Theoretical-computational modelling of the electronic and structural properties of nucleic acids in solution

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My research activity concerns the theoretical-computational modelling of the electronic and structural properties of molecules of biological interest in solution, in particular nucleic acids. The computational approach can give several advantages in this field, but the choice of a proper method is not trivial. In our research group the Perturbed Matrix Method (PMM) [1,2] has been developed. This hybrid QM/MM method allows to describe the molecular electronic properties in complex systems through a mechanical-statistical treatment from which it is possible to extract thermodynamic properties, such as free energy, at a reduced computational cost.

The performances of the method were benchmarked on the determination of the one-electron redox potentials of the 2'-deoxynucleosides in aqueous solution [3]. Then, the complexity of the system was extended to study the effect of the environment on the guanine redox potential [4].

Our data, in agreement with previous experimental findings [5], clearly show that the presence of consecutive guanine bases in both single and double stranded DNA oligomers lowers their reduction potential. Such an effect is even more marked when a G-rich quadruplex (G4) is considered, where the oxidized form of guanine is particularly stabilized. To the best of our knowledge, this is the first computational study reporting on a quantitative estimate of the dependence of the guanine redox potential with respect to sequence and conformational effects in complex DNA molecules, ranging from single-stranded DNA to G-quadruplex in aqueous solution. The one electron reduction potentials of oxidized guanine in single and double strands, with increasing number of adjacent guanine bases in a fully solvated environment are reported in Table 1. We reproduced quantitatively the experimental reduction potential shift (Δ) of each investigated system with respect to the reference compound ss-HG1.

System	*T(K)*	*$E^0(V)^a$ PMM*	*Δ(V) PMM*	*Δ(V) exp.*[2]
ss-HG1	278	0.80	0.00	0.00
ss-HG2	278	0.69	0.11	0.10
ss-HG2	300	0.83	-0.03	0.00
ds-HG2	278	0.69	0.11	0.11
ds-HG4	278	0.55	0.25	0.20
G4	278	0.40	-	-

Table 1. Calculated reduction potential (E^0, vs SHE) of oxidized guanine in each substrate, calculated and experimental potential shift (Δ). [a]The estimated standard error is ± 0.04 V.

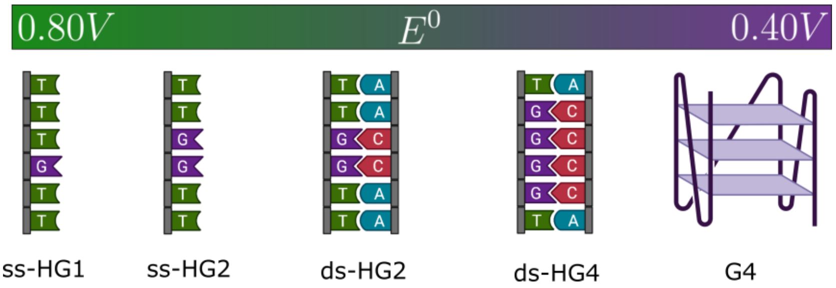

Figure 1. Colorbar of the calculated reduction potentials (E^0, vs SHE) of the oxidized guanine base in the indicated substrates in solution.

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