

## DNA-TATA box binding protein interactions: analysis of ionization potentials of the nucleotides

Ravindra Amunugama and Harshica Fernando\*

Department of Chemistry, University of Colombo, Colombo 3

Structural analyses of x-ray crystallographic coordinates of the human TATA box binding protein (TBP) complexed with the TATA box of an adenovirus major late promoter reveal that the 8-mer sequence of the core promoter region (5' TATAAAAG 3') has undergone extensive deformation to attain a unique TA-DNA conformation whilst creating a bend. This work extensively investigates whether these structural distortions are also reflected in the reactivities of the nucleotides by analysing the uncorrected gaseous  $\pi$  ionization potentials (IPs) of the isolated mononucleotides, the dinucleotides and the dinucleotide steps by *ab initio* self-consistent field (SCF) molecular orbital calculations. Also, the effect on IPs upon insertion of two phenylalanine side chains (Phe284 and Phe193) into the first and last steps respectively, the most significant hydrophobic protein-DNA interactions that occur within the TATA box, has been analysed.

The results of anionic isolated mononucleotides indicate that guanine nucleotide possesses the lowest IP. Thymine mononucleotides, one of the predominantly occurring nucleotides in the TATA box, of the termini of the TATA box are more reactive with respect to the ones towards the centre, as they hold a lower  $\pi$  IP. The evaluation of IPs of the homodinucleotides (dithymines and diadenines) reveals that the lower IP always occurs on the 5'-side nucleotide, implying that the highest occupied molecular orbital is localised on the same nucleotide. The decreased IP values of the dinucleotides and the dinucleotide steps with respect to the isolated mononucleotides is due to the base - base hydrophobic stacking interactions. The variability of  $\pi$  IP of the nucleotides of the same type is a consequence of differences in the glycosidic bond dihedral angles ( $\chi$ ).

The insertion of phenylalanine side chains into the first and last dinucleotide steps has perturbed the  $\pi$  IP of the four nucleotides of each step. Whilst decreasing the IP of the nucleotide base, with which the amino acid makes the closest contact, IP values of the other three nucleotides have been augmented due to disruption of stacking interactions. Such evidence can be instrumental in the development and understanding the mechanistic aspects of DNA alkylating drugs for the treatment of various malignancies.

\*hafernan@UTMB.edu

Tel: