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# Charge transfer between the $PO_4^-$ groups of DNA and the arginine$^+$ and lysine$^+$ side chains of proteins

A. Bende [a,b], F. Bogár [c,b], J. Ladik [b,*]

[a] National Institute for Research and Development of Isotopic and Molecular Technologies, Str. Donath 71-103, C.P. 700, Cluj Napoca RO-400293, Romania
[b] Chair for Theoretical Chemistry and Laboratory of the National Foundation for Cancer Research, Friedric-Alexander-University-Erlangen-Nürnberg, Egerlandstr. 3, 91058 Erlangen, Germany
[c] Supramolecular and Nanostructured Materials, Research Group of the Hungarian Academy of Sciences, University of Szeged, Dóm tér 8, 6720 Szeged, Hungary

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**Abstract**

Using the HF + MP2 methods with full geometry optimizations the charge transfer (CT) from the $PO_4^-$ groups of DNA to the arginine or lysine side chains of the proteins forming the nuclohistone cores were calculated. (X-ray investigation shows that in the nucleohistone core there are eight histones which are wrapped around by a DNA superhelix). We have found 0.21e and 0.26e CT, respectively.

Knowing the structure of nucleohistones one can estimate a charge transfer at every fourth base pair. Taking as average 0.10e CT (there are also other attractive interactions) one can compute the concentrations of holes in DNA. From these one can obtain the dc conductivity for polyguanilic acid (the mobilities are known).


## 1. Introduction

In two recent articles the crystal structure of the nucleosome core particle (NCP) [1] and the structure of DNA in the nucleosome [2] were reported at 2.8 Å and 1.9 Å resolution, respectively, obtained by the Richmond Group at ETH with the help of X-ray diffraction experiments.

They have found that the nucleosome core consists of eight histone molecules. These proteins are in the forms of α-helices or loops [1].

Around the NCP a 147 base pairs long DNA superhelix is wrapped. This superhelix has 167 turns [2] is flat and left-handed. (The intricate packing of the DNA superhelix around the NCPs causes that when the nucleosome molecules form chromatins in the nucleus of a single eukaryotic cell, a 3.5 km long DNA chain can be accommodated).

At the higher resolution [2] it has turned out that contrary, to an ideal 147 base pairs long superhelix (β form of DNA , uniformly distributed base pairs with a radius of 41.9 Å and a pitch of 25.9 Å of the superhelix. Each base pairs step containing two adjacent base pair contributes 4.53° to the curvature of the ideal superhelix) in the nucleosomes DNA is not bent uniformly, because of the anisotropic flexibility of DNA, local structural deviations from the ideal form and irregularities caused by the underlying histones octamer. These features (irregular bending and twisting of the DNA superhelix in the nucleosomes causing excess DNA curvatures) most probably cause the ability of the NCPs to 'slide' along DNA without releasing it [3].

This ability of the NCPs to slide along DNA makes it very probably possible for RNA polymerase to transcribe the sequence of nucleosomal DNA to RNA [4].

The interaction between DNA and histones in the nucleosomes is first of all due to the charge transfer between the negative phosphate groups or O-atoms of the bases (thymine or guanine) and the positive side chains (arginine, lysine, and histidine) of the histone molecules. Additionally there are attractive interactions between the $PO_4^-$ groups of DNA and the positive dipole moments of the main chains

* Corresponding author. Fax: +49 9131 8527736.
*E-mail address:* JanosLadik@chemie.uni-erlangen.de (J. Ladik).

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of the proteins. Of course these interactions are significant only if the negative sites of DNA face the protein. (At about 2.5 turns of the DNA superhelix when H-bonds can be formed between DNA and the histone molecules.)

On the basis of the data given in [1] the number of interactions (charge transfer via H-bonds) can be estimated to be roughly at 40 sites that is at every fourth base pair.

To have an idea about the amount of charge transferred from DNA to the histone molecules and the interaction energy between them we have performed ab initio quantum chemical calculations for the supermolecules $PO_4^-$–arginine and $PO_4^-$–lysine, respectively. For these computations we have used a sophisticated basis both at the HF and MP2 level. The geometry of the systems was fully optimized at both levels.

## 2. Methods

In Figs. 1 and 2 the $PO_4^-$–arginine and $PO_4^-$–lysine systems are shown. In both figures the broken lines indicate H-bonds.

The two supermolecules were first calculated by the HF method using a Gaussian triple zeta + valence polarization functions (TZVP) basis. The geometry in both cases was minimized using the GAUSSIAN 03 (C.02) program [5]. As next step using the results of the HF calculation an MP2 computation was performed for both supermolecules applying the same geometry optimization procedure.

To start the geometry optimizations we have used the structure of methylguanidium dihydrogenorthophosphate determined by X-ray diffraction of its crystal [6].

The rather large computations where performed on an FSC PRIMERGY Fujitsu–Siemens computer on four AMD OPTERON processors of HPC Center at the University of Szeged. The calculation took 168 h for the phosphate–arginine system and 96 h for the phosphate–lysine system, respectively.

## 3. Results and their discussion

In Table 1 we show the obtained H-bond distances at the HF and MP2 levels for both systems.

The interaction energies were found for the phosphate–arginine system 4.79 eV at the HF case and 4.98 eV at the MP2 level (after geometric optimization in both cases). Corresponding values for the phosphate–lysine system were 5.24 eV (HF) and 5.67 eV (MP2), respectively.

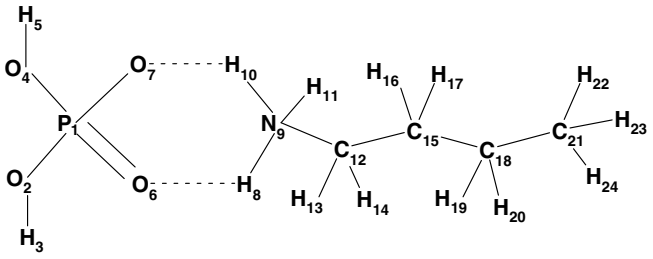



Fig. 2. The $PO_4^-$–lysine systems. The broken lines indicate the H-bonds. The numbering of the atoms is similar as in Fig. 1.

Table 1
The H-bond distances of the phosphate–arginine and phosphate–lysine systems at the HF and MP2 levels (in both cases after geometry optimizations)

| H-bond distances (in Å)s | | | | | |
|---|---|---|---|---|---|
| Phosphate–arginine | | | Phosphate–lysine | | |
| H-bond | HF | MP2 | H-bond | HF | MP2 |
| $O_6 \cdots H_8$ | 1.662 | 1.518 | $O_6 \cdots H_8$ | 1.770 | 1.688 |
| $O_7 \cdots H_{11}$ | 1.674 | 1.579 | $O_7 \cdots H_{10}$ | 1.755 | 1.598 |

Finally the charge transfer between the two systems were 0.15e at the HF level and 0.21e at the MP2 level (from phosphate to arginine) and 0.14e at the HF level, 0.26e at the MP2 level (from phosphate to lysine). One should observe in the case of the calculations with correlation that the increased charge transfers are in accordance of the shortening of the H-bond distances at MP2 as compared to the HF cases (see Table 1).

At the H-bonds between the O-atoms of the bases and the positive parts of the proteins (side chains with positive charges and positive dipole moments) one would expect a somewhat smaller charge transfer from DNA to the histone molecules. The same is true for the charge transfer between the phosphate groups of DNA and the positive dipole moments of the main chain of the proteins (if they are in the right relative position). For these reasons we have estimated the average charge transfer between DNA and the histone molecules as 0.10e. This value was used for

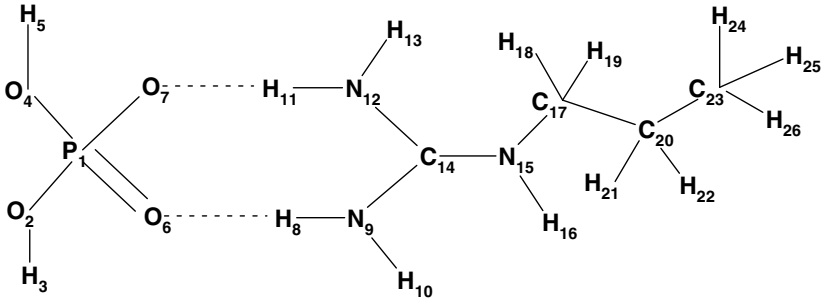
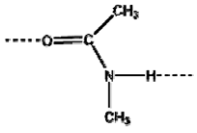



Fig. 1. The $PO_4^-$–arginine$^+$ systems. The broken lines indicate the H-bonds. The atoms in the supermolecule are numbered consecutively.

the calculation of dc conductivity of a guanine–sugar–phosphate chain in the presence of water and $Na^+$ ions [7].

## 4. Conclusion

The rather large change transfer values obtained between the $PO_4^-$ groups of DNA and the arginine and lysine side chains of the histones forming the nucleosome core makes it rather probable that if the two macromolecules are together in the nucleosomes (see introduction) there is a hole conduction in DNA and an electronic conduction in the nucleosome core. To have an estimate of their conductivities we have performed a HF crystal orbital [8] calculation for a periodic guanine–sugar–phosphate chain in the presence of water molecules and $Na^+$ ions [7]. Further we have executed with the same method [8] a computation for an infinite chain perpendicular to the main chains of proteins [9] (with the unit cell;



Coulson's model [10]) to obtain an estimate for the dc electronic conductivity in proteins.

Until the DNA and protein molecules are close to each others both will be either hole or electronic conductors, respectively. If, however, due to an external perturbation (presence of foreign chemical compounds including carcinogens, radiations, etc.) their relative conformation in the nucleosomes can change in such a way that the attractive interactions between them become much smaller (if the distances between their negative and positive groups become substantially larger). In this case the 147 base pair DNA chain wrapped around a nucleosome core can separate itself from the histones [1]. If this happens there will be no charge transfer between them and therefore both the DNA chain and the protein become insulators.

In this case all the genes of the DNA chain can be freely read by ribonuclease molecules to transcribe them to mRNA molecules. If this happens, the known biochemical mechanisms of cancer initiation can freely take place.

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## References

[1] K. Luger, W. Mäder, R.K. Richmond, D.F. Sargent, T.J. Richmond, Nature 389 (1997) 251.
[2] T.J. Richmond, C.A. Davey, Nature 423 (2003) 145.
[3] S.C.R. Elgin, J.L. Workman (Eds.), Chromatin Structure and Gene Expression, Oxford University Press, Oxford, 2000.
[4] See for instance: W.M. Studitsky, G.A. Kassavetis, E.P. Geiduschek, G. Felsenfeld, Science 278 (1997) 1960.
[5] M.J. Frisch et al., Gaussian 03, Revision C.02, Gaussian, Inc., Wallingford CT, 2004.
[6] F.A. Cotton, V.W. Day, E.E. Hazen Jr., S. Larsen, J. Am. Chem. Soc. 95 (1973) 4834.
[7] J. Ladik, A. Bende, F. Bogár, J. Chem. Phys., submitted for publication.
[8] See for instance: J. Ladik, Phys. Rep. 313 (1999) 171.
[9] A. Bende, F. Bogár, J. Ladik, Chem. Phys. Lett., to be submitted.
[10] C.A. Coulson, personal communication.