

### Molecular modeling of DNA Protein interactions in nucleosome

The organization of DNA in chromatin shows arrays of nucleosomes. Two copies of each histone protein, H2A, H2B, H3 and H4 are assembled into an octamer. This has 145-147 base pairs of DNA wrapped around it to form a nucleosome core. In all eukaryotic genomes this highly conserved nucleoprotein complex occurs essentially at every  $200 \pm 40$  bp throughout.

Both histone /histone and histone / DNA interactions depend on the folding domains of histones and, the well ordered structure elements extending from this. To contact neighbouring particles, histone amino - terminal tails pass over and extend between the DNA superhelix. Due to lack of uniformity between multiple histone/DNA binding sites DNA deviates from the ideal superhelical geometry. Much of the biochemistry and biophysics of DNA relies on the electron donating properties of nucleotides. This in the simplest sense, is reflected in the ionization energies.

Gas phase Ionization potentials (IP's) were evaluated for anionic 2'-deoxyguanosine-5'-phosphate (5'-dGMP-) in the DNA strand, of the nucleosome core particle. Herein gas phase uncorrected IP's of 5'-dGMP- for 134,137(5'--CA134GGT137GGAT-3'), 280 and 283 (3' - TAGG283TGG280AC-5') positions in the 146 base pair palindromic DNA fragment were obtained from ab initio Hartree-Fock self consistent field (HF-SCF) molecular orbital calculations by employing the Koopman's theorem.

Gaussian 98W program was used for all calculations. The heavy atom bond lengths, bond angles and dihedral angles of all four nucleotides were obtained from X-ray crystallographic data. The H atom bond lengths, bond angles and dihedral angles were optimized at the 3-21G level.

The nucleotide environment strongly influences the gas phase IP's. In water-counterion environments the highest occupied orbital is a base orbital. Nucleotide ionization plays an important role in mechanisms involving radiation induced DNA damage. Results from these calculations, show that nucleotide IP's are largely localized on the base, sugar and the phosphate groups. The highest occupied base orbitals of all four 5'-dGMP- have molecular orbital coefficients similar to the model compound, 9-methyl guanine. This is also consistent with the reported uv photoelectron data for 9-methyl guanine. Comparison of the highest occupied base IP's shows that the 137 5'-dGMP- has the smallest value. This suggests that from the positions examined 137 5'-dGMP- is favored for ionization.