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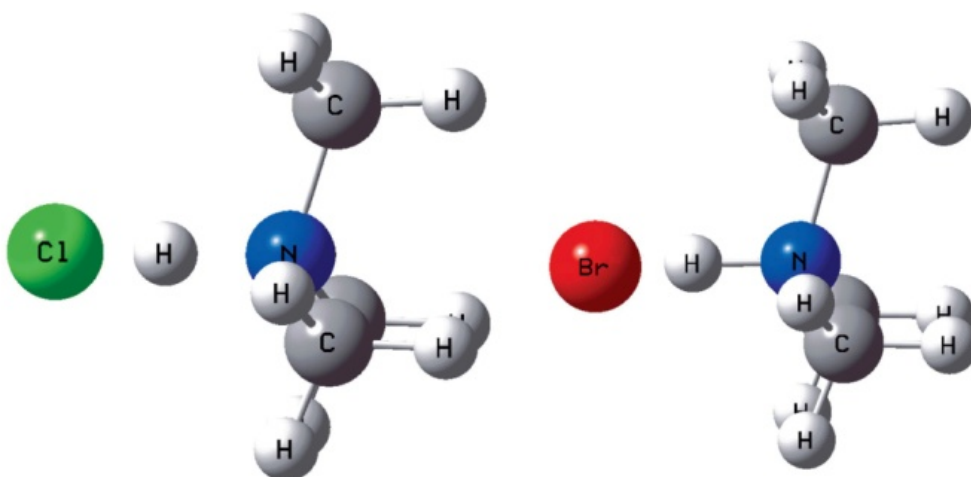
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The role of water and K^+ ion in the charge transfer between PO_4^- groups of DNA and the lysine⁺ and arginine⁺ side chains of histone proteins

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ABSTRACT

We have calculated the charge transfer (CT) between the PO_4^- group of DNA and the lysine (Lys) and arginine (Arg) positive side chains of histones in presence of water and K^+ ions. The calculations were performed at the HF + MP2 level, using the TZVP basis set. The calculations were corrected for basis set superposition error and besides Mulliken's population analysis we have introduced the – for charged systems more reliable – natural population analysis. The results show that the bare PO_4^- -Lys and the PO_4^- -Arg interactions become weaker, mainly, due to the presence of the K^+ ion. We have found 0.067e CT for Lys and 0.050e for Arg.

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1. Introduction

The crystal structure of a nucleosome has currently been determined by the Richmond Group at ETH with the help of X-ray diffraction experiments. The experimental geometrical structure was obtained at 2.8 Å and 1.9 Å resolution [1,2], respectively. The nucleosome consists of a 147 base pair long double-stranded DNA B superhelix and 8 histone molecules [nucleosome core particle (NCP)]. Subsequent investigations have shown that there are 120 H-bonds between the DNA superhelix and the protein side chains [3].

In a previous Letter [4] we have calculated the charge transfer between the PO_4^- groups of DNA and the lysine and arginine side chains of histones. We have found at the HF + MP2 level with triple ζ + polarization functions at the valence shells of the atoms (TZVP) basis of Ahlrichs [5] 0.26e charge transfer (CT) from the PO_4^- group to lysine and 0.21e CT to arginine, respectively.

In the mentioned calculations the presence of water molecules and K^+ ion was not taken into account. Therefore we have repeated the previous calculations in their presence.

We have investigated also the possibility whether there could be a CT between the O-atoms of thymine, guanine, and cytosine, respectively and the lysine or arginine side chains.

The motivation of this new calculation is to obtain more realistic values for the CT. Namely we have calculated in detail the band structures of the homopolynucleotides poly(guanilic acid) [6], poly(adenilic acid), polythymidine and polycytidine [7]) in

presence of water and Na^+ ions. From these band structures we are proceeding to calculate the direct current (d.c.) conductivities at room temperature due to the transferred charge from the PO_4^- groups of DNA to the positively charged side chains (lysine and arginine) of the nucleohistones.

2. Methods

Similarly to our previous study [4], we have used again the supermolecule approach to find out the CT from the PO_4^- groups to the histone side chains. The supermolecular system is built up by a single DNA chain containing two neighbouring thymine molecules, two sugar and one PO_4^- moieties together with 3H₂O molecules which are close to the K^+ ion, one K^+ ion and the lysine or arginine amino acid side chains (see Figs. 1 and 2).

The geometry optimization was performed using the two-layer ONIOM method [8–10], implemented in the GAUSSIAN 03 program package [11], where the water molecules, the K^+ ion and the PO_4^- group of the sugar-phosphate chain as well the lysine or arginine side chains, respectively, were considered to form the *model* system (see the ball and stick molecular fragments in Figs. 1 and 2). The *real* (supermolecular) system was treated using the Hartree–Fock (HF) method with the 6-31G basis set, while for the *model* system both Hartree–Fock and second order Møller–Plesset perturbation theory methods were applied using the Ahlrichs's basis set with polarization functions (TZVP) [5]. Taking the supermolecular geometry structures in such a way we were able to exclude the spatial coincidence of the positions of the water molecules and the K^+ ion with DNA constituents which could happen if the sugars were omitted from the model. For the starting geometry of the

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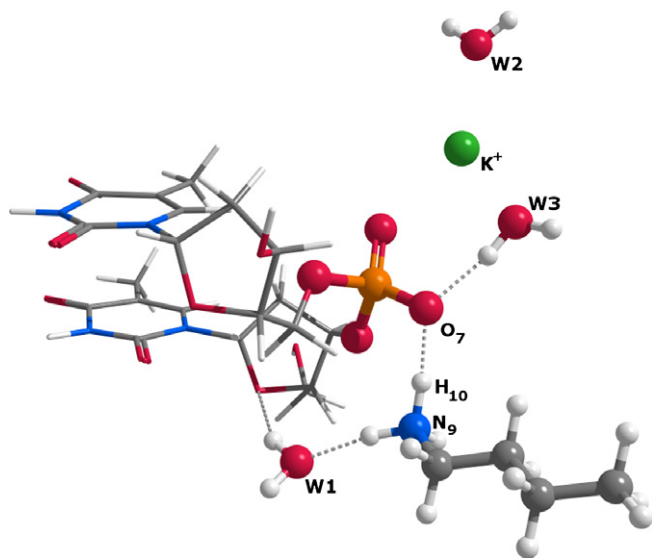


Fig. 1. The optimized geometry of the *model* system of lysine- PO_4^- - $3\text{H}_2\text{O}$ - K^+ obtained with the help of the ONIOM method (indicated by balls and thick sticks) without counterpoise correction (see text). The geometry of the *real* system not included in the *model* system (see text) was taken from experiment [12] (thin sticks).

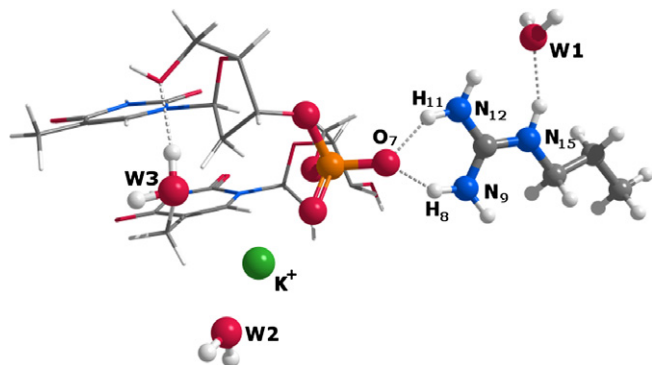


Fig. 2. The optimized geometry of the *model* system of arginine- PO_4^- - $3\text{H}_2\text{O}$ - K^+ obtained with the help of the ONIOM method (indicated by balls and thick sticks) without counterpoise correction (see text). The geometry of the *real* system not included in the *model* system (see text) was taken from experiment [12] (thin sticks).

supermolecular system the experimental geometry of double-stranded DNA B considering the average results of several X-ray diffraction investigations reported by Olson et al. [12] was used, while for the PO_4^- group – amino acid conformations our previous results were taken [4]. During the geometry optimization those atoms that do not belong to the *model* system were kept frozen. As further correction we have used the counterpoise (CP) method to avoid the basis set superposition error (BSSE). In this case only the repeated geometry optimization of the *model* system was performed. The K^+ ion and $3\text{H}_2\text{O}$ were kept at the same position as obtained using the ONIOM method without BSSE. The reason of this fact is that in the GAUSSIAN 03 program package the simultaneous use of the ONIOM method and the counterpoise correction is not possible. The development of a new program which makes this possible would require a major effort (which we are willing to do in the coming year). On the other hand as one can see from Tables 1 and 2 (see below) BSSE does not cause large changes in the bond distances and in the CT. The atomic fractional charges were calculated considering both Mulliken's population- and the natural bond orbital (NBO) [13,14] analyses on the *model* system.

Table 1

Hydrogen bond distances (in Å-s) between the PO_4^- group of DNA and the positive side chains of lysine and arginine (for the numbering of the atoms see Figs. 1 and 2)

H-bond distances (Å)							
Phosphate-lysine			Phosphate-arginine				
H-bond	HF	MP2	H-bond	HF	MP2		
$\text{O}_7 \cdots \text{H}_{10}$	Uncorr.	1.817	1.684	$\text{O}_7 \cdots \text{H}_8$	Uncorr.	1.857	1.761
	CP-corr.	1.717	1.634		CP-corr.	1.841	1.791
				$\text{O}_7 \cdots \text{H}_{11}$	Uncorr.	1.886	1.768
					CP-corr.	1.892	1.834

Table 2

Charge transfer from the PO_4^- group of DNA to the lysine or arginine side chains occurring in the nucleohistones

	HF		MP2		
	Mull.	NBO	Mull.	NBO	
Lysine	Uncorr.	0.070e	0.044e	0.098e	0.070e
	CP-corr.	0.073e	0.052e	0.096e	0.067e
Arginine	Uncorr.	0.073e	0.039e	0.093e	0.062e
	CP-corr.	0.075e	0.041e	0.080e	0.050e

To investigate the possibility whether CT through H-bonds could occur between the O-atoms of thymine or the O-atom of guanine and the lysine or arginine side chains of histone we have used the Brookhaven Protein Data Bank structure *1aoi* (cited in [1]). Using the VMD molecular graphics program [13] for this structure we have found that the protein side chains, even if they penetrate the shallow or the deep groove of DNA, cannot get close enough to the mentioned O-atoms to form H-bonds with them.

3. Results and discussion

In Table 1 we present the H-bond distances between the PO_4^- group of DNA and the positive side chains of lysine and arginine, respectively, for the uncorrected and CP corrected cases.

In Table 2 we present the transferred charge from the PO_4^- group of DNA to the positive side chains of the histones, again for both the uncorrected and CP corrected *model* geometry.

There are two H-bonds between the PO_4^- group and the lysine and arginine molecule, respectively, if there are no H_2O molecules and a K^+ ion between them. As a deviation from the former case now the lysine side chain forms only one H-bond with the O_7 atom of PO_4^- . The same atom enters into a H-bond with one of the H_2O molecules and there is another H-bond between the lysine and another H_2O molecule (see Fig. 1).

In the case of arginine there are two H-bonds. They are however, between O_7 of PO_4^- and the N_9 and N_{12} atoms of arginine, respectively (see Fig. 2).

One should observe also that the lengths of H-bonds are at the MP2 level longer in the screened (with water molecules and K^+ ion) than in the unscreened case for lysine. The same is true for the H-bonds of arginine. The BSSE correction hardly changes these H-bond distances.

Considering the HF + MP2 CT between the PO_4^- group and the amino acid side chains in presence and absence of water and K^+ ion, one can see that in present case (with the water and K^+ ion) the CT are much smaller for both amino acids, 0.098e for lysine and 0.093e for arginine than those obtained in our previous study [4] (0.26e for lysine and 0.21e for arginine). The latter two values refer for the case when no BSSE correction was applied before Mulliken's population analysis. After the BSSE correction the transferred charge decreases from the 0.098e to 0.096e for lysine and from 0.093e to 0.080e for arginine. One can see that in these cases the correction for BSSE is insignificant for lysine and not too large

for arginine. On the other hand using the NBO [13,14] population analysis the CT-s are smaller: $0.070e$ (uncorrected) for lysine and $0.062e$ (uncorrected) for arginine. The correction for BSSE has again no dramatic effects (0.067 for lysine and 0.050 for arginine).

The K^+ ions gain according to the more relevant NBO population analysis in the case of lysine only $0.006e$ and of arginine $0.005e$ charge. Thus their role is negligible for the CT from the PO_4^- groups to the positive side chains of the histones.

One should mention that most probably if we would have been able to improve further our basis set with the introduction of diffuse functions, the value of the transferred charge would have increased somewhat.

4. Conclusion

The diminished CT between the PO_4^- groups of DNA and the positive side chains (lysine and arginine) of the nucleohistones, means that the strength of the hole current in DNA and the electronic one in the histones becomes smaller. However, due to the large number of CT-s between them they are still strong enough to provide an attraction between DNA and the histones.

The qualitative conclusion is that if the relative position of DNA and histones changes, the attraction between them diminishes or disappears. This means that in the absence of CT the hole conduction in DNA and the electronic one in the histones gets disrupted. If this happens at many places simultaneously (like in the case of carcinogene molecules binding to DNA, or radiation damage on DNA)

this can finally cause the departure of larger segments of DNA from their protein covers. In such cases several genes become readable and cause the occurrence at unexpected places and time points of oncoproteins through the well-known biochemical mechanisms. This can seriously disturb the self-regulation of an eukaryotic cell. In such a way the cell could go over to such a new stationary state which is precancerous. Of course many other factors influence the self-regulation of a cell but the described one may be such which also seriously influences it.

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