1.79	17.9
	TpT	-9.90 ± 0.05	-94.5	-4.95	-2.57	4	-7.52	1.26	7.4
	ApT	-9.55 ± 0.05	-58.0	-5.36	-2.73	10	-8.09	1.79	17.9
	UpU	-10.98 ± 0.05	-137.7	-5.16	-2.38	6	-7.54	1.28	7.6
	GpG	-10.97 ± 0.05	-120.0	-4.45	-4.04	13	-8.49	2.23	38.9
	CpC	-12.50 ± 0.05	-172.6	-5.34	-2.84	9	-8.18	1.88	20.7
	GpC	-11.18 ± 0.05	-104.9	-4.75	-3.81	12	-8.56	2.30	42.1
	H_2O^*	-6.26 ± 0.05		-6.26					
80	ApA	-9.12 ± 0.05	-50.8	-5.90	-2.58	12	-8.48	1.66	14.7
	TpT	-8.75 ± 0.05	-94.2	-6.03	-1.52	4	-7.55	0.73	3.0
	ApT	-9.21 ± 0.05	-53.1	-6.66	-1.89	10	-8.55	1.73	16.1
	UpU	-9.27 ± 0.05	-136.1	-5.91	-1.67	5	-7.58	0.76	3.2
	GpG	-9.85 ± 0.05	-130.5	-5.94	-2.60	15	-8.54	1.72	15.8
	CpC	-10.19 ± 0.05	-168.3	-6.23	-1.86	8	-8.09	1.27	7.5
	GpC	-9.91 ± 0.05	-111.3	-6.36	-2.15	11	-8.51	1.69	15.2
	H_2O^*	-6.82 ± 0.05		-6.82					
100	ApA	-8.61 ± 0.01	-45.9	-6.06	-2.10	13	-8.16	1.09	5.6
	TpT	-8.59 ± 0.01	-92.6	-6.30	-1.36	4	-7.66	0.59	2.4
	ApT	-8.87 ± 0.01	-61.1	-6.77	-1.49	9	-8.26	1.19	6.6
	UpU	-9.12 ± 0.01	-132.3	-6.36	-1.44	6	-7.80	0.73	3.0
	GpG	-9.33 ± 0.01	-118.7	-6.59	-1.78	15	-8.37	1.30	7.9
	CpC	-9.62 ± 0.01	-170.2	-6.37	-1.55	7	-7.92	0.85	3.7
	GpC	-9.25 ± 0.01	-111.9	-6.28	-1.84	10	-8.12	1.05	5.2
	H_2O^*	-7.07 ± 0.01		-7.07					
400	ApA	-8.641 ± 0.005	-48.8	-7.86	-0.66	11	-8.52	0.35	1.6
	TpT	-8.602 ± 0.005	-93.8	-7.96	-0.40	5	-8.36	0.19	1.2
	ApT	-8.718 ± 0.005	-41.6	-8.06	-0.56	9	-8.62	0.45	1.9
	UpU	-8.745 ± 0.005	-137.1	-7.97	-0.43	5	-8.40	0.23	1.3
	GpG	-8.799 ± 0.005	-119.7	-7.89	-0.69	15	-8.58	0.41	1.8
	CpC	-8.880 ± 0.005	-169.6	-7.93	-0.43	7	-8.36	0.19	1.2
	GpC	-8.656 ± 0.005	-106.4	-7.92	-0.63	12	-8.55	0.38	1.7
	H_2O^*	-8.174 ± 0.005		-8.17					

DMPs but also on the interaction of DMPs with solvent. With the above statement of the problem in view we used the conception of the excess energy of hydration ΔU_{hyd} and a time of a dipole relaxation of water molecules in a bound state τ_d for analysis of our simulation results. The excess energy of hydration ΔU_{hyd} has been applied in [8,14,41–44] as the characteristic of water molecules binding energies with nucleic acids. For determining the contribution of water molecules into the total potential energy of systems DMP–water it is necessary to know the values of their binding energies with the DMPs. From the energy point of view the water molecule may be considered "connected" if its energy of interaction U with molecular sorbing matrix exceeds an average energy of interaction water–water U_0 in a liquid phase. The excess energy of hydration was determined as $\Delta U_{hyd} = U - U_0$. So knowing the excess energy of hydration ΔU_{hyd} we can estimate the interaction of solute (DMP) with water environment.

Experimentally ΔU_{hyd} is determined in three ways [1]. The first method is based on the detailed analysis of the IR-spectra of water sorption on nucleic acids matrix (frequency shifts of the stretch vibration band of sorption water). From the frequency shifts the binding energy of water molecules with nucleic acids was approximately estimated [41,42]. The second way is based on the analysis of isotherms of hydration obtained at different temperatures by thermogravimetric method [43]. In the third method the evaporation enthalpy of water molecules from nucleic acids was determined directly calorimetrically at various water contents [14,44]. The agreement of the

values for binding energy of water molecules determined by these three independent methods was found to be satisfactory [1].

We have obtained the excess energy of hydration on the basis of our simulation data the following way: $\Delta U_{\rm hyd} = U_{\rm SUM/1} - U_{\rm WW/1(pure\ water)}$; where $U_{\rm SUM/1} = U_{\rm WW/1} + U_{\rm WD/1}$ and $U_{\rm WW/1(pure\ water)}$ is an average interaction energy water–water per one water molecule for pure water cluster (H_2O^* terms in Tab. 1). We have also calculated time of a dipole relaxation of water molecules in a bound state $\tau_{\rm d}$ using the formula $\tau_{\rm d} = \tau_0 \exp(\Delta U_{\rm hyd}/RT)$, where $\tau_0 = 0.9 \times 10^{-11}$ s – time of a dipole relaxation for water molecules in pure water at room temperature; T – temperature in kelvins; R – gas constant. Thus we can estimate the mobility of water molecules around investigated compounds in dependence of their composition and relative humidity. These data are also represented in Table 1 (column 10).

As it is shown from data in Table 1 GC-sequences connected with water molecules better in systems with low RH. In systems simulating a dilute solution (water clusters with 400 water molecules) the interaction of all investigated DMPs with water differ a little. The analysis of values $\Delta U_{\rm hyd}$ represented in the Table 1 (columns 9) allows us to offer the sequences of changing the excess energies of hydration for different types of DMP (on decreasing their absolute values) for low RH: GpG > GpC > CpC > ApA > ApT > UpU > TpT and for clusters corresponding to a dilute solution: ApT > GpG > GpC > ApA > UpU > TpT, CpC. Such sequences correlate with known representation, that the GC-sequences are hydrated more [12,13,17,45] though the AT-sequences have more ordered hydrated shell [7,13,17,38–40].

To estimate the free energy of hydration, the entropic term has to be taken into account. But on the basis of IR-spectroscopic, microcalorimetric and thermogravimetric data the enthalpic part of the energy of hydration and the excess energy of hydration were estimated. Thus we can compare our simulation results (the values of the excess energy of hydration $\Delta U_{\rm hyd}$, Tab. 1) and data of IR-spectroscopic studying of wet films and microcalorimetric measurements of the dehydration energy of polynucleotides and natural DNA with different AT/GC composition reporting in [1,14,41–44]. The magnitudes of $\Delta U_{\rm hyd}$, obtained by IR-spectroscopic investigation change from ~ 2.5 kcal/mol for polyrG-polyrC polynucleotide at low RH (32% RH or near 2–3 water molecules per nucleotide) to $\sim 0.5{-}1.0$ kcal/mol at high RH (98% RH or ~ 25 water molecules per nucleotide). For polyrA-polyrU polynucleotide $\Delta U_{\rm hyd}$ changes from $\sim$ 2.1 kcal/mol at low RH to ~ 0.01 kcal/mol at high RH and for polydA-ploydT it value decreases from ~ 2.0 kcal/mol at low RH to ~ 0.01 kcal/mol at high RH. The analogous dependencies of $\Delta U_{\rm hyd}$ on RH have obtained for natural DNA. It is observed from experimental data [1] that all functions $\Delta U_{\rm hyd}$(RH) are monotonously decreasing, *i.e.* the binding energies decrease with process of sorption of water molecules with hydration-active centers of nucleic acids and connected water molecules. For the GC-enriched nucleic acids (polyrG-polyrC and DNA from *M.lysodiekticus*, $\sim$ 72% GC base pairs) the dependence of $\Delta U_{\rm hyd}$(RH) is higher for all RH than for AT- or AU-enriched nucleic acids. These results the authors [1] explained by the fact that water molecules form stronger hydrogen bonds with hydration centers of the GC-enriched nucleic acids. The same dependencies of $\Delta U_{\rm hyd}$ on water contents and AT/GC composition are received in microcalorimetric investigations [14]. But the comparison of our data for $\Delta U_{\rm hyd}$ and experimental results shows that the experimental values are lesser than those given in Table 1. One can think that the interaction potentials for water–solute (DMP) interactions we used leads to an overestimation of solute–solvent (water–DMP) interactions. In other words, nucleic acids are hydrated in water clusters higher than in real water. Then it would be expected that terms responsible for water–DMP interactions will be somewhat smaller in more realistic "water". However, the comparison of our values for water–water and DMP–water interaction energy and analogous types of energies received with the other type of atom–atom potential functions and periodic boundary conditions [7] does not support this assumption. The values of the hydration energy represented in [7] are also more (on an absolute value) than experimental results summarized in [1]. On the other hand, it could be assumed that the overestimation of DMP–water interactions is due to the underestimation of water–water interactions from the use of cluster theory, since the competition between water–water and water–solute interaction.

The calculated values of times of a dipole relaxation of water molecules in a bound state $\tau_{\rm d}$ (see Tab. 1, last column) indicate that water molecules in system with the DMPs containing G and/or C residues are less mobile at low RH. With increasing number of water molecules in system, *i.e.* with increasing RH, the increasing mobility of water molecules for all investigated systems is observed. At the level of RH corresponding to a dilute solution the mobility of water molecules near AT- and GC-sequences differ a little and approximating of the characteristics of a liquid water. These results are correlated with the values of times of a dipole relaxation of water molecules in a bound state $\tau_{\rm d}$ obtained from NMR investigations of DNA oligonucleotides [5,16] and molecular dynamics simulations of GC- and AT-oligomers [12,13]. Thus our results of computer simulation are not contradictory to the appropriate experimental data.

As it is known the question about various hydration of nucleic acids with different AT/GC composition is not solved up to now. Our calculations show that it is actually difficult to speak about preferability of a hydration of nucleic acids with various nucleotide composition without consideration of concrete conditions, namely, at what values RH there is an investigated system. At low RH there is a considerable dependence of a hydration on nucleotide composition, whereas in solution such dependence is expressed less. If for nucleic acids with the high content of G and/or C residues the total potential energy of systems at low RH is higher (on an absolute value), in solutions

energetically more favourable will be systems with a larger content of A and/or T (U) residues.

Thus with the purpose of understanding the nature of apparent differences in a hydration of AT- and GC-sequences we have performed a Monte Carlo computer simulation of the hydration of systems containing various DMPs with changed RH. It is shown that DMPs containing guanine and/or cytosine residues have higher value of conformational energy (on an absolute value). Moreover at low RH they destruct the water structure strongly and make more hydrogen bonds with water molecules in comparison with DMPs containing A and/or T(U) residues. With increasing RH the interaction of both types of DMPs (A, T(U) residues or G, C residues) with water does not differ by the total potential energy of systems in a great degree. DMPs containing G and/or C residues cause the greater destruction of the water structure than DMPs containing A and/or T residues compensated by increasing GC-interaction with the nearest water molecules for all levels of relative humidity. Obtained results correlate with data represented in literature, therefore one can state that the hydration environment of nucleic acids can be described at the level of their components – deoxynucleoside monophosphates and the nucleic acids hydration depends on their nucleotide composition.

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