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The role of different positively and negatively charged ions on the stability of the histone nucleosome core particle

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SUMMARY. The role of different positively (Na^+, K^+, Mg^{2+}) and negatively (Cl^-) charged ions on the interaction between the negatively charged PO_4^- group of DNA and the positively charged histone protein side chains of lysine and arginine amino acids have been investigated using *ab initio* quantum chemical methods. The analysis of the intermolecular interaction have shown that the positively charged ions polarize the negative charges on the PO_4^- group which weaken the electrostatic interaction between the negative side of the DNA and the positive part of the histone protein. Similarly, the negatively charged Cl^- ion can drastically change the charge distribution on the positively charged lysine or arginine amino acids and again weaken the electrostatic interaction between the negative side of the DNA and the positive part of the histone protein.

Keywords: *Ab initio* methods, DNA, histone, ions, nucleosome

Introduction

Nucleosomes are the basic building blocks of the chromatins and the fundamental repeating units in the cell nucleus. Its crystal structure has been identified by the Richmond Group initially at 2.8 Å atomic resolution (Luger *et al.*, 1997) using X-ray diffraction experiments, which they subsequently refine at 1.9 Å resolution (Richmond *et al.*, 2003). According to this crystal structure, the double-stranded B-DNA superhelix (147 base pair long sequence) is wrapped around the nucleosome core built by eight histone proteins. A detailed structural investigation (Davey *et al.*, 2002) has shown that there are over 120 direct protein–DNA interactions as salt bridges between the main chain amides of the histone and the DNA backbone phosphates. These protein-DNA interactions are further enhanced by several hundred water mediated bridges where the water molecule is intercalated between the charged ends of the salt bridges.

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Materials and methods

The supramolecular system was built up considering two neighboring guanine molecules of a single-stranded DNA chain, together with two sugar and one PO_4^- groups which binds to the lysine or arginine amino acid side chains of the proteins. Positively charged (Na^+, K^+, Mg^{2+}) ions were set close to the PO_4^- fragment, while the negatively charged Cl^- ion was placed close to the amino groups groups of the amino acid side chains. Furthermore, three water molecules were also introduced in our supramolecular system placed close to the different ions. For the geometry optimization the two-layer ONIOM method (Maseras *et al.*, 1995; Svensson *et al.*, 1996; Dapprich *et al.*, 1999) was applied, implemented in the GAUSSIAN 09 program package (Frisch *et al.*, 2009). In the *model* system the PO_4^- group of the sugar-phosphate chain, the lysine or arginine side chains occurring in the protein chain, the three water molecules, as well as the positively and negatively charged ions are included, while the sugars and the guanine fragments were included only in the *real* system. The *model* system was described using the MP2/TZVP levels of theory, while for the *real* (supramolecular) system the HF/6-31G method was considered.

Results and discussion

The intermolecular interaction energies between the negatively charged PO_4^- group of DNA and the positively charged histone protein side chains of lysine and arginine amino acids including the Na^+, K^+, and the Cl^- ions were analized in our previous works (Bende *et al.*, 2007, 2008, 2012) and the values of these energies are presented Table 1.

Table 1.

Interaction energies (in eV-s) between the PO_4^- group of DNA and the lysine and arginine residues of the histone in the presence of different ions

Geometries	Interactions energies (in eV)	
	HF	MP2
$PO_4^-\cdots Lys^+/Arg^+$	-5.24/-4.79[a]	-5.64/-4.98[a]
$PO_4^-\cdots Lys^+/Arg^+$ with H_2O, K^+	-4.84/-4.38[b]	-5.04/-4.57[b]
$PO_4^-\cdots Lys^+/Arg^+$ with H_2O, K^+, Cl^-	-1.12/-0.95[c]	-1.15/-0.97[c]
$PO_4^-\cdots Lys^+/Arg^+$ with H_2O, Mg^{2+}	+0.33/+0.13	-0.02/-0.12

[a] See (Bende et al., 2007); [b] See (Bende et al., 2008); [c] See (Bende et al., 2012)

Conclusions

Using *ab initio* quantum chemistry methods, the intermolecular interaction energies between the the negatively charged PO_4^- group of DNA and the positively charged histone protein side chains of lysine and arginine amino acids. The results have shown that the presence of differently charged ions with different valence numbers could uniquely influence the strength of the DNA protein interaction inside the nucleosome. Accordingly, the positively charged ions with single valency (Na^+, K^+) could somewhat weaken the interaction but it remains strong enough in order to not come apart the wrapped DNA to the histone. The presence of an extra Cl^- ion close to the positively charged amino acids have a significant influence on the interaction strength, by reducing the magnitude of the interaction energy with almost 80%. The positively charged bivalent ions (Mg^{2+}) can even break the DNA-protein complex and hinder their re-formation and safe packing.

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